

### Skin adhesives for ostomy care applications

Water diffusion in polymer composites & its effect on adhesion

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# Skin adhesives for ostomy care applications Water diffusion in polymer composites & its effect on adhesion





**DTU Chemistry** Department of Chemistry Daniel Hansen June 2020

### Preface

This thesis represents a three year PhD project, which is a part of a larger project named: Smart sweat Removal for prolonged Ostomy bag adhesion and increased substantivity of Topicals (SROT). The SROT project is funded by the Innovation Fund Denmark through the Grand Solution no. #6151-00007B. The project includes three partners: Riemann A/S, a sunscreen manufacturer, the Technical University of Denmark (DTU), and Coloplast A/S, a medical device company. All partners seek to understand how sweat interacts with polymer materials and influence the materials functionality e.g. UV protection for sunscreen and adhesion for ostomy care adhesives. I have throughout my PhD been employed at Coloplast as an industrial PhD student, while being enrolled as a PhD student at DTU. I have spent 50 % of my time at Coloplast and the remaining time at DTU. My main supervisor was Professor Esben Thormann (DTU) and my co-supervisors were

Chief Principal Scientist Kristoffer Hansen (Coloplast) and Professor Kristoffer Almdal (DTU).

### Acknowledgments

The past three years have been absolutely great and I would like to express my graditude to the people who have helped me throughout my PhD. I thank my main supervisor, Esben Thormann, for his extraordinary supervision and support during this project. I have enjoyed our scientific discussions and your optimistic mindset, which I find very inspiring. I consider you a mentor more than a supervisor. I owe many thanks to my industrial supervisor, Kristoffer Hansen, who always helped me whenever I needed it. You have shown me how to carefully prioritize academic questions, which have the greatest potential for solving 'real-world problems' and help develop better products. I appreciate our scientific discussions as well as our conversations about personal development, which have helped me a lot. I would like to give a special thanks to my good friend and colleague, Johannes Eiler, who has also done his PhD as a part of the SROT project. I appreciate our scientific conversations, coffee breaks, and the remarkable synergy of our many collaborations. I thank everyone involved in the SROT project, my colleagues from the group for polymers and functional interfaces at DTU, and all my Coloplast colleagues. I have had the privilege of having nothing but positive and helpful colleagues, which has given me two outstanding work places for the past three years. I gratefully acknowledge the Innovation Fund Denmark (Grand Solutions no. #6151-00007B) and Coloplast A/S for funding my project. Finally, I would like to thank my parents for their tremendous support.

### Abstract

Millions of people world wide live with an ostomy, which is a surgically created outlet in the intestine created to treat e.g. colon cancer or Crohn's decease. To allow these people to live a relatively normal life, an ostomy bag is adhered to the skin to collect waste from the ostomy. The ostomy bag is attached to the skin using so-called skin adhesives, which must provide sufficient adhesion to ensure optimal device functionality, while being easy to remove without damaging the skin. The skin adhesive should also support the user while sweating, which means that it needs to provide sufficient adhesive properties in situations where sweat is released at the skin–adhesive interface. Although, skin adhesives have been used for more than 50 years and the functionality and formulations of skin adhesives have been improved, users are still experiencing problems with leakage of waste, adhesive failure, and skin damage. To develop the next generation of skin adhesives new knowledge is required about diffusion of bodily fluids in adhesives and adhesive performance during wear.

In this project, a new impedance-based technique is developed for probing diffusion of artificial bodily liquids in skin adhesives. The technique is used for investigating how the material chemistry, composition and geometry influence the water absorption functionality of adhesives, which is expected to be important for improving skin health and adhesion during perspiration. Next, a perspiration simulator is developed, where skin adhesion can be evaluated on a skin mimicking substrate during realistic perspiration conditions. The adhesion of carefully designed adhesives is systematically evaluated in different dry and perspiration situations where the link between the adhesive and water absorbing properties of the adhesives is mapped.

In the final phase of this project, the obtained knowledge of adhesion and water diffusion was used for proposing a new type of skin adhesives, which according to the developed performance tests were significantly better than conventional skin adhesives. A patent was recently filed on these new and improved adhesives and this part of the work can therefore not be included in this dissertation.

### Resumé

Millioner af mennesker verden over lever med en stomi, som er et kurigisk udløb i tarmen. Grunde til at lave en stomi inkluderer tarmkræft og Crohns sygdom. For at disse mennesker kan leve et relativt normalt liv, klæbes en stomipose fast til huden for at opsamle afføring. Stomiposen sidder fast på huden med en hudklæber, som skal sikre optimal funktionalitet af stomiposen samtidig med at den ikke må skade eller irritere huden. Hudklæberen skal også håndtere situationer hvor brugeren sveder, hvilket betyder at den skal klæbe selvom sved bliver introduceret i grænsefladen mellem huden og klæberen. Selvom hudklæbere har eksisteret i mere end 50 år og funktionaliteten og formuleringer er blevet forbedret, så oplever brugere stadig problemer med lækage af afføring, tab af klæb og hudirritation. Der er derfor behov for en ny og forbedret generation af hudklæbere.

I dette Ph.d.-projekt, udvikles en ny impedans-baseret teknik til at følge diffusion af kunstig sved i hudklæbere. Teknikken benyttes til at undersøge, hvordan klæberes materialekemi, komposition og geometri påvirker vandabsorptionen i klæbere, som forventes at være vigtig for hudens sundhed og klæbeegenskaber når brugeren sveder. I projektet udvikles derefter en svedsimulator, hvor klæbeevne kan evalueres på kunstig hud under realistiske svedbetingelser. Klæberegenskaberne af forskellige klæbere undersøges systematisk under både tørre og svedlignende betingelser, hvor sammenhængen mellem svedabsorption og klæbeevne kortlægges.

I projektets sidste fase benyttes den nye viden om hudklæb og vanddiffusion til at foreslå og teste et nyt hudklæberkoncept, som har vist sig at være bedre end konventionelle hudklæbere. Dette hudklæberkoncept er ved at blive patenteret og er derfor ikke inkluderet i denne Ph.d.-afhandling.

### Publications

### Appended publications

- Water Diffusion in Polymer Composites Probed by Impedance Spectroscopy and Time-Resolved Chemical Imaging
  Daniel Hansen, Jonathan R. Brewer, Johannes Eiler, Niloufarsadat Mirmahdi Komjani, Kristoffer Hansen, and Esben Thormann
  ACS Applied Polymer Materials, 2020, 2 (2), 837-845, DOI: 10.1021/acsapm.9b01107
- Performance of Polymeric Skin Adhesives During Perspiration Daniel Hansen, Saeed Zajforoushan Moghaddam, Johannes Eiler, Kristoffer Hansen, and Esben Thormann ACS Applied Polymer Materials, 2020, 2 (4), 1535-1542, DOI: 10.1021/acsapm.9b01214
- Water Penetration and Absorption in Skin Adhesives: The Influence of Hydrophilic Particles and Mechanical Properties
  Daniel Hansen, Johannes Eiler, Kristoffer Hansen, and Esben Thormann
  In preparation, 2020

### Other publications

- In Vitro Evaluation of Skin Adhesives during Perspiration Johannes Eiler, Daniel Hansen, Bahar Bingöl, Kristoffer Hansen, Jason Heikenfeld, and Esben Thormann International Journal of Adhesion and Adhesives, 2020, 102574, DOI:10.1016/j.ijadhadh.2020.102574.
- Water Transport in Polymer Composites through Swelling-Induced Networks of Hydrogel Particles
  Johannes Eiler, Søren Bredmose Simonsen, Daniel Hansen, Bahar Bingöl, Kristoffer Hansen, and Esben Thormann
  Submitted, 2020.

# Contents

	Pref	face	Ι			
	Ack	nowledgments	Π			
	Abst	tract	III			
	Resi	umé	IV			
	Pub	ublications				
		Appended publications	V			
		Other publications	V			
Ι	Int	troduction & background	1			
1	Intr	roduction	3			
	1.1	The ostomy bag	3			
	1.2	The challenge of wearing an ostomy bag	4			
	1.3	Scope of this PhD project	5			
<b>2</b>	Bac	Background				
	2.1	Polymeric skin adhesives	7			
		2.1.1 Chemistry & composition	8			
	2.2	Water diffusion in skin adhesives	10			
		2.2.1 Diffusion in polymer materials	10			
		2.2.2 Diffusion models	11			
	2.3	Adhesion	13			
		2.3.1 Thermodynamic work of cohesion and adhesion	14			
		2.3.2 Adhesion of viscoelastic materials	15			
TT	v	laterials and methods	17			
**			11			
3	Mat	terials $\&$ methods	19			
	3.1	Materials & polymer processing	19			
	3.2	Overview of experimental techniques	20			

3.3 Details of key techniques	21					
3.3.1 Impedance spectroscopy	21					
3.3.2 Coherent anti-Stokes Raman scattering microscopy	25					
3.3.3 Shear rheometry 2	26					
3.3.4 Gravimetric analysis	26					
3.3.5 Peel test	26					
III Results and discussion 2	29					
4 Probing water diffusion in skin adhesives 3	31					
4.1 Visualizing water diffusion using CARS microscopy	32					
4.2 Probing water diffusion using impedance spectroscopy	36					
4.2.1 Effective water penetration	38					
4.2.2 Hydrocolloid content & distribution of water	40					
5 Perspiration simulator 4	13					
5.1 The perspiration simulator setup	44					
5.2 Pressure and flow considerations	45					
5.2.1 Perspiration rate and presure	47					
5.2.2 Pressure upon occlusion	48					
5.3 Performance tests	49					
5.3.1 Perspiration peel test	49					
5.3.2 Long-wear test	50					
6 Performance of polymeric skin adhesives 5	53					
6.1 Adhesive design	53					
6.2 Adhesive performance during intense sweating	55					
6.2.1 Dry conditions	55					
6.2.2 Intense sweating	55					
6.3 Adhesive performance during moderate sweating & prolonged wear	57					
IV Conclusion and outlook 5	i9					
7 Conclusion and outlook	31					
7.1 Conclusion $\ldots \ldots \ldots$	61					
7.2 Outlook $\ldots \ldots \ldots$	62					
Bibliography						
Appendices						

A Paper I	81
B Paper II	95
C Paper III	113

## Part I

# Introduction & background

### Chapter 1

### Introduction

### 1.1 The ostomy bag

An ostomy is a surgically-created outlet in the body. The outlet is created for the patient to either discharge feces or urine, since the patient is unable to do so naturally. Reasons for creating an ostomy include removal of parts of the intestine or the bladder due to e.g. bladder cancer, colon cancer or Crohn's decease, which is a chronic intestinal condition [1, 2]. The three most common ostomies are colostomy, ileostomy, and urostomy. A colostomy is a surgically-created opening into the colon, ileostomy is an opening created into the small intestine, and the urostomy is a surgically-created opening to drain urine [3–5]. In this project, the focus will be on colostomy and ileostomy where the ostomy is created using the intestine as illustrated in Fig. 1.1a. According to the United Ostomy Association of America, 725,000 - 1 million live with an ostomy in the U.S. and the number is expected to increase worldwide due to the increasing life expectancy, which also yields an increasing risk of experiencing e.g. colon cancer [6].

Living with an ostomy requires changes in the daily routine. Ostomates typically use a skin adhesive (Fig. 1.1b) to attach a pouch, called an ostomy bag (Fig. 1.1c) to the skin [7]. The adhesive has a hole in the center where the intestine can go through to allow feces to be collected in the ostomy bag. Feces will be referred to as output. Modern skin adhesives consist of two adhesives, a center adhesive and a rim adhesive (Fig. 1.1b). The center adhesive is typically designed to absorb bodily fluids such as leaking output and sweat, while still maintaining adhesion. The rim adhesive gives a secure attachment through stronger adhesion but does not absorb bodily fluids as well as the center adhesive. Different device designs of ostomy bags exist to accommodate different user needs. People with a colostomy have output with regular consistency and may only need to change the bag once a day. Here, the skin adhesive may be detached and the whole device is discarded and a new bag is subsequently attached. Ileostomists, on the other hand, typically have output with more liquid consistency and larger volumes compared to regular feces. Here, the ostomy bag needs to be emptied several times a day. To avoid changing the ostomy bag multiple times every day, some bags can be emptied through an open/close mechanism in the bag. Alternatively, some devices allow to decouple the bag from the adhesive, to discard the bag without detaching the adhesive. A new bag can then be mounted onto the adhesive using a mechanical coupling. These different solutions exist to make the everyday life of the user easier, as frequent change of the skin adhesive is time consuming and may cause skin damage.



Figure 1.1: Illustration of a belly and an ostomy with erythema (skin redness/rash) around it (a). A typical skin adhesive (b) used for attaching the ostomy bag (c) to the skin.

### 1.2 The challenge of wearing an ostomy bag

A big challenge of wearing the ostomy bag every day is maintaining good peristomal (around the ostomy) skin health. Peristomal skin damage is associated with frequent change of the skin adhesive where each change exfoliates and may damage the skin. Furthermore, poor adhesion may lead to leakage of output underneath the adhesive, which have also been reported to cause erythema (rash/skin redness, Fig. 1.1a) and mental problems for the user worrying about leakage [8–10]. In situations where the skin is exposed to moisture for an extended period of time through sweating or leakage of output, skin maceration may also occur [11–13].

Consequently, several requirements for the skin adhesives, used for attaching ostomy bags, exist. The adhesives must provide sufficient adhesion to ensure optimum device functionality, while being easy to remove without leaving residues on the skin. They need to adhere in situations where the user is sweating and sweat therefore is released at the skin–adhesive interface. Furthermore, the adhesive should be able to prevent leakage of output by sealing the ostomy. In the non-ideal situation where leakage does occur, then the adhesive should limit the leak by absorbing the output and adhere to the skin around the leak. The ostomy bag was first invented by the nurse Elise Sørensen in 1953 who later founded the company Coloplast A/S in 1957 together with the plastic manufacturer Aage Louis-Hansen. Since then, the ostomy bag and skin adhesives have evolved a lot. However, new knowledge is needed about the diffusion of bodily fluids in skin adhesives, as well as the skin–adhesive interaction during wear to develop the next generation of skin adhesives for ostomy bags.

### 1.3 Scope of this PhD project

In this 3 years PhD project, I sought to build new tools for investigating and answering fundamental questions about skin adhesives. The new knowledge should lead to new and improved skin adhesives for ostomy care products. Fig. 1.2 shows a mind map of the project. Here, new experimental techniques are developed for probing the diffusion of water in skin adhesives, since the adhesive performance and peristomal skin health are expected to be influenced by the moisture level at the skin–adhesive interface. Next, an *in vitro* perspiration model is built to test how skin adhesives perform under perspiration conditions. These new experimental techniques allow to systematically investigate how the material composition and chemistry of skin adhesives influence their overall material functionality and performance. General knowledge obtained about water diffusion in skin adhesives will support the results obtained in the performance of these adhesives. As indicated in Fig. 1.2, this will be discussed in this PhD dissertation.



Figure 1.2: Mind map of this PhD project. First, experimental techniques are developed for probing water diffusion in skin adhesives and testing adhesive performance during simulated wear conditions. Next, the techniques are used to systematically investigate model adhesives to build fundamental knowledge about the functionality and performance of skin adhesives. This knowledge was then used for proposing new skin adhesives.

As this is an industrial PhD project, joint between the Technical University of Denmark (DTU) and Coloplast A/S, the project is also motivated by development of new and improved products. I have therefore continuously been working on generating and testing ideas for new adhesives in parallel with all the other activities. The results, findings, and experimental techniques presented in this dissertation, have served as the foundation for proposing a new generation of skin adhesives. These adhesives were characterized and tested using the developed experimental techniques and the adhesive formulations were modified through multiple iterations until the new adhesives proved to have significantly enhanced performance compared to conventional skin adhesives. A patent of these adhesives was recently filed and this part of the work is therefore kept proprietary at this moment (Fig. 1.2).

### Chapter 2

### Background

The field of skin adhesives is interdisciplinary and requires knowledge about polymer chemistry, water diffusion in polymer materials, the physical chemistry of interfaces, adhesion, and the surface properties of human skin. In this chapter, a brief introduction will be given to skin adhesives and the material chemistry relevant for this project. Next, diffusion theory will be discussed in relation to water/sweat diffusion in polymer materials, which will be important to understand Chapter 4, *Paper I* (Appendix A), and *Paper III* (Appendix C). Lastly, adhesion and adhesive peel tests will be discussed, as that will give background for Chapter 6, *Paper II* (Appendix B), and help to understand skin adhesive performance in general.

### 2.1 Polymeric skin adhesives

Skin adhesives typically include a hydrophobic and sticky polymer matrix. The matrix normally constitutes of at least one polymer with a glass transition temperature lower than room temperature, which ensures that the matrix can flow and establish good contact with the skin [14, 15]. The hydrophobic nature of the matrix results in bodily fluids, such as sweat or output, being trapped at the skin–adhesive interface. This may cause skin complications as described in Chapter 1, Section 1.2.



Figure 2.1: Schematic illustration a skin adhesive consisting of an adhesive matrix and hydrophilic hydrocolloids.

Consequently, skin adhesive formulations include hydrophilic particles in the hydrophobic matrix (Fig. 2.1) [16–18]. These hydrophilic particles can absorb water/bodily fluids and are typically referred to as hydrocolloids. Hydrocolloids are added in amounts of approximately 30-50 wt.%, which results in the skin adhesive exhibiting continuous water absorption over time [19, 20]. This indicates that the hydrocolloids have formed a particle network where water can diffuse between the hydrocolloids. This will be investigated in Chapter 4 and Paper I (Appendix A).

#### 2.1.1 Chemistry & composition

The chemistry of the different components in skin adhesives dictates the final material functionality and should therefore be carefully considered. The polymer matrix typically consists of apolar hydrocarbon polymers which are sticky due to their ability to form van der Waals interactions with most surfaces. These polymers typically have glass transition temperatures,  $T_g$ , below room temperature, which allow them to flow viscously and wet e.g. skin to form large skin–adhesive contact areas even for rough skin surfaces. In this project, the matrix will consist of two polymers: polyisobutylene (PIB) (Fig. 2.2a) and styrene-isoprene-styrene (SIS) (Fig. 2.2b). PIB has a glass transition temperature of approximately  $T_g = -75$  °C and is viscous at room temperature [21]. The viscous properties of the matrix depend on the molecular weight of the polymer, which can be tailored to the application. The ability of PIB to flow and wet almost any surface is beneficial when bonding to skin [22]. To ensure that the skin adhesive does not flow too much and eventually slide off the skin, SIS is added for mechanical reinforcement. SIS is a triblock copolymer as illustrated in Fig. 2.2b where the styrene blocks form glassy phases, which reinforce the bulk mechanical properties of the matrix by physical crosslinking the rubbery isoprene block [23].



Figure 2.2: Chemistry of the polymers polyisobutylene (a) and styrene-isoprene-styrene (b) used in the adhesive matrix in the skin adhesives. The letters n and m represent integers, which are typically between  $10^1$  and  $10^3$ .

The polymer matrix is responsible for the overall adhesion of the skin adhesive. However, the adhesive needs to absorb bodily fluids to keep the skin healthy. Here, hydrocolloids with different chemical structures can be added in powder form to the matrix. The chemistry of the hydrocolloids used in this project are presented in Fig. 2.3.



Figure 2.3: Chemical structure of caboxymethyl cellulose (a), polyacrylic acid (b), and cetyl hydroxyethyl cellulose (c). Here, n represents an integer,  $n \sim 10^2 - 10^3$ .

The chemical structure dictates the overall hydrophilicity and water absorbing capabilities of the hydrocolloids. Highly water absorbing hydrocolloids include carboxymethyl cellulose (CMC) (Fig. 2.3a) and polycarylic acid (PAA) (Fig. 2.3b). The hydrophilic nature of the carboxylic acid groups and the osmotic pressure upon dissociation of sodium ions during water exposure provides the high water absorbing capabilities of CMC and PAA. These polymers can swell and form hydrogels up to hundreds of times their original dry volume when mixed with water, while the hydrocolloid swelling is expected to be mechanically restricted when dispersed in the polymer matrix [24–26]. The degree of swelling can be influenced by the environment where pH, ionic strength, and ion valency are parameters, which have been shown to influence the water uptake of hydrocolloids [27, 28]. However, the water uptake can also be tailored through the physical and chemical properties of the hydrocolloids. Here, the degree of substitution of acid groups, molecular weight, and chemical crosslinking of the hydrocolloids will influence the water uptake [29–31].

PAA and CMC, will serve as highly absorbing hydrocolloids, while cetyl hydroxyethyl cellulose (CHEC) (Fig. 2.3c) is included as a less water absorbing hydrocolloid. The overall lower hydrophilicity of CHEC compared to PAA and CMC is attributed the cetyl groups, which are hydrocarbon side groups with 16 carbon atoms. Furthermore, CHEC does not have any acid groups but only the less hydrophilic hydroxy groups. Lastly, starch is used as a low/non-absorbing particle (Fig. 2.3d). Starch is expected to absorb even less water compared to CHEC due to its ability to form crystals with low water solubility [32]. Starch will therefore primarily be used to modify the viscoelastic properties of the skin adhesives, which are also altered when adding particles to the matrix. All particles added to the matrix will create physical crosslinks in the matrix, which will increase the mechanical properties of the skin adhesives [33–36]. The change in mechanical properties will depend on amount of particles, particle size, particle shape, and particle-matrix interaction [37–42].

Other components can be added to the skin adhesive formulations to give them other functionalities. Examples of other additives include pH buffers to keep the skin pH constant, tackifiers, and active ingredients such as aloe vera or vitamin E to improve skin health [43–46]. However, in this project, simple adhesives consisting of a matrix and hydrocolloids will be investigated to understand adhesion and water absorption, which are here considered the two primary functionalities of skin adhesives.

### 2.2 Water diffusion in skin adhesives

Water absorption in skin adhesives is expected to be important for skin health and adhesion. The water absorption in skin adhesives is driven by diffusion, which will be discussed in this section. However, the literature on water diffusion in skin adhesives is scarce so water diffusion in polymer materials will therefore be reviewed broadly before selecting relevant diffusion models for data interpretation of experiments done with skin adhesives.

### 2.2.1 Diffusion in polymer materials

The ability to study and understand water diffusion is of high interest for polymer materials with many other applications than skin adhesives. Water diffusion in ion-exchange membranes, marine coatings, protective coatings for microelectronics, medical adhesives, drug delivery systems, and food packaging have been investigated extensively [47–63]. Common for all these applications is that there is a need to understand how penetrants such as water and saline solutions interact with the materials to achieve and improve the desired material functionality and stability [64–67].

Water diffusion in polymer materials is often investigated through gravimetric analysis where a polymer sample of known weight and dimensions is immersed in a liquid, e.g. saline solution with similar composition as sweat or sea water. The sample is subsequently taken-up from the liquid reservoir, excess water is wiped with a high absorbent pad or technical napkin, followed by weighing and re-immersion of the sample. This procedure is repeated as often as desired until the sample is saturated with water. The frequency of measurements yields the time resolution of the experiment, which is typically tens of minutes [68, 69]. The data, i.e. mass gain, is simple to interpret and easily accessible since the only equipment needed is an analytical scale. However, the time-resolution is limited, which may cause inaccurate results for systems where the time-scale of the diffusion process is much faster than the sampling time. Gravimteric analysis does not grant any spatial information about how water is distributed in the material. Consequently, other techniques such as FT-IR, neutron scattering, pulsed NMR, electrochemical impedance spectroscopy and fluorescence spectroscopy are used for probing diffusion of penetrants in polymer systems [70–76].

Examples of other techniques used for probing water diffusion include a study by Debate *et al.*, who used real-time Raman spectroscopy to estimate diffusion profiles of water and methanol in ion-exhange membranes without the need for sample manipulation [77]. Baumgartner *et al.* successfully quantified swelling and erosion of polymers used for oral drug delivery using <sup>1</sup>H-NMR and magnetic resonance imaging [78]. It is clear from the literature that diffusion models are needed to extract quantitative information about the diffusion process, regardless of the techniques used for probing diffusion in polymer systems [79–82].

#### 2.2.2 Diffusion models

Diffusion of fluids is driven by a concentration gradient of the fluid. Typically, the fluid concentration is higher in the environment outside the material compared to inside of the material. Consequently, a chemical potential exists which makes the fluid diffuse into the material. For diffusion processes where the fluid can diffuse without resistance, the diffusion process is referred to as Fickian or passive diffusion. The passive diffusion of fluids was first derived by A. Fick (1855) who adopted principles from heat conduction developed earlier by Fourier (1822). Fick's diffusion model is based on Fick's  $2^{nd}$  law, which was carefully reviewed by J. Crank [83]. Fick's  $2^{nd}$  law is given by:

$$\frac{\partial C}{\partial t} = \nabla \cdot (D\nabla C), \qquad (2.2.1)$$

where D is the diffusion coefficient  $[m^2/s]$ , C is the fluid concentration and t is the time. If the diffusion coefficient is assumed to be constant, then Eq. (2.2.1) can be written as:

$$\frac{\partial C}{\partial t} = D\left(\frac{\partial^2 C}{\partial x^2} + \frac{\partial^2 C}{\partial y^2} + \frac{\partial^2 C}{\partial z^2}\right),\tag{2.2.2}$$

where x, y and z are spatial coordinates. Many experiments are designed to investigate diffusion in one dimension, e.g. x, then Eq. (2.2.2) can be simplified to [84–86]:

$$\frac{\partial C}{\partial t} = D \frac{\partial^2 C}{\partial x^2} \tag{2.2.3}$$

Eq. (2.2.3) can be solved for different sample geometries. For one-dimensional diffusion experiments, a planar geometry is typically preferred. The solution for a planar sheet can be obtained using appropriate boundary conditions and Laplace transform [83]:

$$\frac{M_t}{M_{\infty}} = 1 - \frac{8}{\pi^2} \sum_{n=1}^{\infty} \frac{1}{(2n+1)^2} \exp\left(\frac{-D(2n+1)^2 \pi^2}{4l^2}t\right)$$
(2.2.4)

Here,  $M_t$  is the mass of the sample at time t,  $M_{\infty}$  is the mass of the saturated sample and l is the thickness of the sample. For small values of mass uptake, typically for  $M_t/M_{\infty} < 0.5$ , Eq. (2.2.4) can be simplified to [87, 88]:

$$\frac{M_t}{M_\infty} = 4 \left(\frac{Dt}{\pi l^2}\right)^{1/2} \tag{2.2.5}$$

Eq. (2.2.5) is widely used for extracting the diffusion coefficient from systems exhibiting Fickian diffusion. This can be done by e.g. plotting the experimental sorption data,  $\frac{M_t}{M_{\infty}}$ , against  $t^{1/2}l^{-1}$ . A linear fit can then be fitted to the data where  $\frac{M_t}{M_{\infty}} \leq 0.5$  and the diffusion coefficient is determined from the slope of the linear fit [89–91]. The slope of the linear fit is,  $\alpha = 4 \left(\frac{D}{\pi}\right)^{1/2}$ , and the diffusion coefficient is  $D = \frac{\pi \alpha^2}{16}$ .

Although the Fickian diffusion model describes diffusion well for many systems, deviations from Fickian diffusion is often found for water diffusion processes in polymeric materials [92–96]. Here, polymer relaxation processes occuring within the same time scale as the diffusion process may restrict the Fickian diffusion [97]. For these situations, other models are needed to describe the experimental data. Semi-empirical models are typically used and especially one, which was generalized model by N. A. Peppas and L. Brannon-Peppas have been found usefull within polymer science [84, 98–100]:

$$\frac{M(t)}{M_{\infty}} = k \cdot t^n \tag{2.2.6}$$

Here, k is a proportionality constant containing information about the sample geometry and diffusion rate, while n is the diffusional exponent, which is indicative of the diffusion mechanism. For  $n = \frac{1}{2} \Rightarrow k = 4 \left(\frac{D}{\pi l^2}\right)^{\frac{1}{2}}$  i.e. Fickian diffusion, see Eq. (2.2.5). Processes where n = 1 are referred to as Case II sorption. Here,  $k = \frac{2k_0}{C_0 l}$ , where  $C_0$  is the equilibrium water concentration and  $k_0$  is defined as the Case II relaxation constant [84]. The final expression for Case II sorption is:

$$\frac{M_t}{M_\infty} = \frac{2k_0}{C_0 l}t\tag{2.2.7}$$

Case II sorption is characteristic for polymer systems where the diffusion rate is completely limited by polymer relaxation processes and the diffusion occurs with constant rate (linear), which is determined by the polymer relaxation time. Anomalous diffusion is referred to as an intermediate process between Fickian and Case II sorption:  $\frac{1}{2} < n < 1$ . For anomalous diffusion both Fickian diffusion and relaxation restricted diffusion occur simultaneously. It is suggested that newly acquired data from gravimetric sorption experiments are analyzed using Eq. (2.2.6) to determine the appropriate n for data  $\frac{M(t)}{M_{\infty}} \leq 0.5$  to classify whether the transport process is Fickian or restricted by polymer relaxation processes. The passive diffusion, anomalous diffusion, and Case II sorption are schematically illustrated in Fig. 2.4.



Figure 2.4: Schematic illustration of water uptake as a function of time of passive diffusion (n = 0.5), anomalous diffusion (0.5 < n < 1), and Case II sorption n = 1.

The different diffusion mechanisms (Fig. 2.4) represent different water uptake profiles, which may be tuned by considering the formulation of the skin adhesive. Especially, the hydrocolloid chemistry and content is expected to influence the water uptake profile in skin adhesives, since they are expected to be responsible for the water uptake. This will be discussed later in Chapter 4, *Paper I* (Appendix A), and *Paper III* (Appendix C), where the diffusion models presented here are used for data interpretation.

### 2.3 Adhesion

Skin adhesives attached to the skin do not readily detach due to their adhesive properties. The adhesive properties have two main contributions: thermodynamic work of adhesion and dissipation of energy in the material. In this chapter these concepts will be described to better understand how skin adhesives work. For simplicity, the adhesion between two rigid surfaces is considered first

and followed by considerations of adhesion of viscoelastic materials.

#### 2.3.1 Thermodynamic work of cohesion and adhesion

The thermodynamic work of cohesion and thermodynamic work of adhesion are defined as the energy required to separate two unit surfaces of the same or different composition, respectively [101]. The thermodynamic work of cohesion,  $W_{121}$ , is illustrated in Fig. 2.5a, while the thermodynamic work of adhesion,  $W_{132}$ , is presented in Fig. 2.5b. Here, the materials are surrounded by another medium.



Figure 2.5: Schematic illustration of thermodynamic work of cohesion of a material (1) in medium (2) (a). Illustration of thermodynamic work of adhesion of two different materials  $(1 \neq 2)$  immersed in a third medium (3) (b). This figure is inspired by a similar figure by Jacob N. Israelachvili (Fig. 17.1 in [101]).

By considering Fig. 2.5a, an energy balance is made for the process of separating an unit area of medium 1 in medium 2. The energy balance is based on the respective surface free energy of each interface involved in the separation process:

$$W_{121} = W_{11} + W_{22} - 2W_{12} \tag{2.3.1}$$

Here,  $W_{11}$  and  $W_{22}$  represent the energy gain of having an unit area of material 1 and medium 2 in contact with themselves, while  $2W_{12}$  represents the energy required to create two new unit areas of material 1 and medium 2 in contact.

Similar energy considerations can be made for the work of adhesion,  $W_{132} \equiv W_{ad}$ , of two different materials 1 and 2 (1  $\neq$  2) in medium 3 (Fig. 2.5b):

$$W_{ad} = W_{12} + W_{33} - W_{13} - W_{23} \tag{2.3.2}$$

 $W_{12}$  is the energy gain of having material 1 and 2 in contact and  $W_{33}$  represents the energy gain

of having medium 3 in contact with itself.  $W_{13}$  and  $W_{23}$  represent the energy required to create two new surfaces where a respective unit area of material 1 and 2 are in contact with medium 3. For adhesives, the thermodynamic work of adhesion is positive, which means the materials are

3. For adhesives, the thermodynamic work of adhesion is positive, which means the materials are sticking together due to inter-molecular forces [101–103]. Van der Waals forces have been reported to be the main intermolecular force responsible for the work of adhesion of skin adhesives [45, 104]. The Van der Waals forces occur due to fluctuations in molecular polarization and are dominant in large apolar hydrocarbon polymers such as polyisobutylene used in the sticky adhesive matrix of skin adhesives (Section 2.1). Other inter-molecular interactions such as hydrogen bonding can contribute significantly to the thermodynamic work of adhesion for adhesives where polar molecules are incorporated in the adhesives [105].

The thermodynamic work of adhesion is typically in the order of  $10^1 \text{ mJ/m}^2$  [106–108]. This is far from the energy required to attach medical devices safely to the skin. The adhesion strength of most skin adhesives is  $10^3$  to  $10^4 \text{ mJ/m}^2$ , i.e. something else must contribute to the adhesion other than the thermodynamic work of adhesion [109, 110].

### 2.3.2 Adhesion of viscoelastic materials

The energy required to remove a skin adhesive from a substrate, e.g. skin, typically requires several of orders of magnitude more energy compared to the work required to apply the adhesive to the substrate [111]. This phenomena is referred to as adhesion hysteresis and is common for viscoelastic adhesives [112–114]. Here, the adhesion hysteresis is caused by energy dissipated in the skin adhesive upon removal of the adhesive. The energy dissipation is a consequence of deformation of the adhesive, which cause energy costly polymer chain reorganization [115–117]. Due to the viscous behavior of the adhesives, the energy dissipation and thus the adhesive properties are rate dependent. Various empirical and physical models have been proposed to describe the adhesion of viscoelastic materials where several parameters such as energy dissipation, thermodynamic work of adhesion, separation angle, and separation speed have been included [118–120]. Gent and Schultz proposed a model for the total adhesion energy, G, in 1972 [121]:

$$G = W_{ad} \Phi(a_T V), \tag{2.3.3}$$

where  $\Phi$  is the energy dissipation function,  $a_T$  is a time-temperature shift factor, and V is the separation speed. Since then, a lot of new models have emerged, however, common for most models is that the adhesion energy is proportional to the thermodynamic work of adhesion and the energy dissipation [122]:

$$G \propto W_{ad} \Phi,$$
 (2.3.4)

The bulk mechanical properties and the surface properties of the skin adhesives are therefore important to consider when designing skin adhesives. Another important parameter to consider, is the skin–adhesive contact area. Here, the adhesive's ability to flow and wet the skin as well as the external pressure, used for applying the adhesive, will dictate the skin–adhesive contact area, which is usually smaller than the projected area of the adhesive. The adhesive's ability to flow can be studied using rheometry where both the elastic and viscous properties of the adhesive can be quantified.

The overall adhesive performance is therefore a rather convoluted parameter but can be quantified using different methods such as the tack test where an adhesive is brought into contact with a substrate briefly and subsequently removed again, while measuring the force required to separate the adhesive from the substrate as a function of displacement. The tack test is typically used to quantify short-term adhesive performance, which is also referred to as adhesive tack [123, 124]. Another common adhesive test is the peel test, which will be used in Chapter 6. Peel tests are widely used for quantifying adhesion of tapes and skin adhesives [125–128]. A typical 90°-peel experiment is illustrated in Fig. 2.6. Here, a rigid tape, referred to as the backing tape, is placed on the back-side of the adhesive. This ensures that the adhesive does not extend during peel and the stress is placed at the triple line between the adhesive, skin and air/other medium (Fig. 2.6) [129, 130]. The peel force can be measured as a function of displacement at constant rate of displacement. Alternatively, the change in displacement can be measured at constant force. Experimental details of performed peel experiments will be described in Chapter 3, Section 3.3.5.



Figure 2.6: Schematic illustration of a 90°-peel experiment of an adhesive with a backing tape peeled from skin.

## Part II

# Materials and methods

### Chapter 3

### Materials & methods

### 3.1 Materials & polymer processing

The polymer matrix was composed of polyisobutylene (PIB) and styrene-isoprene-styrene (SIS). PIB was obtained from BASF (Germany) and SIS was obtained from Kraton (USA). The particles added to the matrix included sodium carboxymethyl cellulose (CMC) particles obtained from Akzo Nobel (Netherlands), potato starch from KMC (Denmark), poly(acrylic acid sodium salt)(PAA) obtained from Stewart Superabsorbents (USA), and cetyl hydroxyethyl cellulose (CHEC) acquired from Ashland (USA). The particle size distributions of these particles were obtained using a Malvern Mastersizer 2000 with a dry dispersion unit (Scirocco 2000). Particles were dispersed at a pressure of 2.0 bar. The particle size distributions are presented in Fig. 3.1.



Figure 3.1: Particle size distributions of the PAA, CMC, CHEC, and starch particles.

Here, all particles appear to follow normal distributions. The median diameter,  $d_{50}$ , for each particle type is presented in Table 3.1. Here, the particle densities are also included, which were measured using an AccuPyc 1340 He-pycnometer from Micrometrics (USA).

Chemistry	Density [ $g \text{ cm}^{-3}$ ]	Median diameter, $d_{50}$ [ µm ]
PAA	$1.6491 \pm 0.0003$	63.5
CMC	$1.5809 \pm 0.0004$	56.3
CHEC	$1.3792 \pm 0.0003$	68.1
Starch	$1.5203 \pm 0.0009$	37.7

Table 3.1: Particle chemistry, density, and median diameter.

The particle densities allow us to calculate the particle volume fraction of the adhesives, which is expected to be more important for the functionality compared to the weight fraction. The density of SIS and PIB were both obtained from the respective manufacturer and is  $0.92 \text{ g/cm}^3$  for both polymers.

The final adhesives were obtained by mixing a premix of PIB and SIS in a Brabender mixer (Brabender GmbH & Co KG, Germany). The mix was processed for 45 minutes at 30 rpm and 90 °C under vacuum. Vacuum was applied to minimize air entrapment in the mix. For the majority of the prepared adhesives, the ratio between PIB and SIS was kept at 4:1 by weight and the total mass of each mix was 60 g. A few rigid adhesives were prepared with a PIB:SIS ratio of 2:1. Particles/hydrocolloids were mixed with the premix to yield adhesives with a well-known volume fraction of particles. After the particles were added to the matrix, vacuum was applied to minimize air entrapment in the final skin adhesives. The mix was subsequently processed for 45 minutes at 30 rpm and 90 °C. After mixing, 10-20 g of material was placed between two pieces of silicone release paper and pressed between two horizontal steel plates using a hydraulic press (Stenhøj, Denmark). The mix was pressed for 30 seconds under a load of 10 tons at 90 °C. Steel spacers with known thickness were used for controlling the final adhesive thickness. Mixes were pressed to thicknesse ranging from 350-1600  $\mu$ m. After pressing, the thickness was measured using a thickness gauge (Mitutoyo Europe GmbH, Germany). Finally, the desired sample geometry was obtained by punching.

### 3.2 Overview of experimental techniques

Different experimental techniques were used in this PhD project. Table 3.2 provides an overview of all the experimental techniques used in this project, the parameter or process the technique probes as well as the system under investigation.

Technique	Measured property	System
He-pycnometry	Particle density	Hydrocolloids
Laser diffraction	Particle size distribution	Hydrocolloids
Gravimetric analysis	Water absorption	Adhesives
Impedance spectroscopy	Water penetration	Adhesives
CARS microscopy	Imaging water absorption	Adhesives
Shear rheometry	Rheological properties	Adhesives
Peel test	Adhesion	Adhesives
Quartz crystal with dissipation	Water vapor uptake	Gelatin film
Atomic force microscopy	Nano-scale topography	Artificial skin
Contact angle goniometry	Water contact angle	Gelatin film
Thickness gauge	Adhesive tickness	Adhesives
Profilometer	Micron-scale roughness	Artificial skin

Table 3.2: Experimental technique, measured property, and system under investigation.

I will not go into detail with all the techniques here, however, a detailed description of the procedure and measuring principle for the most important techniques is presented in the following section.

### 3.3 Details of key techniques

### 3.3.1 Impedance spectroscopy

Impedance spectroscopy was used for probing the penetration of NaCl solution in different skin adhesives. The experimental setup is schematically illustrated in Fig. 3.2. The adhesive was adhered to a stainless steel plate, which was the working electrode, and a glass cell was clamped to the adhesive. The glass cell was filled with NaCl solution so the adhesive surface was in contact with the solution. A graphite rod was immersed into the saline solution and acted as both the counter- and reference electrode. The counter- and working electrode were connected to an Autolab potentiostat (PGSTAT128N) with a frequency response analyzer module (FRA32M) and a multiplexer module (MUX.SCNR8), all obtained from Metrohm Nordic (Denmark). The frequency response analyzer module allowed to do spectroscopic impedance measurements, while the multiplexer module provided up to eight channels so multiple experiments could be done in series. The impedance cell was placed in an incubator (KS 4000i control, IKA, Germany) for temperature control (Fig. 3.2). Experiments were done at room temperature  $T = 23 \pm 1$  °C and at  $T = 32 \pm 1$  °C, which is the human skin surface temperature [131].



Figure 3.2: Schematic illustration of the impedance setup, which consists of a working electrode, a glass cell clamped to the working electrode, and a counter electrode. Both electrodes are connected to a potentiostat, which applies a potential and measures the electrical current.

The impedance measurements were done with an oscillating potential with an amplitude of 10 mV. The potential was kept small to reduce perturbation of ion diffusion without compromising the signal to noise ratio. As saline solution penetrates into the adhesive, the impedance changes. Here, I describe some key electrical concepts and electrical assumptions relevant for interpretation of the impedance signal.

For a simple system, where a constant direct current (DC) potential, U, is applied across a resistance, R, the resulting current, I, is constant. The relationship between these three electrical parameters is described by Ohm's law, which states that, U = RI. A potential oscillating with angular frequency,  $\omega = 2\pi f$ , can be described as:

$$U = |U|\cos(\omega t), \tag{3.3.1}$$

where |U| is the magnitude of the potential and t is the time. Applying an alternating potential across a resistance typically results in a phase shift,  $\phi$ , between the potential and current. The current is then described as:

$$I = |I|\cos(\omega t - \phi) \tag{3.3.2}$$

Polar representations of the potential and current are convenient to work with and are therefore rewritten as:

$$U = |U|e^{i\omega t} \tag{3.3.3}$$

$$I = |I|e^{i(\omega t - \phi)} \tag{3.3.4}$$

Here,  $i = \sqrt{-1}$ . According to Ohm's law the resistance is the ratio between the potential, Eq. (3.3.3), and current, Eq. (3.3.4). The resistance is complex due to the phase shift and is referred

to as the impedance, Z [132].

$$Z = \frac{|U|}{|I|} \frac{e^{i\omega t}}{e^{i(\omega t - \phi)}} \ \blacklineskip$$
$$Z = |Z|e^{i\phi}, \tag{3.3.5}$$

where  $|Z| = \frac{|U|}{|I|}$  is the magnitude of the impedance. Using the Euler relationship, the impedance can be written as:

$$Z = Z' + iZ'', (3.3.6)$$

where Z is the impedance, and Z' and Z'' are the real and imaginary parts of the impedance, respectively.



Figure 3.3: Schematic illustration of impedance, Z, where Im and Re represents the imaginary and real axis, respectively.

From geometrical considerations of Fig. 3.3, the magnitude of the impedance is obtained:

$$|Z| = \sqrt{Z'^2 + Z''^2} \tag{3.3.7}$$

To interpret the physical meaning of the impedance of a skin adhesive, assumptions of the electrical behavior of the adhesive are needed. The adhesives consist of particles and a matrix. Assuming the fillers are homogeneously distributed in the matrix, the adhesive can be assumed to behave as a homogeneous and isotropic material, since the particle size is much smaller than the dimensions of the adhesive used in the impedance experiment. Next, the electrical properties of the adhesive can be described by a (RC)-circuit, i.e. a resistance, R, and capacitance, C, in parallel (Fig. 3.4).



Figure 3.4: Schematic illustration a skin adhesive containing hydrocolloids (left) and the electrical representation of the adhesive, which is the parallel (RC)-circuit (right).

The resistance describes the electrical conductivity in the adhesive, while the capacitance describes the adhesive's ability to store electrical charge at the surface. The impedance of the parallel (RC)-circuit is defined as:

$$\frac{1}{Z} = \frac{1}{R} + i\omega C, \qquad (3.3.8)$$

which can be rewritten to:

$$Z = \frac{R}{i\omega CR + 1} \tag{3.3.9}$$

Eq. (3.3.9) is expanded to find separate expressions for the real and imaginary parts of the impedance by multiplying by the complex conjugate:

$$Z = \frac{R}{i\omega CR + 1} \cdot \frac{1 - i\omega CR}{1 - i\omega CR}$$
(3.3.10)

Next, the impedance is rewritten to:

$$Z = \frac{R}{1 + (\omega CR)^2} (1 - i\omega CR)$$
(3.3.11)

Eq. (3.3.11) is reduced to yield the final expression for the impedance, which holds a real and an imaginary part, which correspond to the output of the impedance measurements.

$$Z = \frac{R}{1 + (\omega CR)^2} + i\left(-\frac{\omega CR^2}{1 + (\omega CR)^2}\right)$$
(3.3.12)

In Eq. (3.3.12) the real and imaginary part are both frequency dependent. To investigate the frequency response of the impedance of the adhesive, limiting values of the frequency are evaluated in Eq. (3.3.12). For  $\omega \ll RC, Z \to R$ , which means for low frequencies the impedance is dominated by the resistance. For  $\omega \to \infty, Z \to -\frac{1}{\omega C}$ , the dielectric properties of the adhesive dominate the impedance.

The resistance and capacitance can readily be calculated using the real part,  $Z' = \frac{R}{1+(\omega CR)^2}$ ,
and imaginary part,  $Z'' = -\frac{R\omega CR}{1+(\omega CR)^2}$ , of the impedance:

$$R = \frac{Z'^2 + Z''^2}{Z'} \tag{3.3.13}$$

$$C = -\frac{Z''}{\omega \left(Z'^2 + Z''^2\right)} \tag{3.3.14}$$

The definition of a parallel plate capacitance,  $C = \frac{\varepsilon_0 \varepsilon_r A}{l}$ , where A is the area of the material (plate), l is the material thickness (separation between the plates),  $\varepsilon_0$  is the permittivity of vacuum,  $\varepsilon_0 = 8.85 \cdot 10^{-12}$  F/m and  $\varepsilon_r$  is the dielectric constant of the material, which is the permittivity of the material relative to the vacuum permittivity, i.e. unit less. The dielectric constant describes a material's ability to be polarized by an external potential. Materials with low dielectric constant, e.g. polymer materials  $\varepsilon_{r,polymer} \approx 8$  are not as easily polarized as water  $\varepsilon_{r,H_2O} \approx 82$ , which has a higher dielectric constant [133, 134]. This means the effective dielectric constant of the skin adhesive will increase as it absorbs water. The increase in dielectric properties for increasing water absorption, the definition of the parallel plate capacitance, and Eq. (3.3.14) will be important for the interpretation of impedance data presented in Chapter 4, Paper I (Appendix A), and Paper III (Appendix C).

#### 3.3.2 Coherent anti-Stokes Raman scattering microscopy

Coherent anti-Stokes Raman scattering (CARS) microscopy provides label-free chemical contrast by imaging specific molecular vibrations associated with particular chemical species [135]. Besides chemical contrast, the technique also intrinsically provides high 3D spatial resolution and video-rate time resolution, which makes it ideal for probing dynamic process such as diffusion [136–138].



Figure 3.5: Schematic illustration of the CARS setup where the skin adhesive sample is imaged while exposed to water. The CARS imaging is obtained through the pump and Stokes lasers and detected using the epi-CARS detector and a dichroic mirror.

The used CARS setup is schematically illustrated in Fig. 3.5. Here, a skin adhesive sample is imaged while being exposed to water. The CARS signal is obtained through the so-called pump and Stokes lasers and detected using a dichroic mirror and the epi-CARS detector. For a detailed description of the CARS principle see: *Coherent Anti-Stokes Raman Scattering Microscopy: Chemical Imaging for Biology and Medicine* by C. L. Evans and X. S. Xie [135].

The CARS imaging was performed with a Leica (Germany) TCS SP8 CARS microscope. A skin adhesive with dimensions of  $25 \times 25 \times 1 \text{ mm}^3$  was adhered to a cover slip and placed on the sample stage (Fig. 3.5). For imaging water diffusion in adhesives, 50 µL water were placed at the edge of the adhesive. All images were acquired at room temperature ( $23 \pm 2 \text{ °C}$ ). The highest chemical contrast between the matrix and hydrocolloids (Chapter 4, Section 4.1) was determined with a fixed Stokes laser at 1064 nm, while varying the pump laser (PicoEmerald pump laser, APE, Germany). The pump laser was varied from 780 nm to 820 nm with 1 nm increments resulting in wavenumbers ranging from 3400 cm<sup>-1</sup> to 2800 cm<sup>-1</sup>. For video-rate imaging, sequences were acquired at wavenumber 2997 cm<sup>-1</sup> (pump laser: 807 nm) with time intervals of 13.2 s and pixel size of 1.405 × 1.405 µm<sup>2</sup>. All image analysis was done in MATLAB (The Mathworks, Inc.) using the Image Processing toolbox.

#### 3.3.3 Shear rheometry

Shear rheometry was used for quantifying the viscoelastic properties of the adhesives. The rheological analysis was done in the linear viscoelastic region where only small reversible deformations are done. The linear viscoelastic region was identified through a so-called amplitude sweeps where the total deformation of the adhesive was gradually increased. The linear region is indicated by a plateau in the complex modulus,  $G^*$ , as a function of oscillation strain,  $\hat{\gamma}$  (amplitude). The amplitude sweeps were done at an oscillation frequency of 1 Hz with an axial force of 1.00 N. All rheometry was done using a Discovery hybrid rheometer from TA Instruments (Denmark) with parallel plate geometry. Frequency sweeps are a series of deformations of the adhesive with varying deformation frequency but fixed shear strain (amplitude). Here, the frequency sweeps were performed at shear strain,  $\hat{\gamma} = 0.3$  %, where the appropriate shear strain was determined from the amplitude sweeps. The frequency sweeps were done with frequencies ranging from 10<sup>2</sup> Hz to 10<sup>-3</sup> Hz with five frequencies per decade. All measurements were performed in triplicates at 32 °C.

#### 3.3.4 Gravimetric analysis

Gravimetric analysis was done to study how much NaCl solution/artificial sweat the adhesives can absorb as a function of time. Skin adhesive samples with dimensions of  $25 \times 25 \times 1 \text{ mm}^3$ were adhered to polystyrene plates and immersed in 154 mM NaCl solution. The samples were weighed prior to immersion and after certain immersion times using an analytical balance (XS105, Mettler Toledo, Denmark). The temperature of the solution was kept at 32 °C. Assuming the saline solution is absorbed at the adhesive top surface and not the edges, the absorption per area is readily calculated by normalizing by the adhesive area,  $A = 6.25 \text{ cm}^2$ .

#### 3.3.5 Peel test

The adhesive properties were evaluated by peel tests using an Instron 5943 Universal testing system with a 50 N load cell (Instron, Sweden), which allows to measure force as a function of displacement.

The dimensions of the adhesives were  $100 \times 25 \times 1 \text{ mm}^3$ . Adhesives were applied to a substrate, e.g. the artificial skin presented in Chapter 5, with known pressure of either 1680 or 4320 Pa for 60 s using a silicone pad and a load. The adhesives were peeled with constant displacement of 304 mm/min, at an angle of 90° using a backing tape (4124, Tesa, Denmark). The force required to peel the adhesive from the substrate was recorded as a function of displacement. Recorded forces were averaged over displacements from 20 to 80 mm for each measurement, which was done in triplicates.

# Part III

# **Results and discussion**

## Chapter 4

# Probing water diffusion in skin adhesives

Skin adhesives' ability to absorb water/bodily fluids is expected to influence the overall performance of the adhesive. The ability to probe diffusion of water in skin adhesives is therefore of high importance and can help the understanding of the material functionality and screening of new materials and formulations. Traditionally, water diffusion is probed through gravimetric measurements, where skin adhesive samples are immersed in a solution simulating a bodily liquid such as sweat. Gravimetric analysis has limitations and uncertainties including a poor time resolution (order of minutes), inter-operator variation, potentially misleading results due to elution of species from the sample, and sample damage due to the need for sample manipulation when weighing. Fig. 4.1 shows a picture of a skin adhesive sample, which has been immersed in saline solution for 24 h. Here, a weak gel is formed of hydrocolloids. The gel indicate that hydrocolloids have diffused out of the skin adhesive and that the gel may disintegrate upon sample manipulation needed for weighing. Other experimental techniques, which can probe water diffusion in skin adhesives *in situ* with high time resolution are therefore needed.



Figure 4.1: Skin adhesive sample after 24 h of immersion in 154 mM saline solution.

In this chapter water diffusion in selected skin adhesives will be visualized through time-resolved chemical imaging using coherent anti-Stokes Raman scattering (CARS) microscopy. The CARS imaging will help to understand how water is diffusing through the hydrocolloids embedded in the hydrophobic polymer matrix. Next, impedance spectroscopy will be used for probing water diffusion where the assumptions for the data interpretation were obtained through the CARS imaging of the water penetration process. Most of the key concepts, definitions, and results were published in *Paper I* (Appendix A) [139] but will be briefly reviewed here.

#### 4.1 Visualizing water diffusion using CARS microscopy

First, skin adhesives containing 27.1 vol.% PAA dispersed in a 4:1 PIB:SIS (wt:wt) matrix were investigated. Here, a so-called lambda scan was performed where a Raman scattering spectrum was obtained, to identify molecular vibrational energies resulting in high PAA-matrix contrast. The skin adhesives were scanned at wavenumbers ranging from 3400 to 2800 cm<sup>-1</sup>, which covers the O–H and a part of the C–H stretching regions. The results are shown in Fig. 4.2 where Fig. 4.2a-d represent CARS images obtained at different wavenumbers, which are indicated in the spectrum in Fig. 4.2e. Fig. 4.2e shows the normalized intensity as a function of wavenumber for the PAA and matrix, respectively.



Figure 4.2: PAA containing skin adhesives imaged at wavenumbers ranging from 3400 to 2800 cm<sup>-1</sup>. Selected images at wavenumbers 3184, 2997, 2905, and 2830 cm<sup>-1</sup> are shown in (a)-(d). Two regions of interests, representing the PAA particles and the matrix were marked in the images and the corresponding spectrum is shown in (e) where the wavenumbers for the images (a)-(d) are indicated. Reprinted from [139] with permission from ACS Applied Polymer Materials.

Fig. 4.2 shows that the highest contrast is obtained at 2997 cm<sup>-1</sup> (Fig. 4.2b). Here, C–H and aromatic C–H bonds are yielding high intensity from the matrix, while the PAA particles remain dark due to lack of aromatic groups and only a few C–H bonds. The CARS imaging was then

fixed at wavenumber 2997 cm<sup>-1</sup> and time sequences were acquired of the PAA containing adhesive, while being exposed to water. A montage of the PAA containing adhesive is shown in Fig. 4.3a. Here, the dark areas, corresponding to the PAA particles, are swelling and displace the PIB/SIS matrix over time. From the montage it is clear that PAA particles at the adhesive–water interface absorb water and swell to connect with additional particles inside the adhesive, which will proceed to absorb water. To better understand the PAA swelling behavior, each image of the time sequence was binarized and divided into segments perpendicular to the flow front direction (see Fig. 4.3b). The width of each segment was kept at 100  $\mu$ m, which is comparable to the particle size. The particle area for each segment was calculated as a function of time using the image processing toolbox in MATLAB (MathWorks, inc). The PAA particle area relative to the total segment area is plotted as a function of time in Fig. 4.3b for each segment.



Figure 4.3: CARS imaging time montage of a skin adhesive composed of PAA particles (dark spots) dispersed in a PIB/SIS matrix (red region) (a). The sample is exposed to water. The scale bar is 100 µm. Particle area relative to the total segment area plotted as a function time for each of the three segments (b). Adapted from [139] with permission from ACS Applied Polymer Materials.

The initial dry particle area is 25-35 %, which is in agreement with the particle content of 27.1 vol.%. As the PAA particles absorb water and swell the area of the dark regions increases. The first segment (0-100  $\mu$ m) swells initially, followed by the second (100-200  $\mu$ m) and third segment (200-300  $\mu$ m). Here, the saturation of each segment is approximately 90 %, indicated by arrows in Fig. 4.3b, which means the PAA particles absorb at least 60 % of their own volume in water.

Next, skin adhesives containing both PAA (6.5 vol.%) and CHEC (23.4 vol.%) particles dis-

persed in a 4:1 PIB:SIS (wt:wt) matrix were imaged at  $\tilde{\nu} = 2997 \text{ cm}^{-1}$ . A time montage of the adhesive exposed to water is shown in Fig. 4.4.



Figure 4.4: CARS time montage of a skin adhesive containing PAA and CHEC particles dispersed in a PIB/SIS matrix exposed to water. The dark regions correspond to PAA particles, the green regions are CHEC particles, while the red region represents the matrix. The scale bar is 100 µm.

The matrix exhibits CARS signal, while the PAA particles do not as explained above. The CHEC particles also do not exhibit any CARS signal and would consequently also remain dark in the images. However, the CHEC particles do emit a second-harmonic generation (SHG) signal, which is a signal typically occurring when two photons interact with a crystal without a center of symmetry, and have previously been reported to occur in fibrous cellulose materials [140–142]. The SHG signal was overlaid with the CARS signal in Fig. 4.4 where the CHEC particles are represented by the green regions. Consequently, triple-contrast is obtained between the PAA particles, CHEC particles and the adhesive matrix. After 3 min of water exposure, the SHG intensity decreases in the CHEC particles near the adhesive–water interface (indicated by an arrow, Fig. 4.4). This indicates that the particles are wetted, however, they do not appear to swell. After 13 min, a few PAA particles (indicated by the arrow, Fig. 4.4), located approximately 150 µm from the water–adhesive interface, swell significantly. I.e. water transport may occur from the CHEC particles to the PAA particles. Here, a mix of different particle chemistries could be beneficial for tuning the

overall water uptake and swelling of the adhesive to ensure structural integrity over time.

#### 4.2 Probing water diffusion using impedance spectroscopy

Impedance measurements were done as described in Chapter 3, Section 3.3.1 where the impedance of an adhesive immersed in NaCl solution was measured as a function time. The impedance can be probed spectroscopically where the impedance is measured at different potential frequencies. The measurements can also be done at fixed frequency, f = 100 kHz, which will yield a higher time-resolution compared to the spectroscopic measurements. A typical impedance–time plot at fixed frequency is shown in Fig. 4.5a. Initially, at time,  $t_0$ , the impedance represents the dry adhesive



Figure 4.5: Typical impedance data at fixed frequency (a) obtained of an adhesive immersion in NaCl solution. Different times on the curve correspond to specific situation, which are marked in (a) and illustrated schematically in (b)-(e). The situations include dry adhesive (b), wetted adhesive (c), adhesive fully penetrated by NaCl solution (d), and fully saturated adhesive (e).

(Fig. 4.5b) and the impedance has its highest value, while the phase angle is  $\phi = -90^{\circ}$ , which indicates purely capacitive behavior, i.e. no bulk conductivity occurs through the adhesive [133]. Over time, water is absorbed by the adhesive and the overall dielectric properties of the adhesive increase, which results in a gradual decrease in the impedance (Fig. 4.5c) [143]. At some point, NaCl solution will reach the working electrode (Fig. 4.5d). This will result in bulk conductivity occurring through the adhesive. The bulk conductivity, can be detected in the impedance signal, where both the phase angle and impedance drops dramatically (Fig. 4.5a). The characteristic time at which the NaCl solution has penetrated the adhesive is denoted,  $t_p$ , and is arbitrarily but consistently defined as the time where the phase angle has changed by 5 % from its original value,  $\phi_p = 0.95\phi_0$ . The time of penetration is indicated by the asterisk in Fig. 4.5a. After,  $t_p$ , the impedance may be influenced by the electrical properties of the working electrode. Here, the oxide layer on the working electrode surface may hold a significant contribution to the signal. Additionally, corrosion processes may also perturb the signal. However, after a long time,  $t_{\infty}$ , the impedance reaches values comparable to the resistance of the NaCl solution, which suggests that the adhesive has taken up enough NaCl to have electrical properties similar to NaCl solution (Fig. 4.5e).

The impedance was measured spectroscopically and at fixed frequency of adhesives containing either 27.1 vol.% PAA or 27.1 vol.% CHEC particles dispersed in 4:1 PIB:SIS (wt:wt) matrix. The results are shown in Fig. 4.6. Here, Fig. 4.6a and 4.6b show spectroscopic impedance data for the



Figure 4.6: Impedance–frequency plots for the PAA (a) and CHEC (b) contianing adhesives. Impedance–time plots at fixed frequency, f = 100 kHz for the PAA (c) and CHEC (d) containing adhesives. Reprinted from [139] with permission from ACS Applied Polymer Materials.

PAA and CHEC containing adhesives, respectively. The impedance was measured at frequencies ranging from  $10^{-2}$  to  $10^{6}$  Hz, where each frequency sweep was repeated over time. Initially, the impedance is inversely proportional to the frequency with an average slope of -0.954  $\pm$  0.010,

which is in agreement with the theoretical slope of -1, which is obtained from the definition of parallel plate capacitors,  $|Z| = \frac{1}{i\omega C}$ . I.e. the inverse proportionality indicates pure capacitive behavior throughout the frequency range, which means that the NaCl solution has not penetrated through the adhesives to reach the working electrode. Over time, the impedance deviates from the inverse proportionality, which indicates that NaCl now has penetrated the adhesives and reached the working electrode. Fig. 4.6c and 4.6d show impedance-time curves for the PAA and CHEC containing adhesives, respectively. The impedance-time curves were obtained at 100 kHz. The high frequency was chosen for increased sensitivity to dielectric changes, which was explained in Chapter 3, Section 3.3.1. The impedance-time curves follow the general trend as presented in Fig. 4.5. The time of penetration for the PAA and CHEC containing adhesives was determined to be  $t_p = 141.0 \pm 10.3$  min and  $t_p = 1151 \pm 72$  min, respectively. The penetration time for the CHEC containing adhesive is almost an order of magnitude longer than the penetration time for the PAA containing adhesive. This means that PAA is much more effective at transporting water compared to CHEC, which is in agreement their respective chemistries and the CARS analysis in Section 4.1. To extract more information about the water diffusion from the impedance data, additional modeling is needed.

#### 4.2.1 Effective water penetration

In this section, a model for probing the water diffusion from the impedance data is proposed. The model and assumptions are described in detail in *Paper I*, Appendix A [139]. From the CARS images of the adhesives exposed to water, it was seen that the adhesives are capable of absorbing large quantities of water where local sample segments could contain more than 60 % of water. The high water content means that the effective dielectric thickness of the adhesive may change as a function of time, i.e. parts of the adhesive may become perfectly conducting. Additionally, the dielectric properties of the adhesive changes as water is absorbed as discussed in Chapter 3, Section 3.3.1. These two changes in the electrical properties of the adhesives can be probed through changes in sample capacitance, which can be modeled through an equivalent circuit model as previously described (Chapter 3, Section 3.3.1). Here, an effective water penetration,  $\hat{l}$ , is defined as:

$$\hat{l} = 1 - \frac{C_0}{C_t},\tag{4.2.1}$$

where,  $C_0$  and  $C_t$  are the initial capacitance and the capacitance at time, t, respectively. Using the expression for a parallel plate capacitor,  $C = \frac{\varepsilon_0 \varepsilon_r A}{l}$  and assuming the adhesive area, A, does not change during water absorption, Eq. (4.2.1) can be rewritten to:

$$\hat{l} = 1 - \frac{\varepsilon_{r,0}}{l_0} \frac{l_t}{\varepsilon_{r,t}},\tag{4.2.2}$$

where  $\varepsilon_{r,0}$  and  $\varepsilon_{r,t}$  are dielectric constants and  $l_0$  and  $l_t$  are dielectric sample thicknesses of the adhesive at time t = 0 and t, respectively. The effective water penetration holds two contributions,

the change in dielectric thickness and the change in dielectric constant. The change in dielectric thickness is influenced by the spatial water penetration, while the dielectric constant changes with increasing overall water absorption.

The effective water penetration was calculated from the impedance measurements at fixed frequency, f = 100 kHz, for the PAA and CHEC containing adhesives using Eq. (3.3.14) (Chapter 3, Section 3.3.1) and Eq. (4.2.1). The results are plotted in Fig. 4.7. Here, the curves hold infor-



Figure 4.7: Effective water penetration plotted as a function of time for the PAA (a) and CHEC (b) containing adhesives. The time of penetration and electrical saturation are marked by an asterisk and circle, respectively. A power law was fitted to the curves to probe the diffusion mechanism. Adapted from [139] with permission from ACS Applied Polymer Materials.

mation about the water diffusion kinetics, which can be extracted using a power law as presented in Chapter 2, Section 2.2.1.

$$\hat{l} = kt^n, \tag{4.2.3}$$

where k is constant related to the rate of diffusion and sample geometry and n is the diffusional exponent, which indicates the diffusion mechanism as explained in Chapter 2, Section 2.2.1. For the PAA containing adhesives (Fig. 4.7a), the diffusion exponent is,  $0.68 \pm 0.03$ , which indicates anomalous diffusion (0.5 < n < 1). The anomalous diffusion is characteristic for systems where both Fickian and relaxation-restricted diffusion occur simultaneously. The CHEC containing adhesive (Fig. 4.7b) exhibit a diffusional exponent of  $0.97 \pm 0.03$ , which indicates Case II sorption  $(n \approx 1)$ . Case II sorption is characteristic for systems, where diffusion is highly restricted by polymer relaxation processes. This implies that the polymer relaxation times of CHEC are longer compared to PAA, which is in agreement with the CARS images where the PAA swelled/relaxed much faster compared to the CHEC particles.

The proportionality constant, k, cannot readily be compared between two systems exhibiting different diffusion mechanisms. However, k, was used in *Paper I* for evaluating reproducibility by comparing the values of samples with different thicknesses. Here, good agreement was found of constants obtained for adhesives with different thicknesses. A time of electrical saturation,  $t_s$ , is arbitrarily but consistently defined as the time where the effective penetration is 2 % from its maximum value. The electrical saturation time indicates that the adhesive has taken up a lot of water to the extend where the electrical capacitance no longer changes significantly. The electrical saturation time was found to be  $176.9 \pm 8.0$  min and  $1151 \pm 72$  for the PAA and CHEC containing adhesives, respectively. This again indicates that the PAA containing adhesives absorb water much faster compared to the CHEC containing adhesives (Fig. 4.4).

The penetration time, saturation time, and the effective penetration front are all parameters, which can be used for probing the diffusion processes in polymeric skin adhesives to investigate the effect of e.g. particle chemistry, particle content, and matrix rigidity.

#### 4.2.2 Hydrocolloid content & distribution of water

In *Paper III* (Appendix C), the developed impedance technique was used for investigating the influence of hydrocolloid content and matrix rigidity on the water penetration in skin adhesives. The penetration time was measured for adhesives containing 5.8, 9.0, 12.2, 19.3, and 27.1 vol.% PAA particles dispersed in matrices with different mechanical properties. One matrix contained 20 wt.% SIS, while the other contained 40 wt.% SIS. Here, the matrix with high SIS content was more rigid compared to the low SIS content matrix as shown by the rheological properties presented in the Supporting information of *Paper III* (Appendix C). Fig. 4.8 shows the average penetration times for each adhesive formulation having a thickness of 1000 µm. The penetration time generally



Figure 4.8: Penetration time for adhesives with different PAA particle volume fractions dispersed in either 40 wt.% or 20 wt.% SIS containing polymer matrices. Each data point represents an average of three measurements with the errorbars representing their respective standard deviations.

decreases for increasing PAA content until the PAA content reaches 19 vol.% where a plateau in

the penetrations is observed (Fig. 4.8). This indicates that the PAA particle connectivity improves for increasing PAA content until 19 vol.% where the particle network is so effective that additional PAA particles do not contribute to faster water penetration through the adhesive. The differences in penetration time between the 20 and 40 wt.% SIS adhesives are decreasing for increasing PAA content, i.e. the mechanical properties of the matrix are more important for the water penetration in adhesives with poor hydrocolloid connectivity. Here, the PAA particles are required to swell more to form a path for water to penetrate. On the other hand, the penetration times for the 27.1 vol.% PAA adhesives are independent of the mechanical properties. This suggests again, that the water front propagates in a well-connected hydrocolloid network without the need for excessive displacement of the matrix.

Next, the penetration time is resolved for adhesives with different thicknesses to probe the flow front position l = z against time. Here, adhesives containing 27.1 vol.% PAA, dispersed in either a 20 or 40 wt.% SIS matrix, were investigated. The flow front position is plotted against the penetration time in Fig. 4.9a. The flow front position as a function of time (Fig. 4.9a) is similar



Figure 4.9: Flow front position, z, as a function of time for PAA containing adhesives with 20 and 40 wt.% SIS matrices (a). Water absorption per unit area as a function of time for PAA containing adhesives with 20 and 40 wt.% SIS matrices (b). The water absorption data in (b) was obtained by Johannes Eiler.

for both adhesives, which indicates that the inter-particle distance of the PAA particles is small enough to allow water to penetrate through the adhesive with no significant effect of the matrix rigidity. However, the mechanical properties of the matrix proved to affect the water absorption in the adhesives significantly (Fig. 4.9b). Here, the high content SIS adhesive shows a significantly lower water uptake at all times compared to the low SIS content adhesive. This implies that the overall water uptake is restricted by the mechanical properties of the matrix. I.e. the amount of water distributed in the adhesives is different but the water front propagates similarly in both adhesives. These results indicate that the penetration of water can be tuned by the hydrocolloids content and that the amount of water absorbed can be adjusted by the mechanical properties of the polymer matrix.

## Chapter 5

## **Perspiration simulator**

Skin adhesives perform differently depending on their material composition, way they are applied to the skin, and wear conditions such as perspiration, body movement or leakage. Clinical studies can be conducted to probe the performance of skin adhesives where the performance is typically quantified through peel tests or recording the wear time until the adhesive detaches from the skin [144–146]. Although, clinical studies can be useful, they are costly and require a large number of subjects to yield results of statistical significance due to large intra- and intersubject variations [147–149]. Studying the performance of skin adhesives on sweating subjects adds another layer of complexity. Each person will have a unique response to physical activity, differences in sweat gland density and perspiration rate [150, 151]. Additionally, there are technical challenges associated with measuring the sweat rate underneath the adhesive, which is expected to be different from the naked skin [152]. There is therefore a need for *in vitro* models, which simulate human skin and realistic perspiration conditions where adhesives can be tested in a controlled and reproducible manner. A number of perspiration simulators are represented in literature for testing textiles [153, 154]. However, since these models are not optimized for testing skin adhesives, they are often too brittle.

We have previously adapted the perspiration simulator, developed by Hou *et al.* [154], to test the performance of skin adhesives under realistic perspiration conditions [155]. This model includes a brittle artificial epoxy skin, which limits the study to skin adhesives and conditions to low peel forces (F < 5 N), since the artificial skin otherwise will fail cohesively. Another challenge with the epoxy substrate, is that it cannot operate under high sweating pressures e.g. 6 kPa without excessive bulging or even breaking, which consequently compromises the experiments. The general principle of Hou *et al.* was therefore adapted and the dimensions were changed to fit a traditional peel experiment with adhesives having dimensions of  $25 \times 100$  mm<sup>2</sup>. Furthermore, an artificial skin with increased mechanical properties compared to the skin by Hou *et al.*, while still providing skin-like properties was developed. The design of this perspiration simulator was published in *Paper II* (Appendix B) [156].

In this chapter the key aspects of the perspiration simulator, as presented in Paper II, will

be briefly reviewed. In addition, the technical details associated with the development of the model and flow/pressure considerations of the artificial skin will be discussed. Lastly, different performance tests using the perspiration simulator will be described as they will be used later in Chapter 6.

#### 5.1 The perspiration simulator setup

The perspiration simulator setup is schematically illustrated in Fig. 5.1 and includes a tank supplying artificial sweat to a reservoir. The tank hangs with an adjustable height, h, above the reservoir, which creates a pressure inside the reservoir of  $\rho gh$ , where  $\rho$  is the density of the artificial sweat and  $g = 9.82 \text{ m/s}^2$  is the gravitational constant. The reservoir has an aluminum bottom, which allows to heat the artificial sweat to skin temperature, T = 32 °C, using a water bath. The rest of the reservoir is made of transparent PMMA to allow detection of trapped air bubbles. An outlet valve is placed in the reservoir opposite to the inlet. Here, trapped air bubbles are readily released from the reservoir through the outlet. A substrate mimicking skin, referred to as the artificial skin, is taped to a PMMA frame using double-sided adhesive. The PMMA frame is readily mounted on the reservoir using 6 screws and an O-ring for proper sealing.

The artificial skin consists of a track-etched membrane laminated to a fiber-reinforced polyimide support using an acrylic adhesive. The support has holes drilled in it to mimic sweat pores. The support is coated with a thin gelatin layer, which mimics the surface properties of the skin. The gelatin coating process was optimized to have a thin and strong layer, which allows to peel adhesives from it without compromising the gelatin layer. The gelatin should also not block the sweat pores. The gelatin coating process is described in the Supporting Information of *Paper II*, Section 2. In *Paper II*, we furthermore characterized the surface properties of the artificial skin. Here, the average surface roughness parameter was determined using profilometry to  $R_a = 8.4\pm4.5$  µm, while the water contact angle of the skin was 77.5 ± 0.8°, which are both similar to human skin [157–160]. Using quartz crystal microbalance with dissipation, it was found that the gelatin coating hydrates when exposed to a humid environment, which is also a feature human skin possess [161, 162]. Finally, the setup includes a flow sensor, which is placed in between the tubing from the tank to the reservoir. The flow sensor is connected to a flow reader, which allows to read the flow rate (µL/min). Both the flow sensor and reader were obtained from Elveflow (France).

An adhesive can be applied to the perspiration simulator for testing. For situations where the adhesive occludes the artificial sweat pores, a pressure from the reservoir will build up at the adhesive–sweat pore interface. Here, the pressure needs to be in the range of what a natural sweat pore can provide, while the free flow for non-occluded pores needs to be in realistic perspiration rate ranges. Both the pressure upon occlusion and perspiration rate are expected to influence adhesive performance and depend on the properties of the chosen track-etched membrane and the polyimide substrate. In the following section, the flow and pressure in the artificial sweat pores and the principle of the track-etched membrane which also ensures homogeneous sweating throughout the skin, will be described.



Figure 5.1: Schematic illustration of the artificial perspiration simulator. Adapted from [156] with permission from ACS Applied Polymer Materials.

#### 5.2 Pressure and flow considerations

There are two purposes of including the track-etched membrane in the artificial skin. One purpose is to have a flow-pressure relationship mimicking real sweat pores by providing an appropriate flow resistance, which will be discussed in Section 5.2.1. The other purpose is to create a pressure drop before the polyimide support, which is greater than the difference in Laplace pressure between different sweat pores caused by variations in pore diameter, d. This pressure drop ensures more homogeneous sweating throughout the artificial skin. The Laplace pressure,  $P_L$ , is given by:

$$P_L = 4\gamma \frac{\cos\left(\theta\right)}{d} \tag{5.2.1}$$

As an example, the difference in Laplace pressure can be calculated for a variation in the pore diameter of e.g. 5 µm for a polyimide support having a water contact angle of  $\theta = 80^{\circ}$ , using Eq. (5.2.1). The difference in Laplace pressure is,  $\Delta P_L = 24$  Pa. L. Hou *et al.* gives a rule of thumb that the pressure drop across the track-etched membrane,  $P_m$ , should be at least an order of magnitude larger than the difference in Laplace pressure  $P_m > 10\Delta P_L$  [154]. For this example, this means the minimum pressure drop through the track-etched membrane should be  $P_m > 240$ Pa to obtain homogeneous artificial sweating through the polyimide support with variations in pore diameter of 5 µm.

The complete pressure drop,  $P_0$ , across the artificial skin, holds contributions from each layer:

$$P_0 = P_m + P_S, (5.2.2)$$

where  $P_S$  is the pressure drop across the gelatin coated support (substrate). According to Poiseuille's

Law, the pressure drop in a pore is defined as:

$$P = R \cdot Q_n, \tag{5.2.3}$$

where  $Q_n$  is the flow rate in a single pore and  $R = \frac{128\eta l}{\pi d^4}$  is the resistance of the pore. Note that the pressure drop is proportional to the flow rate meaning it may be easier to have homogeneous sweating at higher flows. The resistance is a function of the fluid viscosity,  $\eta$ , layer thickness, l, and pore diameter, d. A pore in the substrate with diameter,  $d_s$ , will have multiple tracketched membrane pores with diameter,  $d_m$ , depending on the membrane pore density,  $\alpha$ . For the track-etched membrane the pressure will be:

$$P_m = R_m Q_n \tag{5.2.4}$$

The total resistance of the track-etched membrane for a single sweat pore is:

$$R_m = \frac{128\eta l_m}{\pi d_m^4} \cdot \frac{1}{\pi d_S^2 \alpha/4}$$
(5.2.5)

Here,  $\pi d_S^2 \alpha/4$  is the number of track-edge membrane pores under a single sweat pore in the polyimide support. The Laplace pressure in the track-etched membrane is assumed to be negligible since it consists of polycarbonate, which means it is hydrophilic and water readily spreads on it [154].

The pressure drop in the substrate (gelatin + support),  $P_S$ , is given by:

$$P_S = R_S \cdot Q_n + P_L, \tag{5.2.6}$$

where the resistance of the substrate is  $R_S = \frac{128\eta l_S}{\pi d_S^4}$ . Next, the flow rate for one sweat pore can be calculated at a given pressure,  $P_0 = \rho gh$ , using Eq. (5.2.2), Eq. (5.2.4) and Eq. (5.2.6):

$$Q_n = \frac{\rho g h - P_L}{R_m + R_S} \tag{5.2.7}$$

The track-etched membrane chosen here have a resistance much higher than the substrate, i.e.  $R_m \gg R_S$ . The resistance of the substrate,  $R_S$ , is therefore negligible and Eq. (5.2.7) can be rewritten using Eq. (5.2.1) and Eq. (5.2.5):

$$Q_n = \frac{\pi^2 d_m^4 d_S \alpha}{512\eta l_m} \left(\rho g h d_s - 4\gamma \cos(\theta)\right) \tag{5.2.8}$$

Eq. 5.2.8 can now be used for modeling different combinations of track-etched membranes with the polyimide support to have pressure and flow values, which are found in human sweat pores.

#### 5.2.1 Perspiration rate and presure

Two different track-etched membranes were obtained from Sterlitch (USA). The track-etched membranes will be referred to as T.-E.M. 1 and T.-E.M. 2. Before Eq. (5.2.8) can be used for evaluating the flow rate as a function of applied pressure, it must be ensured that the resistance of the tracketched membranes is much larger than the resistance in the support,  $R_m \gg R_S$ , i.e.:

$$d_m \ll \left(\frac{4d_s^2 l_m}{\pi \alpha l_s}\right)^{\frac{1}{4}} \tag{5.2.9}$$

For T.-E.M. 1, with  $d_m = 0.1 \text{ µm}$ ,  $l_m = 12 \text{ µm}$  and porosity,  $\alpha = 4 \text{ pores/µm}^2$  and a support with  $l_S = 510 \text{ µm}$  and  $d_S = 250 \text{ µm}$ , Eq. (5.2.9) is used to obtain  $d_m \ll 4.7 \text{ µm}$  for the assumption to hold. Since the pore size of the T.-E.M. 1 is 47 times smaller, the assumption is expected to hold. For T.-E.M. 2 with  $d_m = 0.08 \text{ µm}$ ,  $l_m = 6 \text{ µm}$  and porosity,  $\alpha = 4 \text{ pores/µm}^2$  and the same support, Eq. (5.2.9) gives:  $d_m \ll 3.9 \text{ µm}$ . The pore diameter of T.-E.M. is  $\approx 48$  times smaller than the 3.9 µm and the resistance of the support is also here found to be negligible.

Using Eq. (5.2.8), the theoretical perspiration fluxes, Q, are plotted as a function of applied pressure,  $p = \rho gh$ , for both track-etched membranes (Fig. 5.2). The flux was calculated by multiplying the flow rate of a single pore,  $Q_n$ , by the polyimide support pore density of 100 pores/cm<sup>2</sup>, which is similar to the sweat pore density in the abdomen area [151]. From Eq. (5.2.8)



Figure 5.2: Theoretical and experimentally measured flow rates of polyimide supports with different hole diameters and different track-etched membranes. Each data point represents an average of three different artificial skins where the errorbars represent the standard deviation.

it is known, that the slope of the linear Q-p relation is proportional to the inverse resistance, while

the intersect with the primary axis is the Laplace pressure,  $P_L$ . Fig. 5.2 shows that T.-E.M. 1 and T.-E.M. 2 theoretically have the same Laplace pressure, while the resistance of each artificial skin are different as expected from the different track-etched membranes. Here, T.-E.M. 1 has a lower resistance to flow and therefore yields higher perspiration rates compared to T.-E.M. 2 at a given pressure. Both track-etched membranes gives perspiration rates and pressures within literature values, where pressures up to ~6 kPa and perspiration rates up to ~5  $\mu$ L/min/cm<sup>2</sup> have been reported [150, 163]. The T.-E.M. 1 was chosen to challenge the adhesives more by supplying more sweat faster at a given pressure. The perspiration rate as a function of pressure was measured for skins including T.-E.M. 1 using the flow sensor. The results are included in Fig. 5.2. Here, the Laplace pressure is in agreement with theoretical calculations. However, the slope of the experimental data is approximately 30 % larger, meaning the resistance of the actual skin is lower, compared to the theoretical skin. This could be due to mechanical deformation of the track-etched membrane due to the high pressure or slightly larger pores in the polyimide support. However, the perspiration rates and pressures of the artificial skin are still within literature values and it is therefore found appropriate for the adhesive performance testing.

#### 5.2.2 Pressure upon occlusion

The pressure in the reservoir and the perspiration rate were monitored at different levels of occlusion of the artificial skin to check if the artificial sweat flow indeed is proportional to the non-occluded area or the occlusion would influence the flow in non-occluded areas. This is important to know, since it could change the perspiration conditions depending on the adhesive's ability to occlude the sweat pores. The pressure was monitored using a pressure gauge, which was connected to the outlet in the perspiration simulator. Fig. 5.3 shows the flow rate and pressure as a function of the occluded area. The occlusion was made with acrylic adhesive.



Figure 5.3: Flow rate and pressure as a function of % occluded area. Each data point represent an average of temporal flow at a given occlusion, while the errorbars represent the standard deviation of the average flow.

The pressure was 3.8 kPa and was independent of the occluded area as expected from the considerations of the resistance of the artificial skin. The flow rate, measured with the flow sensor, proved to be inversely proportional to the occluded area. This means that pressure will build up at the artificial–skin adhesive interface where the adhesive occludes the artificial skin, while non-occluded areas will sweat with the chosen perspiration rate. I.e. the artificial perspiration works as intended and can now be used for testing the performance of skin adhesives.

#### 5.3 Performance tests

#### 5.3.1 Perspiration peel test

The adhesive performance is evaluated by 90°-peel experiments from the perspiration simulator. Here, the adhesive is applied to the perspiration simulator using a soft silicone pad and a load. The silicone pad helps to distribute the pressure evenly throughout the adhesive, which is critical for even bonding and reproducible results. The load and the time under load influences the initial bonding, i.e. the initial skin–adhesive contact area. To simulate different application conditions, two different bonding conditions were used: 420 g (1680 Pa) for 60 s and 1080 g (4320 Pa) for 60 s. The low load of 420 g simulates very poor bonding where the adhesive barely is applied to the skin. This bonding condition is expected to expose poorly performing adhesives. The bonding condition using the load of 1080 g, simulates moderate bonding. After application, the adhesive is either left dry or exposed to artificial perspiration followed by a 90°-peel (Fig. 5.4) of the adhesive where the force is measured as a function of displacement using an Instron 5943 Universal testing system with a 50 N load cell. The adhesive is peeled using an acrylic backing tape which is adhered to the backside and partly underneath the adhesive to create a flap for the Instron to grip. The backing tape also ensures that the stress from the peel is at the skin–adhesive contact line. The adhesive dimensions are  $100 \times 25 \times 1 \text{ mm}^3$  (length  $\times$  width  $\times$  thickness). The peel is conducted at a fixed



Figure 5.4: Schematic illustration of an adhesive peeled from the perspiration simulator. Reprinted from [156] with permission from ACS Applied Polymer Materials.

displacement of 304 mm/min, which is similar to standard 90° peel tests. The perspiration pressure was fixed at 4.5 kPa, which gives a perspiration rate of  $1.6 \pm 0.2 \ \mu L/min/cm^2$  for uncovered skin. With this perspiration pressure, high intensity sweating is simulated since it is close to the highest

perspiration pressures reported in literature. I.e. the perspiration peel test is a stress test where the adhesive performance is quantified after 10-20 min of high intensity perspiration.

#### 5.3.2 Long-wear test

The long-wear test is designed to test how the adhesives perform under moderate perspiration conditions for a prolonged period of time. Here, the adhesive is applied to the perspiration simulator under low bonding conditions using the 1680 Pa for 60 s as for the perspiration peel (Section 5.3.1). After application the perspiration simulator is hung upside-down using a stand. A small weight of 12 g is attached to the adhesive to initiate the failure. The adhesive dimensions are  $40 \times 20 \times 1 \text{ mm}^3$  (length × width × thickness) to ensure that the adhesive does not stick to a dry edge of the perspiration simulator, which delays the failure dramatically. The smaller adhesive dimensions allow for testing of two adhesives in a single experiment (Fig. 5.5). The perspiration pressure is kept



Figure 5.5: Schematic illustration of the perspiration simulator hanging upside down using a stand. Two adhesives are adhered to the artificial skin and each adhesive has a load hanging

at 3.5 kPa to simulate moderate sweating. A camera is placed in front of the perspiration simulator and captures an image every 15 seconds to detect when the adhesives detach from the perspiration simulator. The time of adhesive detachment will be referred to as the *time of failure* and will indicate the adhesive's ability to stick to human skin under moderate perspiration conditions. Here, the adhesive staying on the perspiration simulator for the longest time, is expected to exhibit improved performance under perspiration conditions  $in\ vivo.$ 

## Chapter 6

# Performance of polymeric skin adhesives

The performance of a skin adhesive will depend on several parameters and circumstances such as skin roughness, rheological properties of the adhesive, the adhesive's ability to absorb bodily fluids, wear time, bonding conditions, sweating, humidity, and body movement. Most of these parameters are difficult to adjust, reproduce or even probe accurately. Consequently, clinical studies of skin adhesives often yield results with large variations or ambiguous results, which may make it difficult to evaluate hypotheses or answer fundamental questions about skin adhesion. A perspiration simulator was therefore developed in Chapter 5 to simulate realistic wear conditions. The developed perspiration simulator, will here be used for investigating adhesives which were carefully designed for understanding how water absorption, application pressure, sweating, and viscous flow influence the adhesive performance during realistic perspiration conditions. Most of the results presented in this chapter were published in *Paper II* (Appendix B). It is suggested to read *Paper II* prior to this chapter, since this chapter summarizes and expands some points presented in *Paper II*. Additionally, performance experiments complementary to *Paper II* are presented in Section 6.3.

#### 6.1 Adhesive design

Three adhesives were designed to have the same rheological properties but different abilities to absorb water. This was done to decouple the bulk mechanical properties' contribution to the measured adhesion from events occurring at the skin–adhesive interface. The three different adhesives contain the same volume fraction of 28 vol.% particles dispersed in a 4:1 PIB:SIS (wt:wt) matrix. Here, potato starch was chosen as a non-absorbent particle, while CMC was chosen as an effective water absorbent particle. Both particle types are cellulose derivatives and were chosen to have as similar chemistry and physical particle properties as possible, as an attempt to obtain similar

rheological properties, while providing different water absorbing functionality. Three different adhesives were designed and contain, 28 vol.% CMC, 14 vol.% CMC + 14 vol.% starch, and 28 vol.% starch, respectively. The three adhesives will hereafter be referred to as the CMC, CMC–Starch, and Starch adhesives, respectively. The rheological properties, water absorption and impedance data of the three adhesives are shown in Fig. 6.1. Here, the rheological properties are indistin-



Figure 6.1: Storage modulus, G', loss modulus, G'', and  $\tan \delta$  as a function of deformation frequency, f, of the CMC, CMC–Starch and Starch adhesives (a). Water absorption as a function of time (b). Impedance as a function of time of Starch (c), CMC–Starch (d), and CMC (e) adhesives immersed in NaCl solution. All measurements were done at T = 32 °C. Adapted from [156] with permission from ACS Applied Polymer Materials.

guishable for all three adhesives (Fig. 6.1a). The adhesives absorb different amounts of water (Fig. 6.1b). The CMC adhesive absorbs water continuously over the 2 h, while the CMC–Starch adhesive absorbs water within the initial 10 min and hereafter plateau at  $\approx 0.06 \text{ g/cm}^2$  for the remainder of the time. The Starch adhesive does not absorb any water within 2 h, which indicates that Starch indeed does not absorb water under these conditions. This is in agreement with the impedance measurements where the Starch adhesive does not transport water as seen by the constant impedance signal (Fig. 6.1c). The impedance of the CMC–Starch adhesive shows a subtle decrease in the magnitude of the impedance until the time of penetration,  $141 \pm 46$  min, which indicates a low water uptake and that the CMC particles are able to swell and form a path for NaCl solution to reach the working electrode (Fig. 6.1d). The impedance of the CMC–Starch, which

indicates greater water uptake and is in agreement with the water absorption measurements (Fig. 6.1e). The penetration time of the CMC adhesive was determined to  $t_p = 107 \pm 3$  min. The penetration times represent averages of three measurements and the errorbars represent their respective standard deviations.

#### 6.2 Adhesive performance during intense sweating

The performance of the CMC, CMC–Starch and Starch adhesives was quantified using the perspiration simulator. First, the adhesive performance during simulated intense sweating was probed using the method developed in Chapter 5, Section 5.3.1. Before investigating the adhesive properties on sweating skin, the adhesives were investigated on dry artificial skin to see the effect of application pressure and dwell time.

#### 6.2.1 Dry conditions

Each of the three adhesives were tested on the perspiration simulator by 90°-peel experiments. The adhesives were applied with two different application pressures, 4320 Pa (Fig. 6.2a) and 1680 Pa (Fig. 6.2b), which were kept for 60 s. The adhesives were then peeled from the perspiration simulator immediately after application (0 min) and after 20 min of dwell time. There were no significant differences between the adhesives in peel forces at 0 min for both application pressures. However, the peel force was  $\approx 4$  N for the low application pressure, while it was  $\approx 20$  N for the high application pressure. I.e. the application pressure has a great influence on the initial adhesion, which is due to the increased skin–adhesive contact area for increasing application pressure. 20 min after application, the peel forces increased for all adhesive compared to the 0 min peel at both application pressures. This indicates that the adhesives continue to flow after the initial application and establish additional contact with the skin as illustrated in Fig. 6.2c.

#### 6.2.2 Intense sweating

The adhesives were tested under intense sweating conditions where a pressure of approximately 4.5 kPa was applied to yield a perspiration rate of  $1.6 \pm 0.2 \,\mu\text{L/min/cm}^2$  for uncovered skin. Due to partial occlusion of the skin by the adhesives, the flow rates reduced to approximately  $1.0 \pm 0.1 \,\mu\text{L/min/cm}^2$  in all cases (see Supporting information of *Paper II*, Appendix B [156]). First, the adhesives were exposed to 20 min of artificial sweating immediately after application. For the high application pressure (Fig. 6.2a), the peel forces reduced compared to the 20 min dry peel. This indicates that the artificial sweat introduced at the skin–adhesive interface restricts the viscous flow of the adhesive and thus limits the bonding as illustrated in Fig. 6.2d. The CMC and CMC–Starch adhesives gave peel forces, which were comparable to their 0 min values, which means that the initial skin–adhesive contact area remained, while further bonding was restricted. For the Starch adhesive, however, the peel force reduced significantly compared to the initial peel force (0 min), which suggests that some of the initial skin–adhesive contact area was compromised.



Figure 6.2: Average peel forces of the CMC, CMC–Starch and Starch adhesives peeled from the perspiration simulator. The peel forces were evaluated of the adhesives applied with application pressures of 4320 Pa (a) and 1680 Pa (b) under dry and perspiration conditions. The peel forces represent averages of three measurements where the errorbars represent their repective standard deviations. The horizontal bars represent groups with equal mean according to a two sample t-test with 95 % confidence level. Schematic illustrations of the skin–adhesive interface region under dry dwelling (c), perspiration with a non-absorbent adhesive (d), and perspiration with an absorbent adhesive (e). Reprinted from [156] with permission from ACS Applied Polymer Materials.

This could be a consequence of the occlusive nature of the Starch adhesive, which does not absorb water.

A similar trend is observed for the low application pressure (Fig. 6.2b) where the peel forces after 20 min of intense sweating was lower than the 20 min dry peel force. Here, the peel forces of the CMC and CMC–Starch adhesive were higher compared to the initial values (0 min), while the Starch adhesive had equal means with the start value. This indicates that a certain level of water absorption allows the adhesive to flow and bond further with the substrate under perspiration conditions (Fig. 6.2e). To further investigate this, the sweating time was reduced to 10 min to introduce a lower amount of artificial sweat, however, the adhesives were still left for an additional 10 min to keep the total time of 20 min. The CMC adhesive now exhibits a peel force significantly higher compared to the Starch adhesive. The peel force of the Starch adhesive is unchanged compared to the peel force after 20 min of sweating. I.e. the sweat introduced within 10 min was

sufficient to restrict further bonding for the Starch adhesive. The CMC–Starch adhesive seems to perform similarly to the CMC adhesive, which indicates that the level of absorption in the CMC–Starch adhesive is sufficient to manage these short intensive sweating conditions.

### 6.3 Adhesive performance during moderate sweating & prolonged wear

The CMC and CMC–Starch adhesives were tested on the 'long-wear test', which was presented in Chapter 5, Section 5.3.2. This was done to test if the continuous water absorption of the CMC adhesive makes a difference compared to the initial water absorption of the CMC–Starch adhesive under prolonged wear conditions. Here, the adhesives were applied with low application pressure (1680 Pa for 60 s) and a sweating pressure of 3.5 kPa was applied while the adhesives were hung upside-down with a load attached. The *time of failure* was recorded for each adhesive formulation and is reported in Fig. 6.3. Here, the average *time of failure* for the CMC–Starch



Figure 6.3: The average *Time of failure* for the CMC–Starch and CMC adhesives with errorbars representing the standard deviations. The measurements were done in triplciates.

adhesive is  $\sim 100$  min. The CMC adhesive exhibits a consistent *time of failure* of 500 min, which is much greater compared to the CMC–Starch adhesive. This could be due to the continuous water uptake of the CMC adhesive, which allows it to continuously remove artificial sweat from the skin–adhesive interface and perhaps avoid pressure build-up at the skin–adhesive interface. The CMC–Starch adhesive, on the other hand, only absorbs water initially, which seems to only allow it to adhere to the artificial skin for a short time compared to the CMC adhesive. I.e. based on these results, continuous water absorption in skin adhesives seem to be an important feature to maintain consistent performance under prolonged perspiration conditions, while short-term absorption is important for intense sweating for a limited time.

# Part IV

# Conclusion and outlook
## Chapter 7

## **Conclusion and outlook**

### 7.1 Conclusion

The objective of this PhD project was to gain fundamental understandings of skin adhesives' interaction with sweating skin and how the different material properties would affect the adhesive performance.

First, water diffusion in different skin adhesives was investigated, as the adhesives' ability to absorb water/sweat was expected to influence adhesive performance and skin health. Here, CARS microscopy was used for obtaining chemical contrast between the polymer matrix and hydrocolloids in skin adhesives. Skin adhesive samples were subsequently imaged while exposed to water. The CARS imaging revealed that water diffuse through the hydrocolloids, which physically connect when swelling.

Next, a new impedance based technique was developed for probing water diffusion in situ and in real-time. Here, the impedance of skin adhesive samples immersed in saline solution were monitored as a function of time. A model was proposed for estimating an effective water penetration front, which was then used for probing the diffusion mechanism using a power law. The impedance measurements showed that water diffusing in skin adhesives containing PAA hydrocolloids follow anomalous diffusion, while CHEC containing skin adhesives exhibit Case II sorption. This indicates that the polymer relaxation times of CHEC are slower compared to PAA when exposed to water, which is in agreement with their respective chemistries. A characteristic penetration time was defined, as the time where the saline solution has penetrated through the entire thickness of the adhesive. Here, a clear signal was observed in the phase angle of the impedance. The penetration time was shown to decrease for increasing hydrocolloid hydrophilicity and for increasing hydrocolloid content. The mechanical properties of the polymer matrix were then increased, which showed that water absorption was reduced. However, for skin adhesives containing large amounts of hydrocolloids, e.g. 27 vol.%, the penetration time was independent of the matrix rigidity. I.e. water penetrated a highly connected network of hydrocolloids but the total amount water absorbed was reduced, which revealed that the distribution of water could be tuned by considering the matrix rigidity and hydrocolloid content.

To gain understanding of adhesive performance in realistic wear situations, a perspiration simulator was developed. The perspiration simulator had the ability to sweat with an adjustable pressure and included an artificial skin substrate based on gelatin, which had similar surface properties as human skin. The perspiration simulator was first used for evaluating peel forces of three adhesives with indistinguishable rheological properties but with different abilities to absorb artificial sweat. Here, a non-absorbent adhesive proved to have the poorest adhesive performance, while absorbing adhesives exhibited significantly higher peel forces after artificial perspiration. This suggested that having hydrocolloids included in the adhesive formulation allowed the adhesive to absorb sweat introduced at the skin–adhesive interface and further bond to the skin, which increased the adhesion over time. The perspiration peel tests did not show any significant differences between skin adhesives exhibiting continuous water uptake through a hydrocolloid network compared to an adhesive with a few hydrocolloids, which only provided an initial water absorption through the hydrocolloids connected to the adhesive surface.

However, the perspiration simulator was then used for testing adhesive detachment during simulated prolonged wear under moderate perspiration conditions. Here, the adhesives were hung upside-down with a small load attached, while a camera recorded the time of adhesive detachment, which was referred to as *time of failure*. Here, the adhesive exhibiting the continuous water absorption stayed on the artificial skin approximately 5 times longer compared to the adhesive only absorbing artificial sweat initially. I.e. continuous water absorption is important for maintaining adhesion under prolonged wear with perspiration.

### 7.2 Outlook

Due to the industrial nature of this project, I cannot discuss the ideas for new formulations and designs of improved skin adhesives. I will therefore restrict this outlook to some of the remaining academic questions, which are relevant for skin adhesives and polymer technology in general.

It would be beneficial for the general understanding of water diffusion in polymer composites and skin adhesives if well-defined hydrocolloids could be obtained, e.g. through collaboration with skilled polymer chemists. The hydrocolloids could then be tailored to systematically investigate the effects of molecular weight, size, degree of crosslinking and degree of substitution. Next, further impedance studies are needed to discover the general relationships between water absorption, water penetration, and the relative change in the capacitance (effective water penetration) of skin adhesives containing different hydrocolloid types and content. Such general correlations would allow one to derive e.g. the water absorption from the impedance measurements as well as the water penetration depth. Ultimately, the temporal water concentration profile should be extracted.

As skin adhesives are exposed to liquids for an extended period of time, they are plasticized, which will change the rheological properties. Consequently, the energy dissipation in the material is affected and thus the adhesive properties are also expected to change. Most of the adhesion tests in this project were designed to keep the rheological properties of the adhesives as constant as possible to decouple events occurring at the skin-adhesive interface from the bulk mechanical properties. However, in further studies it would be important to understand how the rheological properties change as a function of water absorption. Here, extensive rheometry studies of adhesive samples, with known amounts of water absorbed, are needed. The distribution of water in the adhesives is expected to affect the rheological properties as well, i.e. these studies could be combined with the newly developed impedance technique where the distribution of water can be probed.

Although, the developed perspiration simulator mimics relevant skin and perspiration parameters, a final validation of the model is needed. Here, the results obtained from the perspiration simulator should be compared with clinical results, where the same adhesives are tested on humans under similar conditions. As a part of the SROT project, we have made a few pilot trials, however, the clinical trial should ideally include as many healthy volunteers as possible to increase the chance of obtaining statistically significant results. The volunteers could be exercising in a controlled manner, e.g. cycling while producing a set power, while wearing different adhesives. The perspiration rate could be measured gravimetrically by the use of absorbent pads attached to the body. These pads would collect sweat and different pads could be detached and weighed at different times to resolve the temporal development in the perspiration rate.

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# Appendices

## Appendix A

# Paper I

Article

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### Water Diffusion in Polymer Composites Probed by Impedance Spectroscopy and Time-Resolved Chemical Imaging

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Supporting Information

**ABSTRACT:** The ability to probe water diffusion in polymer composites is of significant importance for materials characterization and performance evaluation. Here, we investigate water diffusion in polymer composites using coherent anti-Stokes Raman scattering microscopy and impedance spectroscopy. Coherent anti-Stokes Raman scattering microscopy provides real-time information about evolution in the polymer composite structure during water uptake, which supports a method for evaluation of impedance data obtained in a water penetration



process. The method extracts the water diffusion kinetics from the relative change in the temporal capacitance, which includes contributions from changing dielectric properties and thickness. Specifically, the method is used for investigating two model composites relevant for medical adhesives consisting of a hydrophobic and rigid polymer matrix mixed with either poly(acrylic acid) or cetyl hydroxyethyl cellulose particles. Based on our analysis, these two composites exhibit anomalous diffusion and case II sorption, respectively, corresponding to faster relaxation processes in the poly(acrylic acid) containing composites compared to the cetyl hydroxyethyl cellulose containing composites during the water uptake process. Furthermore, the cetyl hydroxyethyl cellulose containing composites. In agreement with known chemical properties of these materials, this implies a lower water affinity for cetyl hydroxyethyl cellulose compared to poly(acrylic acid).

**KEYWORDS:** impedance spectroscopy, coherent anti-Stokes Raman scattering (CARS) microscopy, polymer composites, water diffusion, case II sorption, anomalous diffusion

#### 1. INTRODUCTION

Polymer composites are used for a wide range of applications including paints, protective coatings, wind turbine blades, and adhesives. Such composites consist of a polymer matrix and fillers. One function of the matrix is to hold the geometrical shape of the composite, while the fillers give the material application-specific properties depending on the type of filler. Filler types include pigments for coloring, fibers for directional rigidity, and hydrophilic particles for enhanced water permeability.<sup>1-5</sup> Water diffusion in polymer composites is of great interest for manufacturing anticorrosive paints, protective coatings for microelectronics, hydrogels, and medical adhesives.<sup>6–10</sup> The ability to accurately probe water diffusion is required for rational material formulation and screening of material performance. Consequently, there exists a continuous drive to develop and refine experimental techniques for investigating water diffusion in polymer composites.

Diffusion studies are typically conducted using gravimetric measurements, while spectroscopic techniques represent an alternative approach.<sup>11–13</sup> The choice of method depends on

sample geometry, functionality, and time scale of diffusion. Obtaining accurate water uptake data presents a challenge using gravimetric measurements for degrading systems where significant sample mass is lost due to elution of species or cohesive fracture.<sup>14,15</sup> Fredj et al. demonstrated the occurrence of leaching processes in marine coatings by comparing gravimetric measurements with impedance spectroscopy. Impedance spectroscopy proved not to be as sensitive to eluting species as gravimetric measurements and yielded more accurate uptake kinetics.<sup>16</sup> Later, Grammatikos et al. emphasized the benefits of impedance spectroscopy to detect moisture uptake in fiber reinforced polymer composites without the contribution of sample loss.<sup>17</sup> Other advantages of impedance spectroscopy include high time resolution, noninvasive nature, and the ability to detect electrochemical reactions. However, assumptions about the electrical behavior

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of the system are required for physical interpretation. Complementary techniques should therefore be used in combination with impedance spectroscopy to ensure correct data interpretation. Reuvers et al. studied the water uptake in nylon films using electrochemical impedance spectroscopy and magnetic resonance imaging. The imaging was used to track the bulk water front since it was found to only detect moisture levels higher than 2%. Meanwhile, impedance spectroscopy was found to be sensitive enough to detect low concentrations of water ahead of the bulk water front, which also made it suitable for studying the water penetration in the films.<sup>11</sup>

Experimentally obtained sorption curves are typically interpreted by using diffusion models to obtain quantitative information, such as the diffusion coefficient, which is useful for intersample comparison. Diffusion models can also help link together the material composition and performance, since The they hold molecular information about the system.<sup>18</sup> nature of sorption kinetics strongly depends on the samplepenetrant interactions.<sup>19</sup> Polymer systems with a high degree of chain mobility are typically above their glass transition temperature and can accommodate diffusion of penetrants with a high activity without the buildup of internal stress. Such systems will exhibit Fickian diffusion behavior.<sup>20</sup> On the other hand, for polymeric systems where the time scales of the polymer relaxation processes are comparable with the time scales for penetrant diffusion, non-Fickian sorption kinetics are expected. These sorption processes will typically exhibit a sharp flow front propagating in the material.<sup>2</sup>

In the work presented here, we investigate polymer composites relevant for medical-grade adhesives composed of a hydrophobic matrix and hydrophilic particles. The water transport is expected to occur in the hydrophilic particles due to the low water permeability of the matrix. In this study, we select two different fillers that are expected to exhibit different water transporting properties due to differences in their hydrophilicity. Poly(acrylic acid) (PAA) was selected as a highly hydrophilic filler. PAA is typically categorized as a superabsorbent polymer, which is attributed to sodium ion dissociation upon wetting and its hydrophilic acid groups. Cetyl hydroxyethyl cellulose (CHEC) was chosen as a moderately hydrophilic particle due to its hydrophobic cetyl side chains and nonionic nature.<sup>25,26</sup> We seek to understand how water interacts with the fillers by probing the diffusion kinetics using impedance spectroscopy and by imaging structural changes using coherent anti-Stokes Raman scattering (CARS) microscopy. CARS microscopy provides label-free chemical contrast by imaging specific molecular vibrations associated with particular chemical species.<sup>27</sup> The technique is typically used for imaging dynamic processes in biological systems, since besides the chemical contrast, it also intrinsically yields high 3D spatial resolution and video-rate time resolution.  $^{28-30}$  We take advantage of CARS microscopy to obtain chemical contrast between fillers and matrix and probe real-time structural changes in the composite during water absorption. This allows us to probe the bulk water absorption indirectly by following the swelling of the hydrophilic particles, which will aid in the physical interpretation of the obtained impedance results.<sup>31</sup>

#### 2. MATERIALS AND METHODS

**2.1. Materials.** Polyisobutylene (PIB) was obtained from BASF (Germany), styrene-isoprene-styrene (SIS) was obtained from Kraton (Houston, TX), the poly(acrylic acid sodium salt) (PAA)

particles were obtained from Steweart Superabsorbents (Hickory, NC), and the cetyl hydroxyethyl cellulose (CHEC) particles were obtained from Ashland (Lexington, KY). The volume-weighted average diameter of each particle type was determined by laser diffraction (Malvern Mastersizer 2000, United Kingdom) to  $d_{PAA} =$ 68.4  $\mu$ m and  $d_{CHEC}$  = 93.1  $\mu$ m. Details on the laser diffraction measurements and the particle size distributions are provided in the Supporting Information (see Figure S1). PIB and SIS were mixed for 45 min at 30 rpm and 90 °C under vacuum in a Brabender mixer (Brabender GmbH & Co KG, Germany). The ratio between PIB and SIS was kept at 4:1 by weight, and the total mass of each mix was 60 g. Particles were then mixed with the matrix to yield composites containing 40.0 wt % PAA particles corresponding to 27.1 vol %. CHEC containing composites with the same volume fraction corresponding to 35.8 wt % were also mixed. Particle volume fractions were calculated from particle densities  $\rho_{\text{PAA}} = 1.6491 \pm 0.0003 \text{ g cm}^{-3} \text{ and } \rho_{\text{CHEC}} = 1.3792 \pm 0.0003 \text{ g cm}^{-3} \text{ obtained with an}$ AccuPyc 1340 He pycnometer from Micrometrics (Norcross, GA). After the particles were added to the matrix, vacuum was applied to minimize air entrapment in the composites. The mix was subsequently processed for 45 min at 30 rpm and 90 °C. After mixing, 20 g of material was pressed between two horizontal steel plates for 30 s under a load of 10 tons at 90  $^{\circ}$ C. The sample mixes were pressed to thicknesses of 1050  $\pm$  25 and 550  $\pm$  25  $\mu m.$  The thickness was subsequently measured by using a thickness gauge (Mitutoyo Europe GmbH, Germany). After pressing, the desired sample geometry was obtained by punching. A saline solution for the impedance measurements was prepared from ultrapure water (arium pro, Satorius, Germany) and sodium chloride (Sigma-Aldrich, Denmark).

**2.2. Impedance Spectroscopy.** Impedance spectroscopy was performed by using a two-electrode system connected to an Autolab potentiostat (PGSTAT128N) with a frequency response analyzer module (FRA32M) both obtained from Metrohm Nordic (Denmark). The sample was adhered directly to a type 316L stainless-steel plate (working electrode) and clamped to a glass cell (Figure 1a). A



Figure 1. (a) Experimental setup for the impedance measurements consisting of a glass cell clamped to the polymer composite and working electrode. The counter electrode is fixed above the composite, which is immersed in a 154 mM NaCl solution. (b) Schematic illustration of CARS imaging of a polymer composite exposed to water. The CARS imaging is obtained through a pump and a Stokes beam, and the CARS signal is detected through the epi-CARS detector.

graphite rod was used as both the counter and the reference electrode. The sample was exposed to 154 mM NaCl solution. The sample area was chosen to be 9.6 cm<sup>2</sup>, which is much larger than the particle sizes, to average out sample inhomogeneities. An oscillating potential with an amplitude of 10 mV was applied between the two electrodes, and frequencies from 10 mHz to 1 MHz with one frequency per decade were scanned. A small potential was chosen to minimize perturbations of the water diffusion process. The measurements were done at room temperature, which was  $23 \pm 2$  °C. We note that impedance results obtained after the electrolyte solution has penetrated through the entire polymer composite and reached the working electrode may have a significant contribution from the resistive and capacitive properties of an oxide layer at the surface of the working electrode.

#### Article



**Figure 2.** Bode (a, b) and impedance–time (c, d) plots of 565 and 1053  $\mu$ m PAA containing composites, respectively. The Bode plots are plotted at different times representing the entire duration of the experiments, while the impedance–time plots continuously show the impedance and phase angle as a function time at fixed frequency, f = 100 kHz.

However, the detailed diffusion analysis is performed for times much shorter than the time of penetration, and this contribution can therefore be considered insignificant since a thick layer (at least 250  $\mu$ m) of polymer composite remains on the working electrode and will dominate the impedance signal over the oxide layer.

The capacitance was obtained from the impedance by using an equivalent circuit model. Here, we model the polymer composite as a (RC) circuit, i.e., a resistor and a capacitor in parallel. The resistor and capacitor represent bulk conductivity and the dielectric properties of the sample, respectively. The resistance of the hardware and electrolyte solution is neglected. Additionally, the resistive and capacitive properties of the oxide at the working electrode surface can be neglected until the electrolyte solution is close to the working electrode. The capacitance, C, of a (RC) circuit is readily obtained as

$$C = -\frac{Z''}{\omega(Z'^2 + Z''^2)}$$
(1)

where  $\omega$  is the angular frequency of the potential, Z' is the real part of the impedance, and Z'' is the imaginary part of the impedance.

**2.3. CARS Imaging.** CARS imaging was performed on a Leica TCS SP8 CARS microscope (Germany). A thick sample  $(25 \times 25 \times 1 \text{ mm}^3)$  was adhered to a coverslip and placed on the sample stage (Figure 1b). For the water absorption experiments, 50  $\mu$ L of water was placed at the edge of the sample, and the water was absorbed into the sample. All images were acquired with a field of view of 718 × 718

 $\mu$ m<sup>2</sup> at room temperature (23 ± 2 °C). The highest chemical contrast was determined with a fixed Stokes laser at 1064 nm, while varying the pump laser (PicoEmerald pump laser, APE, Germany). The pump laser was varied from 780 to 820 nm with 1 nm increments, resulting in wavenumbers ranging from 3400 to 2800 cm<sup>-1</sup>. The sample was exposed to water to investigate changes during water sorption. Here, image sequences were acquired at wavenumber 2997 cm<sup>-1</sup> (pump laser: 807 nm) with time intervals of 13.2 s and pixel size of 1.405 × 1.405  $\mu$ m<sup>2</sup>. Image segmentation was done in MATLAB (The Mathworks, Inc.) by using the Image Processing toolbox. The images were binarized by using the *im2bw* function where the optimum threshold was determined from gray scale histograms, which were obtained using the *imhist* function.

#### 3. RESULTS AND DISCUSSION

The goal of the present work is to develop a new method for probing water diffusion in polymer composites. This is done by first determining the temporal impedance of composites exposed to saline solution. Then, structural changes during the diffusion process are imaged by using CARS microscopy. From these findings, we finally describe a new model for impedance interpretation, which we use for comparing composites containing PAA and CHEC particles.



Figure 3. PAA containing composite imaged at wavenumbers ranging from 3400 to 2800 cm<sup>-1</sup>. Selected images at wavenumbers 3184, 2997, 2905, and 2830 cm<sup>-1</sup> are presented in (a)–(d), respectively. The spectra (e) illustrate the signal from the PAA particles and the matrix.

3.1. Impedance Spectroscopy of PAA Containing Composites. PAA containing composites, with thicknesses of  $550 \pm 25 \ \mu m$  and  $1050 \pm 50 \ \mu m$ , were investigated by using impedance spectroscopy, while exposed to a 154 mM sodium chloride solution. The results are displayed in Figure 2 as Bode plots (Figure 2a,b) and impedance-time plots at fixed frequency, f = 100 kHz (Figure 2c,d). At short times (20 min) after the sample was exposed to salt solution, the Bode plots show that the impedance is inversely proportional to the frequency, which indicates purely capacitive behavior. For capacitive behavior,  $|Z| = \frac{1}{i\omega C}$ , the proportionality constant theoretically is -1 in a log-log plot of impedance vs frequency.<sup>32</sup> The slope of the linear frequency sweeps was determined to be  $-0.954 \pm 0.010$ , which is in agreement with the theoretical value of -1. The reported value represents an average and standard deviation of five independent frequency sweeps. The capacitive behavior is also observed in the impedance-time plots where the phase angle,  $-\phi$ , is close to  $90^{\circ}$ .<sup>33</sup> Over time, the saline solution penetrates into the composites through the hydrophilic particles, resulting in a steady decrease in impedance. After some time, sudden drops are observed in both the impedance and the phase angle for all composites. This means the composites no longer behave purely capacitive and implies that saline solution has fully penetrated the composites, i.e., reached the working electrode. The phase angle is less sensitive to small variations in the capacitance compared to the magnitude of the impedance. The time of full penetration,  $t_{\rm p}$ , is therefore arbitrarily but consistently defined as the time at which the phase angle has decreased by 5% from its original value,  $\phi_{\rm p}$  = 0.95 $\phi_{\rm 0}$ . After full penetration of the saline solution corrosion may occur at the surface the working electrode. This increases the complexity of the obtained data, and we will therefore limit our diffusion analysis to times much shorter than the penetration time. The impedance and phase angle continue to change after full penetration in all cases. This indicates the composites are not saturated at that point and continue to absorb saline solution. The impedance eventually reaches constant values,  $|Z| \sim 20 \Omega$ , which is comparable to the impedance of the electrolyte solution. This means the composites have absorbed enough saline solution to exhibit impedance values similar to the free saline solution.

Quantitative information about the diffusion kinetics can be extracted from impedance data by making appropriate assumptions about the sample capacitance. One approach represented in the literature is the Brasher-Kingsbury model where the capacitive changes are attributed to changes in the system's dielectric properties, while the dielectric thickness is assumed to remain constant.<sup>34</sup> The water uptake can subsequently be estimated by calculating the dielectric properties relative to the dielectric constant of water. The Brasher-Kingsbury model assumptions work well for systems absorbing low quantities of water, typically <10 vol %, and have been successfully applied to evaluate water diffusion kinetics in protective coatings.  $^{35-38}$  Because the impedance values of our systems reach values comparable to the electrolyte solution for long immersion times, the water content is expected to be high why the Brasher-Kingsbury model is not expected to be suitable. However, to find the most appropriate model conditions for water diffusion in our materials, complementary techniques are needed. Here, we use CARS microscopy to evaluate the composite during water exposure to identify appropriate modeling assumptions.

**3.2. Imaging Water Diffusion Using CARS Microscopy.** PAA containing composites were imaged by using CARS microscopy. To identify energies resulting in high particle-matrix contrast, composites were imaged at wavenumbers,  $\tilde{\nu}$ , ranging from 3400 to 2800 cm<sup>-1</sup>, which cover the O-H and some of the C-H stretching regions. Figures 3a-d show resulting images collected at different wavenumbers indicated by letters (a-d) in the spectra (Figure 3e). The dashed lines in the spectra indicate the intensity difference between PAA and the matrix. Similar intensity differences were obtained at several different wavenumbers; however, the highest relative contrast between PAA and matrix was found at  $\tilde{\nu} = 2997$  cm<sup>-1</sup>. Here, the aromatic groups of the styrene in SIS give a high intensity signal from the matrix, while the PAA

particles do not exhibit molecular vibrations corresponding to this energy due to the lack of aromatic double bonds and thus remain dark in the images.

Image sequences were acquired at  $\tilde{\nu} = 2997 \text{ cm}^{-1}$  during water exposure (Figure 4). The water was supplied as



Figure 4. CARS image montage of a sample exposed to water. The composite in the montage contains 40 wt % PAA particles, which appear to swell as water propagates in the sample. The scale bar is 100  $\mu$ m.

illustrated in Figure 1b. Here, the evolution of the water transport is observed as swelling of the dark regions corresponding to the hydrophilic PAA particles, which shows that the particles indeed are responsible for the water transport. The matrix (red region) is displaced due to particle swelling as the water front is propagating through the sample. Water does not contribute significantly to the signal at the measured wavenumber. To help visualize the particle swelling, the images were divided into segments perpendicular to the flow front direction. The segment width is 100  $\mu$ m (Figure 5), which is comparable to the particle size. The particle area of each segment was subsequently determined relative to the total segment area. The changes in relative particle area in each image segment were plotted as a function of time and are displayed in Figure 5. The plots show that the relative particle area in each segment is approximately 25-35% in the dry state, which is in agreement with the particle fraction of the mix at 27.1 vol %. The relative particle area at saturation is around 90%, implying each segment contains at least 60% water at saturation. This is in agreement with the low impedance at saturation, indicating that saturated sample segments are electrically conducting. The time between the start of swelling and saturation, indicated by arrows in Figure 5, is 18 min for the first segment (0–100  $\mu$ m) and 30 min for the third segment (200–300  $\mu$ m). This indicates that the concentration profile of the flow front broadens over time. The initial swelling time of the third segment happens after  $\sim 18-20$  min, which seems to agree with the impedance measurements where full penetration of a 565  $\mu$ m PAA containing composite

happens after 28.9 min. In the following section this information will be used to model the impedance data for two different particle containing composites.

3.3. Diffusion Modeling and Material Variation. From the CARS imaging we found that PAA containing composites exposed to water consist of a dry part, a semiwetted part, and a saturated part. Furthermore, the fraction of each part changes as a function of time. The impedance data and CARS images indicate that saturated sample segments can be assumed to be perfectly conducting, which results in an overall decrease of the effective dielectric thickness. The Brasher-Kingsbury model is not found suitable for data interpretation of these composites since it assumes constant dielectric thickness. Instead, we define an effective water penetration front that includes contributions from saturated, semiwetted, and dry sample segments. The effective water penetration front is here defined as  $\hat{l} = 1 - \frac{C_0}{C_t}$ , where  $C_0$  is the initial capacitance and  $C_t$  is the capacitance at time, t. From the definition of parallel plate capacitance,  $C = \frac{\varepsilon_0 \varepsilon_r A}{l}$ , we obtain

$$\hat{l} = 1 - \frac{\varepsilon_{r,0}}{l_0} \frac{l_t}{\varepsilon_{r,t}}$$
<sup>(2)</sup>

Here,  $\varepsilon_{r,0}$  and  $\varepsilon_{r,t}$  are dielectric constants and  $l_0$  and  $l_t$  are thicknesses of the sample at time t = 0 and  $t_i$ , respectively. This model is valid for times shorter than the time of full penetration,  $t < t_p$ , after which the electrical properties of the substrate are expected to have a significant contribution. The diffusion kinetics are therefore extracted for times much shorter than the time of full penetration,  $t \ll t_{\rm p}$ . The simplest description of capacitive changes for a highly water absorbing system is to consider a binary water concentration profile, where a given sample segment is either dry or fully saturated. The dielectric constant of the sample can then effectively be considered constant  $\varepsilon_{r,t} = \varepsilon_{r,0}$ , while only the dielectric thickness changes over time. Equation 2 is readily reduced to  $\hat{l} = rac{l_0 - l_t}{l_0}$  describing the temporal water penetration. However, CARS observations showed that the water concentration profile is a gradient rather than binary. The dielectric constant must therefore vary spatially with the water concentration,  $\varepsilon_{\rm r,t}$  $= \varepsilon_{r,t}(x)$  (1D diffusion). The effective water penetration front (eq 2) was determined from the temporal capacitance at 100 kHz for increased sensitivity to changes in dielectric properties. The temporal capacitance was calculated via eq 1. The effective water penetration front for PAA containing composites is plotted as a function of time in Figure 6. The curves hold information about the water diffusion kinetics, which can be extracted by fitting a power law (eq 3) previously found useful to classify the water diffusion mechanism in polymeric systems.  $^{21,39}$ 

$$\hat{l} = kt^n \tag{3}$$

where k is a proportionality constant related to the diffusion rate and sample geometry and n is the diffusional exponent indicating the diffusion mechanism. The diffusion model is fitted to data up to half of the full penetration of the thinnest sample for each sample type since the diffusion mechanism ideally is independent of sample thickness.<sup>40</sup> This also ensures that there is no capacitive contributions from the working electrode, since there is a dry polymer layer with a thickness of at least ~250  $\mu$ m covering the stainless steel electrode. The

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Figure 5. Particle area relative to the total segment area plotted as a function of time for each segment. The vertical white lines illustrate the boundaries of the segments having widths of 100  $\mu$ m. The arrows indicate swelling initiation and saturation of each segment. The scale bar is 100  $\mu$ m.



**Figure 6.** Effective water penetration front plotted as a function of time for each sample type: 565  $\mu$ m PAA (a) and 1053  $\mu$ m PAA (b). The fits represent a power law fitted to the data up to half-penetration of the thinnest sample. The points of full penetration (\*) and saturation (O) are also indicated.

point of full penetration (\*) and the point of saturation ( $\bigcirc$ ) are marked in Figure 6. Saturation is arbitrarily but consistently defined as the point where the effective water penetration front is 2% from its maximum value. The time of saturation is denoted  $t_s$ . The difference between the saturation and full penetration time,  $\Delta t = t_s - t_p$ , reflects the width of the concentration profile.  $\Delta t$  increases with increasing thickness, from  $\Delta t(565 \ \mu m) = 16.6 \pm 1.6 \ min to \Delta t(1053 \ \mu m) = 35.9 \pm 3.6 \ min$ . This implies that the width of the concentration

profile is increasing over time, which is in agreement with the CARS observations.

Next, CHEC containing composites with the same PIB–SIS matrix and particle loading were examined. The impedance data, provided as Supporting Information (Figure S2), reached low values similar to the PAA containing composites. This means that these composites also absorb amounts of water, which makes the composites electrically conducting. The data are therefore analyzed following the same approach as for the



Figure 7. Effective water penetration front plotted for each sample type: 565  $\mu$ m CHEC (a) and 1049  $\mu$ m CHEC (b). The fits represent a power law fitted to the data up to half-penetration of the thinnest sample. The points of full penetration and saturation are marked (\*) and (O), respectively.

 Table 1. Penetration Times, Saturation Times, Diffusional Exponents, and Proportionality Constants Summarized for the Four Different Composites<sup>a</sup>

type	$l_0 \ (\mu m)$	$t_{\rm p}~({\rm min})$	$t_{\rm s}~({\rm min})$	$\Delta t \pmod{\min}$	n	$k (s^{-n})$
PAA	565	$28.9 \pm 1.0$	$45.6 \pm 2.6$	$16.6 \pm 1.6$	$0.77 \pm 0.01$	$0.93 \pm 0.08$
PAA	1053	$141.0 \pm 10.3$	$176.9 \pm 8.0$	$35.9 \pm 3.6$	$0.68 \pm 0.03$	$0.32 \pm 0.02$
CHEC	565	$253 \pm 28$	$507 \pm 36$	$254 \pm 28$	$1.04 \pm 0.11$	$0.08 \pm 0.01$
CHEC	1049	766 ± 119	$1151 \pm 72$	$385.0 \pm 48$	$0.97 \pm 0.03$	$0.04 \pm 0.01$
<sup>a</sup> Each value represents an average of three results with their respective standard deviation.						

PAA containing composites. The effective water penetration front for the CHEC containing composites is plotted as a function of time in Figure 7 for composites with thicknesses of 565  $\mu$ m (Figure 7a) and 1049  $\mu$ m (Figure 7b). All impedancederived results are summarized in Table 1 where the reported values are averages of triplicates with their respective standard deviations. The CHEC containing composites also indicate flow front broadening since  $\Delta t$  increases with increasing sample thickness, i.e., from  $\Delta t(565 \ \mu m) = 254.0 \pm 28.0 \ min$  to  $\Delta t(1053 \ \mu m) = 385.0 \pm 47.5 \text{ min.}$  The CHEC containing composites have longer penetration and saturation times compared to the PAA containing composites. This means the CHEC particles transport water less effectively than the PAA particles assuming similar particle dispersion. This implies that the water affinity of the PAA particles is higher compared to the CHEC particles, which is in agreement with the chemical structure of PAA and CHEC. Diffusional exponents of the PAA containing composites are  $n = 0.77 \pm 0.001$  and n = 0.68 $\pm$  0.03 for the 565 and 1049  $\mu$ m composites, respectively. The CHEC containing composites have diffusional exponents of n= 1.04  $\pm$  0.11 and *n* = 0.97  $\pm$  0.03 for the 565 and 1049  $\mu$ m composites, respectively. The diffusional exponents should ideally be independent of sample thickness; however, minor variations are observed for the PAA containing composites. We speculate that it is due to the thickness of the thin composites approaching the particle size, potentially leading to increased influence of variations in filler dispersion along the composite thickness. The largest variations in diffusional exponents are, however, found between the PAA and the CHEC containing composites. The PAA containing composites exhibit anom-

alous diffusion (0.5 < n < 1), while the CHEC containing composites demonstrate case II sorption  $(n \approx 1)$ . The anomalous mechanism is characteristic for systems where both Fickian and relaxation-restricted diffusion processes occur simultaneously. Similar diffusional exponents, obtained through gravimetric measurements, have previously been reported for PAA in the literature.<sup>41</sup> Case II sorption is characteristic for systems where the penetrant diffusion is highly restricted by polymer relaxation processes.<sup>39</sup> This implies the polymer relaxation processes are slower for CHEC compared to PAA. The proportionality constant, k, is only of physical significance for limiting cases, i.e., Fickian diffusion (n = 0.5) and case II sorption (n = 1).<sup>42,43</sup> For case II sorption the proportionality constant holds information about the polymer relaxation and the equilibrium water concentration, and it is inversely proportional to the thickness. Since we do not have knowledge about the equilibrium water concentration, meaningful information cannot be extracted from the proportionality constant. However, one can still compare the constants for each thickness of the CHEC containing composites to evaluate their consistency. This is readily done by multiplying the proportionality constants with their respective thicknesses:  $k \cdot l_0 (565 \ \mu \text{m}) = 4.7 \times 10^{-5} \ \text{m s}^{-1}$ and  $k \cdot \hat{l_0}(1049 \ \mu \text{m}) = 4.3 \times 10^{-5} \text{ m s}^{-1}$ . The two proportionality constants for the CHEC containing composites are in good agreement, which demonstrates that the impedance measurements in combination with the developed model is a consistent tool for probing water diffusion in the polymer composites.

#### 4. CONCLUSION

Impedance spectroscopy was used to evaluate water diffusion in PAA and CHEC containing polymer composites. To aid data interpretation, the diffusion process was imaged for selected PAA containing composites. This was done by monitoring the structural changes of the material during water absorption using CARS imaging. The CARS images showed that the water concentration in the composite was a gradient with the two extremes being dry polymer and highly water saturated polymer containing 60-90% water. An effective water penetration front was subsequently defined as the relative change in the temporal capacitance. Diffusion kinetics were successfully extracted from the effective water penetration front by fitting a semiempirical power law to the results. The diffusion was in all cases limited by polymer relaxation processes. However, the PAA containing composites showed anomalous diffusion, while the CHEC containing composites exhibited case II sorption. This means that the relaxation processes were faster for the PAA containing composites compared to the CHEC containing composites. Characteristic penetration and saturation times were determined and revealed that the concentration profile of the flow front broadens over time. Finally, aqueous solution was found to penetrate and saturate the PAA containing composites approximately an order of magnitude faster compared to the CHEC containing composites. This implies that PAA has higher water affinity than CHEC, as expected from water uptake data for the pure components. Apart from these simple model composites, the developed method can readily be used for examining more complex material formulations such as layered materials or composites containing multiple different filler types and plasticizers.

#### ASSOCIATED CONTENT

#### **Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsapm.9b01107.

Impedance spectroscopy data for the CHEC containing composites (PDF)

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#### Notes

The authors declare no competing financial interest.

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# Supporting Information: Water diffusion in polymer composites probed by impedance spectroscopy and time-resolved chemical imaging

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Particle size distributions of the PAA and CHEC particles were obtained using a Malvern Mastersizer 2000 with a dry dispersion unit (Scirocco 2000). Particles were dispersed at a pressure of 2.0 bar. The obtained particle size distributions are shown in Fig. S1. The volume-weighted average diameter for each particle type were determined as  $d_{PAA} = 68.4$ µm and  $d_{CHEC} = 93.1$  µm.



Figure S1: Particle size distribution of the PAA and CHEC particle obtained through laser diffraction measurements.

Impedance spectroscopy, following the protocol described in Section 2.2, was done on CHEC containing composites with thicknesses of 565 µm and 1049 µm. The results are displayed in Fig. S2 as Bode and impedance-time plots.



Figure S2: Bode (a), (b) and impedance-time (c), (d) plots of 565 µm and 1049 µm CHEC containing composites, respectively. The bode plots show selected frequency sweeps representing the entire duration of the experiments, while the continuous impedance-time plots show the impedance and phase angle as a function time at fixed frequency, f = 100 kHz.

Appendix B

# Paper II

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### Performance of Polymeric Skin Adhesives during Perspiration

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Abstract: Skin adhesives are polymer materials used for attaching medical devices to the skin. Probing the performance of such adhesives is of great interest for rational material formulation. Here, we present a perspiration simulator, which includes a skin mimicking gelatin substrate with controlled roughness and the ability to perspire with a tunable sweat rate. The setup was used for probing peel adhesion of adhesives under realistic wear conditions. Adhesives with indistinguishable rheological properties but different ability to absorb artificial sweat were evaluated. The rheological properties were fixed to decouple the bulk mechanical properties



from events occurring at the substrate-adhesive interface. The effects of application pressure, dwell time, and perspiration were quantified for each adhesive formulation. Here, we found that sweat introduced at the substrate-adhesive interface restricts further bonding of the adhesives by limiting viscous flow. Water-absorbing skin adhesives were found to have significantly higher peel forces compared to nonabsorbing adhesives under sweating conditions where the adhesive could absorb the introduced sweat.

KEYWORDS: skin adhesives, perspiration simulator, peel adhesion, adhesive bonding, artificial skin

#### 1. INTRODUCTION

Skin adhesives represent a class of polymer composites used for attaching medical devices, such as transdermal drugdelivery patches, ostomy bags, wound dressings, and wearable biosensors to the skin.<sup>1-7</sup> Such adhesives must provide sufficient adhesion to ensure optimal functionality of the attached device, while being easy to remove without leaving residues or damaging the skin.  $^{\rm 8}$  These adhesives must also adhere to the skin during perspiration where sweat is released at the skin-adhesive interface. The presence of sweat can compromise adhesion by perturbing the nonspecific interactions between the adhesive and skin.9 Furthermore, prolonged exposure to sweat accumulated between the skin and adhesive causes skin maceration.<sup>10,11</sup> To address this issue, modern formulations include hydrophilic fillers, known as hydrocolloids, in the sticky hydrophobic polymer matrix to remove bodily fluids from the skin-adhesive interface.<sup>12</sup> However, rational formulation of skin adhesives still presents a challenge due to difficulties with probing adhesive performance during wear and balancing the antagonist requirements for adhesion.

Some clinical investigations, where adhesive performance during wear is evaluated, are available in the literature. Here, the adhesive performance is typically quantified through peel tests or by recording the wear time until the adhesive detaches from the skin of resting subjects.<sup>13,14</sup> However, clinical studies are costly and require a large number of subjects to yield results of statistical significance due to large intra- and intersubject variations.<sup>15</sup> Consequently, there is a growing

demand to develop skin models for in vitro adhesive testing, which mimic relevant skin parameters, such as surface roughness, mechanical properties, hydration, and surface energy.<sup>16–19</sup> A limited effort has been put into clinical investigation of the performance of skin adhesives specifically during perspiration. Difficulties associated with controlling, reproducing, and measuring human perspiration introduce sources of variations, which make the results obtained from in vivo sweat studies even more convoluted.<sup>20,21</sup> This further emphasizes the need for a perspiration simulator for systematic adhesive testing.

The requirements for a perspiration simulator depend on the device functionality and materials tested. For biosensors the sweat composition and rate are of high importance, while the friction during perspiration is of interest for textiles.<sup>22–25</sup> For adhesive testing the model needs to exert a pressure from the artificial sweat glands, possess a water contact angle similar to skin, and be tough enough to allow peeling adhesives from the skin.<sup>26–28</sup> Eiler et al. recently adapted a perspiration simulator, developed by Hou et al.,<sup>29</sup> to test the performance of skin adhesives under well-controlled perspiration conditions on a

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polymer substrate mimicking the surface topography and water contact angle of skin.<sup>30</sup> Rigid adhesives were chosen to specifically probe spreading of artificial sweat at the substrate– adhesive interface without the influence of viscous flow of the adhesive. Adhesives with different abilities to absorb artificial sweat were evaluated by peel tests. Here, a delay in adhesive failure was observed for the adhesive absorbing the most artificial sweat. However, it is still unknown how perspiration influences the viscous flow of these adhesives and how the initial adhesive bonding affects the adhesive performance during perspiration for adhesives with different abilities to absorb sweat.

In this work, we present a new perspiration simulator having dimensions appropriate for conventional adhesive peel experiments.<sup>31</sup> The setup provides the ability to control the artificial sweat rate, the hydrostatic pressure upon artificial sweat pore occlusion, sweat composition, and sweat pore density. The outermost layer of the substrate consists of a cross-linked gelatin film, which hydrates during water exposure mimicking human stratum corneum.<sup>32,33</sup> The skin-like gelatin layer is coated on a rigid polyimide support with controlled roughness, hole size, and hole density. The coating process and crosslinking density of the gelatin were optimized to avoid blocking of the artificial sweat pores and cohesive fracturing of the gelatin during peel experiments. The model is used for systematic investigations of the peel adhesion of three different adhesive formulations under realistic perspiration conditions. The adhesive formulations are designed to have indistinguishable rheological properties yet significantly different abilities to absorb sweat. This enables us to decouple the bulk properties from the events occurring at the artificial skin-adhesive interface and separate the effects of water transport from the mechanical contributions to the peel adhesion. Each adhesive formulation is evaluated as a function of application pressure prior to artificial perspiration and different perspiration times to systematically investigate the link between adhesive bonding, amount of artificial sweat, water transport, and peel adhesion.

## 2. MATERIALS AND METHODS

2.1. Materials. Polyisobutylene was obtained from BASF (Germany), styrene-isoprene-styrene was obtained from Kraton (USA), sodium carboxymethyl cellulose (CMC) particles were obtained from Akzo Nobel (Netherlands), and potato starch was obtained from KMC (Denmark). A premix of styrene-isoprenestyrene and polyisobutylene (the adhesive matrix) was mixed for 45 min at 30 rpm and 90 °C under vacuum in a Brabender mixer (Brabender GmbH & Co. KG, Germany). The ratio between polyisobutylene and styrene-isoprene-styrene was kept at 4:1 by weight, and the total mass of each mix was 60 g. The polyisobutylene provides the stickiness of the adhesives, while the styrene-isoprenestyrene is added for increasing the cohesive strength of the adhesives. Next, particles were mixed with the matrix to yield adhesives with a total particle volume fraction,  $\phi_{\rm p}$  = 0.277. Three different adhesives were mixed: one containing only CMC fillers (hereafter CMC adhesive), one having half of the particle volume fraction CMC fillers and the other half starch fillers (hereafter CMC-Starch adhesive), and one only containing starch fillers (hereafter Starch adhesive). Particle densities were measured with an AccuPyc 1330 He pycnometer from Micrometrics (USA). The densities of CMC and Starch were found to be  $\rho_{\rm CMC} = 1.5809 \pm 0.0004 \text{ g cm}^{-3}$  and  $\rho_{\rm Starch} = 1.5203 \pm 0.0009 \text{ g cm}^{-3}$ , respectively. Vacuum was applied after the particles were added to the matrix to minimize air entrapment, and the mix was processed for 45 min at 30 rpm and 90 °C. After mixing, 20 g of material was pressed between two horizontal steel plates for 30

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s under a load of 10 tons at 90 °C. The sample mixtures were pressed to a thickness of 950  $\pm$  25  $\mu m$ . The thickness was subsequently measured by using a thickness gauge (Mitutoyo Europe GmbH, Germany). After pressing, the desired sample geometry was obtained by punching. The artificial sweat solution for the impedance measurements, gravimetric analysis, and artificial perspiration experiments was prepared from ultrapure water (arium pro, Satorius, Germany) and sodium chloride (Sigma-Aldrich, Denmark) at a concentration of 154 mM, which is within the range of the sodium chloride concentration of human sweat.<sup>34</sup>

**2.2. Material Characterization.** *2.2.1. Rheology.* The rheological properties of each formulation were evaluated by shear rheology using a Discovery hybrid rheometer from TA Instruments (Denmark) with parallel plate geometry. Amplitude sweeps at 1 Hz were done for each formulation to identify the linear viscoelastic region. The amplitude sweeps are provided as Supporting Information (Figure S1). Frequency sweeps were subsequently performed on a new sample at fixed shear strain,  $\hat{\gamma} = 0.3\%$ . The frequency sweeps were done with frequencies ranging from  $10^2$  to  $10^{-3}$  Hz with five frequencies per decade. All measurements were performed in triplicates at 32 °C, provided as Supporting Information (Figure S2).

2.2.2. Impedance Measurements. Impedance measurements were performed according to a method that we previously developed for probing water diffusion in polymer materials.<sup>35</sup> The method utilizes a two-electrode system connected to an Autolab potentiostat (PGSTAT128N) with a frequency response analyzer module (FRA32M) and a multiplexer module (MUX.SCNR8) all obtained from Metrohm Nordic (Denmark). The adhesive was adhered to a stainless-steel plate (working electrode) and subsequently clamped to a glass cell. A graphite rod was used as both the counter and reference electrode. The adhesive was exposed to 154 mM NaCl solution. The adhesive area was chosen to be 9.6 cm<sup>2</sup>, which is much larger than the filler sizes, to average out sample inhomogeneities. An oscillating potential with an amplitude of 10 mV was applied between the electrodes, and time scans were performed at 100 kHz. The temperature during the impedance measurements was adjusted to  $32 \pm 1$  °C with an incubator (KS 4000i control, IKA, Germany). The experiments were done in triplicates. The capacitance was obtained from the impedance by using an equivalent circuit model. Here, we model the adhesive as a (RC) circuit, i.e., a resistor and a capacitor in parallel. The resistor and capacitor represent bulk conductivity and the dielectric properties of the sample, respectively. The resistance of the hardware and electrolyte solution was neglected. The capacitance, C, of a (RC) circuit is readily obtained as

$$C = -\frac{Z''}{\omega(Z'^2 + Z''^2)}$$
(1)

where  $\omega$  is the angular frequency of the potential, Z' is the real part of the impedance, and Z'' is the imaginary part of the impedance. The presented equivalent circuit model is valid until saline solution reaches the working electrode; thereafter, the electrical behavior of the working electrode may have a significant contribution.<sup>35</sup>

2.2.3. Gravimetric Analysis. Gravimetric analysis was performed on adhesive samples immersed in 154 mM NaCl solution using an analytical balance (XS105, Mettler Toledo, Denmark). The adhesives were  $25 \times 25 \times 1$  mm<sup>3</sup> and adhered to a polystyrene plate during the experiment. The temperature of the solution was kept at 32 °C. The mass of the adhesives was measured prior to immersion and after 10, 30, 45, 60, and 120 min of immersion. Each measurement was done five times.

**2.3. Perspiration Simulator.** The artificial skin is a multilayer substrate, where each layer holds a functionality. The skin includes a track-etched membrane (obtained from Sterlitech Cooperation, USA) of polycarbonate having a thickness  $l_{\rm m} = 12 \ \mu m$ , pore diameter  $d_{\rm m} = 0.1 \ \mu m$ , and pore density  $\alpha_{\rm m} = 4 \ \mu m^{-2}$ . The track-etched membrane was laminated to the polyimide support by using a double-sided acrylic adhesive. The acrylic adhesive was applied to the polyimide support prior to drilling the artificial sweat pores to ensure the adhesive did not block the pores. The track-etched membrane was

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**Figure 1.** Schematic illustration of the artificial skin, which consists of a track-etched membrane and a polyimide substrate with micrometer-scale roughness coated with cross-linked gelatin. The artificial skin was clamped to a reservoir connected to a flow meter and a tank for artificial sweat with height, h, above the skin surface (a). A roughness line scan of the artificial skin obtained with a profilometer is shown in (b). The artificial perspiration rate is plotted as a function of pressure with a linear model fitted to the experimental data (c). The perspiration data represent averages and standard deviations of three different artificial skins.

carefully laminated to the polyimide substrate, and the skin was left for 24 h with a pressure of 250 Pa to allow the adhesive to bond with the track-etched membrane. The polyimide support has a well-defined micrometer-scale roughness and holes having a diameter  $d_s = 250 \ \mu m$ and hole density  $\alpha_s = 100 \text{ cm}^{-2}$ . The holes in the polyimide support are supposed to mimic the sweat pores. The track-etched membrane provides high flow resistance, which yields a pressure drop much larger than the differences in Laplace pressure of the holes in the polyimide support, which ensures homogeneous sweating throughout the substrate.<sup>2</sup> The polyimide support gives mechanical stability and large scale roughness. The polyimide support was coated with gelatin (Figure 1a) through a dip-coating procedure (details are provided in the Supporting Information, section S2). For less complex adhesion results, the gelatin was highly cross-linked to avoid cohesive failure and elastic deformation of the artificial skin. This is different from human skin, which is elastic and typically allows for removal of superficial skin cells. Gelatin is derived from collagen, which is a natural component of human skin.<sup>36</sup> In the Supporting Information, we furthermore provide quartz crystal microbalance with dissipation measurements to confirm that the gelatin film is hydrated through water exposure (Figure S3) and atomic force microscopy images to illustrate the nanoscale roughness of the gelatin (Figure S4). The thickness of the gelatin layer was estimated to be a few micrometers through atomic force microscopy and gravimetric measurements (Figure S5). The water contact angle was measured to  $77.5 \pm 0.8^\circ$ , which is similar to reported values measured on human skin.<sup>37,38</sup> The experimental details and the data of the water contact angle are provided in the Supporting Information (Figure S6). The mean surface roughness of the artificial skin was measured by using a profilometer (SJ-410 surface roughness tester, Mitutoyo, Germany). A line scan is shown in Figure 1b where the surface height,  $z_i$  is plotted as a function of distance, x. The average roughness parameter was  $R_a$ = 8.4  $\pm$  4.5  $\mu$ m, which is on the same order of magnitude as reported literature values for human skin.<sup>39,40</sup>

The artificial skin was clamped to a reservoir, which was connected a microfluidic flow sensor and a tank supplying the artificial sweat solution (Figure 1a). The flow sensor was connected to a microfluidic flow reader both obtained from Elveflow (France). The flow sensor allowed to measure the artificial sweating rate, which is a function of the tank height, *h*. Flow rates were measured as a function of pressure. The data are presented in Figure 1c. Here, a linear flow rate–pressure relation was found, which was expected from Poiseuille's law:

$$Q_{\rm n} = \frac{\pi^2 d_{\rm m}^4 d_s \alpha_m}{512 \eta l_{\rm m}} (\rho g h d_s - 4\gamma \cos(\theta))$$
<sup>(2)</sup>

where  $Q_n$  is the flow in a single artificial sweat pore,  $\theta$  is the contact angle of the substrate with the artificial sweat, *g* is the gravitational constant, and  $\eta$ ,  $\gamma$ , and  $\rho$  are the viscosity, surface tension, and density of the artificial sweat. The remaining parameters are described above. Equation 2 was derived under the assumption that the resistance in the polyimide support is negligible compared to the resistance of the track-etched membrane. The final expression is a linear relationship between the flow rate in an artificial sweat pore and the pressure, where the proportionality constant is the inverse resistance of the sweat pore and the intercept with the *x*-axis is the Laplace pressure in a pore,  $\Delta p_L = \frac{4\gamma \cos \theta}{d_s}$ .<sup>29</sup>

2.3.1. Peel Test. The adhesive properties were evaluated by using an Instron 5943 Universal testing system with a 50 N load cell (Instron, Sweden). The dimensions of the adhesives were  $100 \times 25 \times$ 1 mm<sup>3</sup>. The adhesives were applied to the artificial skin with either a pressure of 1680 or 4320 Pa for 60 s and were subsequently exposed to artificial perspiration or left to dwell at dry conditions. The adhesives were peeled with constant displacement, 304 mm/min, at an angle of 90° by using a backing tape (4124, Tesa, Denmark). The force required to peel the adhesive from the substrate was recorded as a function of displacement. Recorded forces were averaged over displacements from 20 to 80 mm for each measurement, which was done in triplicates. We note that the artificial skins were not reused for multiple peel experiments and the skins were used within 2 weeks after preparation.

## 3. RESULTS AND DISCUSSION

**3.1. Characterization of Adhesive Formulations.** The rheological properties of the adhesive formulations were characterized by shear rheology in the linear viscoelastic region, which was determined through amplitude sweeps (see Supporting Information, Figure S1). Frequency sweeps were performed at frequencies ranging from  $10^2$  to  $10^{-3}$  Hz with five frequencies per decade at a fixed shear strain,  $\hat{\gamma} = 0.3\%$ . The storage modulus, G', the loss modulus, G'', and the ratio between the loss and storage modulus,  $\tan(\delta) = \frac{G'}{G'}$ , are displayed in Figure 2 as a function of the frequency.



**Figure 2.** Storage modulus, G', loss modulus, G'', and  $tan(\delta)$  plotted as a function of deformation frequency, f, for the CMC ( $\triangle$ ), CMC–Starch ( $\Box$ ), and Starch ( $\bigcirc$ ) adhesives.

The rheological measurements were done in triplicates (see Figure S2) to ensure that the data in Figure 2 represent the general rheological properties. Variations within each adhesive formulation were similar to variations between formulations implying the three adhesive formulations have indistinguishable rheological properties in the measured frequency range. The different adhesives are thus expected to flow similarly when applied to the substrate.

Next, the water transport in the adhesives was investigated by using impedance measurements. The measurements were done with an alternating potential, with an amplitude of 10 mV, oscillating at fixed frequency, f = 100 kHz, to increase the sensitivity to dielectric changes. The results are displayed in Figure 3.

The impedance and phase angle are plotted as a function of time for the Starch adhesives in Figure 3a. Here, the phase angle is constant at  $\phi = -90^\circ$ , indicating pure capacitive behavior. The impedance is constant for at least 1400 min  $(\sim 23 \text{ h})$ , which means no water transport occurs in the Starch adhesive within this time. The CMC-Starch adhesives (Figure 3b) initially exhibit pure capacitive properties,  $-\phi = 90^{\circ}$ , followed by the occurrence of bulk conductivity, indicated by a rapid drop in the phase angle. The conductivity occurs when the NaCl solution has penetrated through the adhesive and reached the working electrode. The rapid drop in phase angle is detected after  $141 \pm 46$  min where the large standard deviation, i.e., large intersample variation, implies poor connectivity of the water transporting CMC particles, which makes the water transport results sensitive to small variations in the particle dispersion between adhesive samples. Finally, the CMC adhesive (Figure 3c) shows the occurrence of full penetration after  $107 \pm 3$  min of immersion, where the small standard deviation indicates continuous transport and good CMC-particle connectivity, which is in agreement with the higher CMC-particle content.

The sweat uptake is further evaluated through the change in temporal capacitance relative to the dry capacitance,  $\frac{C_t - C_0}{C_t}$ , where  $C_t$  and  $C_0$  are the capacitance at a given time, t, and the dry capacitance, respectively. The capacitance is calculated by using eq 1 and the results for the CMC and CMC–Starch adhesives are shown in Figure 4. Here, the increase in the capacitance for the CMC adhesive is larger compared to the CMC–Starch adhesive, which implies that the water uptake in the CMC adhesives are higher than the CMC–Starch adhesives. Such behavior is expected from the respective chemistries of CMC and starch.

The sweat-absorbing properties of each adhesive formulation were also evaluated through gravimetric analysis of the composites immersed in artificial sweat (154 mM NaCl) solution. The absorbing properties were examined for up to 120 min, which is longer than the longest time in the in vitro perspiration experiments. The results are presented in Figure 5, where the mass difference per adhesive area is plotted as a function of time. Each data point in Figure 5 represents an average of five measurements with error bars representing their respective standard deviations.

The CMC adhesives demonstrate a continuous uptake over the entire measured time range, while the CMC–Starch adhesives show an initial uptake within 10 min followed by a plateau indicating poor CMC particle connectivity. Lastly, the Starch adhesives show no water absorption, which again



Figure 3. Impedance as a function of immersion time of Starch (a), CMC–Starch (b), and CMC (c) adhesives. The measurements were done using 154 mM NaCl solution at fixed frequency, f = 100 kHz.



**Figure 4.** Difference in capacitance relative to the dry capacitance as a function of immersion time for the CMC (•) and CMC–Starch ( $\triangle$ ) adhesives. The asterisks (\*) represent the characteristic penetration times,  $t_{\rm p}$ .



Figure 5. Mass uptake as a function of time for the CMC  $(\triangle)$ , CMC–Starch  $(\Box)$ , and Starch  $(\bigcirc)$  adhesives immersed in 154 mM NaCl solution.

confirms that starch does not absorb sweat under these conditions. These results are in agreement with the impedance measurements. The results in Figure 5 represent the absolute uptake per area when the entire adhesive surface area is exposed to artificial sweat. However, in the situation where the adhesive is attached to the perspiration simulator, the adhesive is expected to absorb locally around the artificial sweat pores. The actual uptake in a perspiration situation is therefore expected to be lower compared to the immersion tests.

**3.2.** Adhesive Performance during Artificial Perspiration. The aim of the work presented here is to demonstrate the potential of the perspiration simulator and obtain general knowledge of adhesive performance under realistic perspiration conditions. The adhesive performance was evaluated by peeling the adhesives, with an angle of 90°, directly from the perspiration simulator. The peel results are shown in Figures 6a and 6b where the horizontal bars represent groups with equal means according to a two sample *t* test with 95%

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confidence level. We divide the discussion of the peel results in two parts: adhesion under dry conditions and adhesion after artificial perspiration.

3.2.1. Adhesion under Dry Conditions. First, the adhesives were peeled from the artificial skin without introducing artificial sweat. This was done to study the effect of the application pressure and dwell time. Both dwell time and application pressure will have an effect on the substrateadhesive contact area due to the viscoelastic behavior of the adhesives. To obtain two different initial substrate-adhesive contact areas, we vary the application pressure. Here, each adhesive formulation was applied with respective pressures of 4320 Pa (Figure 6a) and 1680 Pa (Figure 6b) for 60 s. Adhesives peeled immediately after application (0 min after application) showed no significant differences between formulations as expected from their rheological properties and similar chemistries. However, there is a clear effect of the application pressure since the average peel forces were approximately 3 and 20 N for the adhesives applied with 1680 and 4320 Pa, respectively. The increase in peel forces for increasing application pressure is a consequence of increasing viscous flow of the adhesive, which results in a larger initial substrate-adhesive contact area.

Adhesives were also peeled 20 min after application to investigate the effect of dwell time on peel adhesion. Here, the adhesives generally show increments in peel forces indicating the evolution of the substrate-adhesive contact area over time through viscous flow as illustrated in Figure 6c. After 20 min dwell time, differences were found between the CMC adhesive and the two other adhesives. Mixed failure modes were generally observed for peel forces larger than 15 N. During mixed failure, both adhesive and cohesive failure occur, which suggests that the adhesion to the substrate was stronger locally than the cohesion of the adhesives. It also demonstrates that the skin-mimicking gelatin does not delaminate or fracture during peel. The structural integrity of the gelatin makes the peel results less convoluted compared to real human skin where adhesives peeled from the skin typically remove a superficial layer of stratum corneum.<sup>41</sup> We speculate that the differences after 20 min are attributed to differences in nonlinear rheological properties between the CMC adhesive and the other two adhesive formulations.

3.2.2. Adhesion after Artificial Perspiration. Next, the peel adhesion of the adhesives, applied under the same conditions as above (4320 or 1680 Pa for 60 s), was evaluated after 20 min of artificial perspiration with an artificial sweat rate corresponding to  $1.6 \pm 0.2 \ \mu L \ min^{-1} \ cm^{-2}$  for uncovered skin. Because of partial occlusion of the artificial skin, the perspiration rates reduced to approximately  $1.0 \pm 0.1 \ \mu L/(min \ cm^2)$  in all cases (see Figure S7). We note that even though water is an effective plasticizer, <sup>42–44</sup> the changes in peel forces during perspiration are mainly expected to be a result of events occurring at the substrate—adhesive interface. This assumption is based on a conservative estimate of the changes in the bulk mechanical properties of the adhesives during perspiration, which is provided in the Supporting Information (section S4).

Peel forces measured after 20 min of artificial perspiration were lower compared to 20 min of dry dwell after application for all adhesive formulations and both application pressures. This revealed that the viscous flow of the adhesives is restricted due to the artificial sweat introduced at the substrate—adhesive interface as illustrated in Figure 6d. The Starch adhesive shows

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**Figure 6.** Average peel forces recorded of the CMC, CMC–Starch, and Starch adhesives peeled from the perspiration simulator. The adhesives were applied with application pressures of 4320 Pa (a) and 1680 Pa (b) and peeled immediately after application and after 20 min without and with exposure to perspiration. The horizontal bars indicate groups with equal means (two sample *t* test, 95% confidence level). Schematic illustrations of the substrate–adhesive interface region, which are based on the peel results, depicting dry dwell (c), perspiration with a Starch adhesive (d), and CMC adhesive (e).

significantly lower peel force compared to the initial value (0 min) at high application pressure (Figure 6a). This suggests that some of the initial substrate-adhesive contact area is compromised due to the pressure exerted from the artificial sweat glands ( $\sim$ 4.5 kPa), which we speculate is a consequence of the Starch adhesive's occlusive nature. The CMC and CMC-Starch adhesives are less occlusive through their water absorption and consequently do not show this significant drop in peel force. For the low application pressure (Figure 6b), the peel forces after 20 min do not decrease below the initial (0 min) peel forces, which indicates that the initial substrateadhesive contact area remains throughout the perspiration process. Here, the adhesives are less occlusive due to a smaller substrate-adhesive contact area, which will result in a lower overall pressure build up at the interface. However, artificial sweat spreading at the substrate surface restricts further adhesive bonding with the substrate. After 20 min of perspiration, no significant differences are detected between formulations.

Next, the perspiration time was decreased to 10 min to introduce an overall lower volume of artificial sweat at the interface. After 10 min of perspiration, the adhesives were left on the artificial skin for an additional 10 min without perspiration and was subsequently peeled off the artificial skin (Figure 6b). The Starch adhesive shows no change in peel force compared to 20 min of artificial perspiration. This suggests that sufficient artificial sweat accumulates at the interface during 10 min to prohibit further adhesive bonding due to lack of sweat absorption. However, the CMC adhesive shows an increase in peel force and now performs significantly better compared to the Starch adhesive. This indicates that having hydrophilic fillers near the skin–adhesive interface to absorb sweat maintains the adhesive properties during perspiration. The hydrophilic CMC fillers absorb sweat at the substrate–adhesive interface, which allows the adhesive to flow and bond to the substrate and consequently increase the substrate–adhesive contact area over time (Figure 6e). The CMC–Starch adhesive seem to exhibit peel forces in between the CMC and Starch adhesive as expected from its water absorption capacity, which also is in between the two other adhesives.

## 4. CONCLUSION

A new perspiration simulator for evaluating the performance of skin adhesives during realistic wear conditions was successfully developed. The perspiration simulator has a gelatin skin mimicking substrate and the ability to sweat with a controlled sweat rate. Three skin adhesive formulations having indistinguishable rheological properties, but different abilities to absorb the artificial sweat were evaluated by measuring the peel adhesion directly from the perspiration simulator. Artificial sweat introduced at the artificial skin–adhesive interface proved to restrict viscous flow of the adhesives and consequently reduced the adhesive's ability to bond to the substrate. However, highly water-absorbing adhesives were found to bond under perspiration conditions depending on the total amount of artificial sweat introduced. Here, the absorbing

adhesive showed a significant increase in peel adhesion compared to non-sweat-absorbing adhesives.

### ASSOCIATED CONTENT

#### **Supporting Information**

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsapm.9b01214.

Additional rheological measurements, description of the gelatin coating process, characterization of the gelatin, and artificial perspiration rates (PDF)

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#### Notes

The authors declare no competing financial interest.

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# Supporting Information: Performance of Polymeric Skin Adhesives during Perspiration

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# 1 Rheology

The linear viscoelastic region for the adhesives was determined through amplitude sweeps (Fig. S1). The linear regime is indicated by a plateau region in the complex modulus,  $G^*$ , as a function of oscillation strain,  $\hat{\gamma}$ . The measurements were performed at 1 Hz with an axial force of 1.00 N.



Figure S1: Complex modulus,  $G^*$ , as a function of oscillation strain,  $\hat{\gamma}$ , for the CMC ( $\triangle$ ), CMC–Starch ( $\Box$ ), and Starch ( $\bigcirc$ ) adhesives. The data was collected at frequency, f = 1 Hz.

Frequency sweeps at oscillation strain,  $\hat{\gamma} = 0.3$  %, under axial force 1.00 N, were done for each adhesive type. The measurements were done in triplicates and the results are shown in Fig. S2.



Figure S2: Storage modulus, G', loss modulus, G'', and  $\tan(\delta)$  as a function of frequency, f, for the CMC ( $\Delta$ ), CMC–Starch ( $\Box$ ), and Starch ( $\bigcirc$ ) adhesives. Each measurement was done in triplicates under an axial force of 1.00 N and oscillation strain,  $\hat{\gamma} = 0.3$  %.

# 2 Gelatin Coating

The polyimide substrate was coated with a thin layer of gelatin to mimic skin chemistry, hydration and wettability. The polyimide substrates were first rinsed with ethanol, then dried with compressed air. Next, the substrates were plasma-treated (PDC-32G plasma cleaner, Harrick Plasma) using high power under a constant air pressure of 500 mTorr for 10 min. This process was shown to enhance the adhesion between the gelatin and the polyimide substrate, which prevents delamination of the gelatin coating upon peeling. A typical dipcoating procedure was employed to coat the polyimide substrate with gelatin. Accordingly, gelatin (type A from porcine skin, gel strength ~175 g Bloom, Sigma Aldrich) was dissolved in warm ultra pure water (~ 55 °C) for 1 h to yield a 5 wt. % clear solution. Then, the plasma-treated polyimide substrates were dipped into the gelatin solution (~ 3-5 s) and then hung vertically (~ 10-15 s) to remove excess solution. Next, the polyimide substrates were instantly fixed on a vacuum chamber. This step allows for draining the excess gelatin solution so that the artificial sweat glands will remain open. After the gelatin-coated substrates were dried at room temperature, they were exposed to formaldehyde vapor for 48 h. The chemical

crosslinking with formaldehyde not only enhances the mechanical properties of the gelatin film but also decreases the solubility of gelatin in water. Afterward, the coated substrates were left in the fume hood overnight to ensure removal of excess formaldehyde.

## 2.1 Quartz Crystal Microbalance with Dissipation

Quartz crystal microbalance with dissipation monitoring (QCM-D, Q-Sense E1, Biolin Scientific, Gothenburg, Sweden) was utilized to investigate the vapor uptake of the gelatinous film. QSense<sup>®</sup> Humidity module allows adjusting the relative humidity over the sensor by using saturated salt solutions. A gold-coated sensor (Biolin Scientific, Gothenburg, Sweden) was rinsed with ethanol then plasma-cleaned (PDC-32G plasma cleaner, Harrick Plasma) for 1 min using high power under a constant water pressure of 500 mTorr. 5 wt. % gelatin solution was then spin coated on the sensor using 2500 rpm speed, followed by crosslinking with formaldehyde vapor for 48 h. The sensor was then placed in the humidity module, then saturated solution of LiBr was loaded into the cell with a flow rate of 50  $\mu$ l min<sup>-1</sup> to adjust the humidity to  $\sim 6.3$  %. After obtaining a stable baseline in all overtones (3<sup>rd</sup>-11<sup>th</sup>), the following saturated salt solutions were sequentially loaded in the flow cell for 15 min: LiCl (11.3 % RH), MgCl<sub>2</sub> (32.8 % RH), Mg(NO<sub>3</sub>)<sub>2</sub> (52.9 % RH), NaCl (75.3 % RH), KCl (84.3 % RH), and  $\rm K_2SO_4$  (97.3 % RH). The shift in the oscillation frequency of the sensor (for the third overtone) is plotted in Fig. S3. The change in the frequency is interpreted as the change in the sensed mass attached to the sensor, which could be assigned to the vapor uptake by the gelatinous film.



Figure S3: Vapor uptake by the gelatin film studied by quartz crystal microbalance with dissipation monitoring (QCM-D); (top) the frequency shift ( $\Delta F$ ) vs. time, (bottom) the frequency shift ( $\Delta F$ ) vs. relative humidity (adsorption isotherm).

## 2.2 Atomic Force Microscopy

The topographical images of the gelatin coated on the polyimide support were obtained by AFM tapping mode imaging (NanoWizard 4a NanoScience, JPK Instruments AG, Berlin, Germany) using a rectangular cantilever (HQ:NSC18/Al BS, MikroMasch, Bulgaria) with an approximate spring constant of 2.8 N m<sup>-1</sup> and a conic tip of 8 nm radius was used. Surface areas of 100 µm × 100 µm and 20 µm × 20 µm were examined using a scanning rate of 0.2 Hz. The standard software of the instrument (JPKSPM Data Processing) was employed to analyze the images and calculate the root mean square roughness (Rq). The estimated Rq was found to be around 90 ± 5 nm (obtained from 3 images with 100 µm × 100 µm dimension).



Figure S4: Atomic force microscope (AFM) topographical images of the gelatinous film on the polyimide support. (top) 100  $\mu$ m × 100  $\mu$ m (bottom) 20  $\mu$ m × 20  $\mu$ m.

The thickness of the coated gelatin layer was estimated by carefully scratching away gelatin locally and imaging the scratched area using AFM in contact mode. The height profile of the scratched area indicates that the gelatin thickness is approximately 1.5 µm (Fig. S5). The gelatin thickness was also estimated by measuring the weight of the polyimide substrate before and after gelatin coating. Here, the average weight increase and standard deviation of five artificial skins was  $72 \pm 15$  mg after coating the polyimide support with gelatin. Knowing the polyimide support area,  $12 \times 3.5$  cm<sup>3</sup> and assuming the gelatin was evenly coated on both sides of the polyimide support and has a density of 1.4 g/cm<sup>3</sup>, the gelatin thickness was estimated to  $6 \pm 1$  µm.



Figure S5: AFM height image (contact mode) together with cross-section height profile from the scratched area of the gelatin coating (estimated thickness  $\sim 1.5 \ \mu m$ ).

## 2.3 Water Contact Angle

To prepare the samples for contact angle measurements, 5 wt. % gelatin solution was spin coated on a silicon wafer using 500 rpm speed, followed by crosslinking with formaldehyde vapor for 48 h. The thickness was estimated to be around 2 µm using spectroscopic ellipsometry. The static contact angle was measured using Attension Theta Lite optical tensiometer by placing a 2 µL droplet of ultra pure water on the sample surface. The apparent water contact angle value was recorded after 10 s. The average water contact angle was found to be 77.5°  $\pm$  0.8° (obtained from 3 replicas × 3 sampling areas).



Figure S6: water contact angle of gelatin (3 different images are provided, (left) without overlays (right) with overlays).

# 3 Perspiration Rate

The flux of artificial sweat through the artificial skin was measured while the adhesive was adhered to the skin using a flow sensor in connection with a microfluidic flow reader. The results are shown in Fig. S7. The results confirm that there is a significant amount of artificial sweat introduced throughout the experiments. Each value represents an average of three measurements, while the errorbars represent the respective standard deviations. The fluxes range from 0.7 to 1.0  $\mu$ L/min/cm<sup>2</sup>.



Figure S7: Average artificial perspiration flux of artificial perspiration experiments with the CMC, CMC–Starch, and Starch adhesives applied with a pressure of either 4320 Pa or 1680 Pa.

# 4 Bulk Mechanical Properties during Perspiration

During the perspiration experiments, the water absorbing adhesives take up water. Water is an effective plasticizer, which change the bulk mechanical properties of the adhesives as they take up increasing amounts of water. Changes in bulk mechanical properties will influence the measured peel forces. We therefore perform a conservative estimate of the expected changes in bulk mechanical properties of the most water absorbing adhesive (CMC adhesive). Assuming the CMC adhesive absorbs the entire amount of supplied artificial sweat (0.025 g cm<sup>-2</sup>), the total amount of supplied artificial sweat corresponds to 16 % of the uptake capacity at 20 minutes (Fig. 5, in the main article). The driving force for the water penetration process is thus expected to be much smaller for the artificial perspiration compared to the immersion test. In the immersion tests the penetration can be estimated to ~ 20% of the full thickness (Fig. 4, in the main article) and is expected to be much lower under perspiration conditions. The changes in peel force during the perspiration experiments are therefore mainly expected to be a result of events occurring at substrate– adhesive interface with only minor effects of changes in the bulk mechanical properties. Appendix C

# Paper III

# Water Penetration and Absorption in Skin Adhesives: The Influence of Hydrophilic Particles and Mechanical Properties

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## Abstract

Skin adhesives, used for attaching medical devices to the body, are required to adhere to the skin while being exposed to bodily fluids such as sweat. Here, a solution is to have the adhesive absorb the fluids to maintain good skin–adhesive contact. The water absorption and distribution of water in the adhesives influence the overall adhesive properties. Understanding how the material composition impacts the absorption and distribution of water in these adhesives is required for biomedical engineering of new skin adhesives. Here, we probe the water penetration and absorption in different skin adhesives using time-resolved impedance measurements and gravimetric analysis. Skin adhesive formulations similar to typical industrial formulations consisting of hydrophilic particles dispersed in a sticky and hydrophobic polymer matrix were designed. The hydrophilic particle content and polymer matrix rigidity were varied and these adhesives were systematically investigated to link the material composition and water absorption functionality.

# Keywords

Time-resolved impedance measurements, skin adhesive, water penetration, polyacrylic acid, polymer composites

# 1 Introduction

Wearable medical devices such as drug delivery patches, wound dressings, ostomy care appliances, and sensors for patient monitoring, e.g. electrocardiography sensors, rely on skin adhesives to function.<sup>1-4</sup> As skin is a complex biological surface, which can be mechanically deformed, hold different hydration levels, and even release sweat, skin adhesives are required to maintain adhesion under varying conditions such as perspiration. Typical skin adhesives consist of a hydrophobic polymer matrix, which typically constitutes of at least one hydrophobic polymer with a glass transition temperature below room temperature to allow the adhesive to flow viscously and bond effectively to the skin.<sup>5,6</sup> However, water or sweat at the skin surface may prevent bonding of the hydrophobic adhesive matrix. Consequently, such skin adhesive formulations include hydrophilic polymer particles such as carboxymethyl cellulose or polyacrylic acid.<sup>7-9</sup> It was recently shown that these particles can absorb water at the skin–adhesive interface, which subsequently allow the adhesive matrix to bond to the skin and ensure the overall medical device functionality.<sup>10,11</sup>

The water absorption of skin adhesives depends on the content, physical and chemical properties of the hydrophilic particles and the mechanical properties of the polymer matrix.<sup>12</sup> There are thus several adjustable parameters within biomedical engineering of skin adhesives. Consequently, experimental techniques are needed for mapping the influence of the adhesive formulation on the water absorption capabilities. Here, gravimetric analysis is typically done of skin adhesive samples immersed in NaCl solution simulating sweat. The temporal water absorption is monitored through the weight increase over time.<sup>13–15</sup> Although, the total amount of water absorbed by the adhesive is important for its functionality, the spatial distribution of water in the adhesive is also expected to be of high importance. Water is an effective plasticizer and is known to alter the mechanical properties of polymers and polymer composites.<sup>16,17</sup> A high water content near the skin–adhesive interface could yield a weak boundary layer in the adhesive, which has previously been reported to compromise adhesion.<sup>18</sup>

The distribution of water has been investigated in different polymer composites using spectroscopic and imaging techniques such as FT-IR, NMR, electrochemical impedance spectroscopy, and confocal Raman imaging.<sup>19–26</sup> However, the literature on the distribution of water in skin adhesives is very scarce and it is therefore currently not known how the skin adhesive formulation influences the temporal water distribution.

Here, we investigate the distribution of water in skin adhesives with different compositions. The water front propagating in the adhesive is probed through time-resolved impedance measurements. The impedance gives a clear signal when the NaCl solution has penetrated through the adhesive and reached the working electrode.<sup>27</sup> Knowing the adhesive thickness, the position of the diffusion front is determined at the time of full penetration. By preparing adhesives with different thicknesses, the penetration time is readily probed as a function of water front position.

We use the developed impedance methodology to systematically investigate skin adhesives containing polyacrylic acid (PAA) particles dispersed in a viscoelastic and hydrophobic polymer matrix. The water penetration is measured for a wide range of different skin adhesive formulations containing different amounts of PAA dispersed in polymer matrices with different mechanical properties. By combining the water penetration measurements with conventional gravimetric water absorption measurements, we reveal how water is distributed in the adhesives depending on the polymer matrix rigidity and PAA content, which may readily aid the design of novel skin adhesives.

# 2 Materials and Methods

## 2.1 Materials

Adhesives were prepared from a premix of styrene-isoprene-styrene (SIS) (Kraton, USA) mixed with polyisobutylene (PIB) (BASF, Germany). The ratio between PIB and SIS was kept at either 4:1 or 4:2 by weight. The SIS gives the adhesive cohesive strength, while

the PIB provides adhesion. The premix was processed in a Brabender mixer (Brabender GmbH & Co. KG, Germany) for 45 min at 30 rpm and 90 °C under vacuum to minimize air entrapment. Next, poly(acrylic acid sodium salt) (PAA) particles, obtained from Stewart Superabsorbents (USA), were mixed with the premix to yield adhesives with 10, 15, 20, 30, and 40 wt.% PAA particles. The corresponding particle volume fraction was obtained through the particle density,  $\rho_{PAA} = 1.65$  g cm<sup>-3</sup>, which was obtained from an AccuPyc 1340 He pycnometer from Micrometrics (USA). The corresponding particle volume fractions in each respective adhesive was 5.8, 9.0, 12.2, 19.3, and 27.1 vol.% PAA particles. Once the particles were contained in the matrix, vacuum was applied and the mix was processed for 45 min at 30 rpm and 90 °C. The total mass of each mix was 60 g. After mixing, the samples were pressed between two horizontal steel plates for 30 s under a load of 10 tons at 90 °C using appropriate steel spacers to yield the desired thickness. The desired sample geometry was subsequently obtained by punching. Saline solution used for the impedance measurements and gravimetric analysis was prepared from ultrapure (arium pro, Satorius, Germany) and sodium chloride (Sigma-Aldrich, Denmark) at a concentration of 154 mM.

## 2.2 Impedance Measurements

Time-resolved impedance measurements were performed using a two-electrode system as illustrated in Figure 1a. The adhesive was adhered to the working electrode (stainless steel plate) and clamped to the impedance cell. The impedance cell held the NaCl solution in which the counter electrode (graphite rod) was immersed. The working and counter electrode were connected to an Autolab potentiostat (PGSTAT128N) with a frequency response analyzer module (FRA32M) and a multiplexer module (MUX.SCNR8), all obtained from Metrohm Nordic (Denmark). The multiplexer module allowed to do multiple experiments in series but reduce the time-resolution. Up to 6 channels were used for experiments with adhesives with thicknesses greater than 500 µm. For adhesives thinner than 500 µm a single channel was used to give the highest time resolution possible at 1.8 s. The impedance measurements were done with a potential oscillating with fixed frequency, f = 100 kHz. The high frequency provides higher time resolution and greater sensitivity to dielectric changes. The amplitude of the potential was kept at 10 mV. The temperature was fixed at 32 ± 1 °C, corresponding to skin surface temperature,<sup>28</sup> using an incubator (KS 4000i control, IKA, Germany). Using the described setup, the impedance of the adhesives was probed as a function of immersion time.

## 2.3 Gravimetric analysis

Gravimetric analysis was performed on adhesive samples immersed in 154 mM NaCl solution using an analytical balance (XS105, Mettler Toledo, Denmark). The adhesives were adhered to polystyrene plates using double-sided acrylic adhesive. The adhesives had dimensions of  $25 \times 25 \times 1$  mm<sup>3</sup>. The temperature of the NaCl solution was kept at 32 °C. The mass of each sample was assessed prior to immersion and after each immersion time. All measurements were done 6 times.

## 3 Results and discussion

## 3.1 Time-Resolved Impedance Measurements

Impedance measurements were done as described in in Section 2.2 and illustrated in Figure 1a where the impedance of an adhesive immersed in NaCl solution was measured as a function time. A typical impedance-time plot at fixed frequency, f = 100 kHz, is shown in Fig. 1b. Initially, at time,  $t_0$ , the impedance represents the dry adhesive (Fig. 1c) and the magnitude of the impedance holds its highest value, while the phase angle is  $\phi = -90^{\circ}$ , which indicates purely capacitive behavior, i.e. no bulk conductivity occurs through the adhesive.<sup>29</sup> Over time, water is absorbed by the adhesive (Fig. 1d) and the overall dielectric properties of the sample increase due to the large difference in dielectric properties of the polymer and water.<sup>30</sup> This results in a gradual decrease in the impedance. At some point, NaCl solution will reach



Figure 1: Schematic illustration of the impedance setup (a) where an adhesive sample is attached to a working electrode and immersed in saline solution. An oscillating potential is applied and the impedance is measured as a function of time using a potentiostat. A typical set of impedance data i presented in (b) where different times are marked (c-f). These immersion times represent different water absorption stages, which are schematically illustrated in (c-f).

the working electrode (Fig. 1e). This will result in bulk conductivity occurring through the adhesive, which can be detected in the impedance signal where both the phase angle and magnitude of the impedance drop dramatically (Fig. 1b).<sup>30–33</sup> The characteristic time at which the NaCl solution has penetrated the adhesive is denoted,  $t_p$ , and is arbitrarily but consistently defined as the time where the phase angle has changed by 5 % from its original value,  $\phi_p = 0.95\phi_0$ .<sup>27</sup> The time of penetration is indicated by the asterisk in Fig. 1b.

After,  $t_p$ , the impedance may be influenced by the electrical properties of the working electrode. Here, the oxide layer on the working electrode surface may hold a significant contribution to the signal. Additionally, corrosion processes may also perturb the signal. However, after a long time,  $t_{\infty}$ , the impedance reaches values comparable to the resistance of the NaCl solution, which suggests that the adhesive has taken up enough NaCl to have electrical properties similar to the NaCl solution (Fig. 1f).

Adhesives containing 5.8, 9.0, 12.2, 19.3, or 27.1 vol.% PAA particles dispersed in a matrix

consisting of 4 PIB: 1 SIS (wt:wt), were assessed to investigate the correlation between PAA content and penetration time. The magnitude of the impedance and phase angle, representing each composition, are plotted as a function of time in Figure 2.



Figure 2: Impedance as a function of time at 100 kHz for adhesive formulations containing (a) 5.8, (b) 9.0, (c) 12.2, (d) 19.3, and (e) 27.1 vol.% PAA particles. The asterisks indicate, a deacrease in the phase angle of 5 % from the original value.

Here, the impedance data follow the trends as explained in Figure 1. The initial (t = 0 min) magnitude of the impedance is similar for all samples at,  $|Z| \sim 4 \cdot 10^4 \Omega$ , which is in good agreement with all adhesives having the same thickness of 1000 µm. The penetration time for the 5.8 vol.% PAA adhesives is 614 ± 101 min and decrease for increasing PAA content. Adhesives with 27.1 vol.% PAA proved to have a penetration time of 114 ± 12 min. This indicates improved PAA particle connectivity in the adhesive for higher PAA content, which yield more effective water penetration. Since the PAA particles are responsible for the water transport, their ability to swell is also expected to influence the water penetration. The PAA particles' ability to swell may be tuned through the mechanical properties of the polymer matrix.

## 3.2 Polymer matrix rigidity and PAA content

The penetration time through the polymer adhesive with different PAA content and polymer matrix rigidity was investigated. The matrix rigidity was adjusted by adding SIS, which gives increased mechanical strength. The rheological properties of matrices containing 20 and 40 wt.% SIS matrices are provided as Supporting Information (Figure S1). Here, the  $G^*$  is significantly higher and tan  $\delta$  is lower for the 40 wt.% SIS matrix compared to the 20 wt.% SIS matrix, which indicates that the high content SIS matrix indeed makes the adhesive stiffer.

The penetration times for adhesives containing 5.8, 9.0, 19.3, and 27.1 vol.% PAA particles dispersed in either 20 or 40 wt.% SIS matrices are plotted in Figure 3.



Figure 3: The penetration time for different PAA particle volume fractions and 40 wt.% and 20 wt.% SIS containing polymer matrices. Each data point represents an average of three measurements with the error representing the standard deviation.

Each penetration time in Figure 3 represents an average of three measurements where the errorbars are the respective standard deviations. All adhesive thicknesses were kept at 1000 µm. The penetration time generally decreases for increasing PAA content until the PAA content reaches 19 vol.% where a plateau in penetration time is observed for both adhesive

polymer matrices. The plateau indicates that the PAA particles through the adhesives are well connected, effective water penetration occur through the adhesive and the addition of PAA particles does not contribute to faster water penetration.

The adhesives with the more rigid matrix (40 wt.% SIS) exhibit a water penetration time of approximately 1000 min for 5.8 vol.% PAA content and gradually decrease to 100 min for PAA contents of 19.0 and 27.1 vol.%. A similar trend is observed for the softer adhesives (20 wt.% SIS) where the penetration time is approximately 600 min for 5.8 vol.% PAA and approximately 100 min for PAA contents of 12.2 vol.% and above. The large difference in penetration time at low PAA content (5.8 and 9.0 vol.%) between the high a low SIS content adhesives suggest that a stiffer matrix delays the water penetration in adhesives containing hydrophilic particles with poor connectivity where the particles are required to swell more to form a path of water through the adhesive. The stiffer matrix thus provides increased PAA swelling resistance compared to the softer polymer matrix. This is in agreement with findings of water absorption and x-ray computed tomography of similar polymer composites.<sup>34</sup>

The influence of the matrix rigidity decrease for increasing PAA particle content. For the highly filled adhesive with 27.1 vol.% PAA, there is no significant difference in the penetration time for the two different matrices. This indicates that the PAA particle connectivity has reached a level where minimal PAA swelling is required to form a conductive path of NaCl solution through the adhesives.

## 3.3 Probing the Water Penetration Front

The impedance measurements give a clear change in the phase angle when the water front has traveled across the adhesive thickness and reached the working electrode. The water front can thus be probed in one dimension by measuring the penetration time as a function of adhesive thickness. Figure 4a shows the thickness of the adhesive, z in µm, plotted against the measured penetration time for adhesives with 27.1 vol.% PAA and 20 or 40 wt.% SIS matrices.



Figure 4: Water diffusion front (a) and weight uptake per area (b) as a function of immersion time for adhesives containing 27.1 vol.% PAA particles dispersed in either a 20 or 40 wt.% SIS matrix.

Here, the water penetration in the 20 and 40 wt.% SIS adhesives with 27.1 vol.% PAA are indistinguishable for all thicknesses as expected from the penetration time for 1000  $\mu$ m thick adhesives (Figure 3). Both penetration curves follow Fickian diffusion, which suggests that polymer relaxation times are not affecting the diffusion process.<sup>35,36</sup> This indicates that that the polymer matrix does not restrict the water penetration process and that the PAA particle are readily plasticized by water due to their highly hydrophilic nature.<sup>37</sup> Figure 4b show the weight uptake per adhesive area as a function of water immersion time for the two different 27.1 vol.% PAA adhesives. The data represents averages of 6 measurements with errorbars representing the standard deviations. The immersion tests show that the adhesives absorb water continuously over time for both matrices. This suggests that the PAA particles have formed a particle network, which effectively absorb NaCl solution and is therefore in agreement with the impedance measurements. The water uptake in the adhesives with the 20 wt.% SIS matrix is greater at all times compared to the adhesives with the more rigid matrix, 40 wt.% SIS. This indicates that the water uptake is restricted by the matrix rigidity, while the water front propagates similarly in both adhesives as suggested by the impedance measurements (Figure 4a).

Next, the water front is assessed for adhesives containing 9.0 vol.% PAA particles dispersed in either a 20 or 40 wt.% SIS matrix (Figure 5a). Here, the penetration times are longer for adhesives with the rigid matrix, 40 wt.% SIS, compared to the adhesives with the 20 wt.% SIS matrix. However, the water uptake in the adhesives is similar up to 60 min (Figure 5b). The difference in penetration time indicates that the PAA particles are required to



Figure 5: Water diffusion front (a) and weight uptake per area (b) as a function of immersion time for adhesives containing 9.0 vol.% PAA particles dispersed in either a 20 or 40 wt.% SIS matrix.

swell to form a path of NaCl solution through the adhesives. The PAA particles swell faster in the softer matrix compared to the stiffer matrix. The water uptake is similar for times up to 60 min, which indicates that only PAA particles connected to the adhesive surface absorb water. After 120 min, the adhesive with 20 wt.% SIS matrix shows a significantly higher uptake, which means that some PAA particles have swollen to transport water to other PAA particles in the adhesive, while the water uptake in the stiffer adhesive is lower due to the increased swelling resistance of the PAA particles.

## 4 Conclusion

Water penetration and water absorption was probed in different skin adhesive using timeresolved impedance measurements and gravimetric measurements. Adhesives containing from 5.8 vol.% to 27.1 vol.% PAA particles dispersed in hydrophobic polymer matrices with different mechanical properties were systematically investigated. The results showed that the water penetration became independent of PAA content for adhesives with a high PAA particle content >19 vol.%. Here, the water penetration was also independent of the mechanical properties of the polymer matrix, which indicates that the water was readily propagating through a well-connected network of PAA particles. However, the overall water absorption was significantly reduced for increasing mechanical properties of the polymer matrix, which means that a more rigid matrix provides increased swelling resistance for the PAA particles. For adhesives with lower PAA contents, the mechanical properties of the polymer matrix highly influenced both the water absorption and the water penetration in the adhesive. These findings show that the hydrophilic particle connectivity can be adjusted through the particle content and that skin adhesives with a high hydrophilic particle content can be engineered to absorb different amounts of water depending on the matrix rigidity, while maintaining the water penetration.

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# Supporting Information Available

The following file is available free of charge.

• SuppInfo.pdf

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# Supporting Information: Water Penetration and Absorption in Skin Adhesives: The Influence of Hydrophilic Particles and Mechanical Properties

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## 1 Rheology

The rheological properties of the two different polymer matrices (4:1 and 4:2 wt:wt PIB:SIS) were probed by shear rheology using a Discovery hybrid rheometer from TA Instruments (Denmark) with parallel plate geometry. Frequency sweeps were done at fixed shear strain, 0.1 %. The frequency sweeps were performed at frequencies ranging from  $10^2$  to  $10^{-4}$  Hz with five frequencies per decade. The measurements were done a 32 °C.



Figure S1: The complex modulus,  $G^*$ , and loss tangent,  $\tan \delta$ , plotted as a function of deformation frequency for polymer matrices consisting of 20:80 ( $\triangle$ ) and 40:60 ( $\Box$ ) SIS:PIB (wt:wt)

The 40 wt.% SIS matrix has  $\tan \delta < 1$  in the entire frequency range, meaning it can be considered elastic. The 20 wt.% SIS matrix has  $\tan \delta > 1$  from  $10^{-3}$  to  $10^{-1}$  Hz, where it can be considered viscous. Generally, the complex modulus  $G^*$  is higher for the 40 wt.%, which together with the  $\tan \delta$  considerations mean, that it is stiffer than the 20 wt.% SIS matrix.

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