



## Identification of promoters and enhancers induced by carbon nanotube exposure

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## 21 Optimization of flanking region lengths for folding into constrained RNA structures: RNAcop.

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RNA secondary structure prediction is often performed with the aim to identify functional elements. Especially for screens for structured non-coding RNAs or predicted structures in untranslated regions of a mRNAs, the length of such an element is not well defined. For in vitro experiments, however, a smaller part of an entire transcript comprising the predicted structure is usually extracted. Here, the composition of flanking nucleotides can disturb folding into the structure of interest.

Therefore, we developed a computational tool, RNAcop (RNA context optimization by probability), that optimizes folding into the structure of interest. Using constrained folding, our approach computes probabilities for folding into the structure of interest for all pair-wise combinations of flanking region lengths. Our analysis suggests that proper choices of flanking regions are crucial for a number of structures. The results are supported by in vitro experiments. RNAcop is available as web server and command-line tool at <http://rth.dk/resources/rnacop>.

## 22 Identification of promoters and enhancers induced by carbon nanotube exposure .

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Usage of carbon nanotubes (CNTs) is increasing in industry due to their mechanical and electrical properties. However, pulmonary exposure to CNTs induces, an asbestos-like toxicological response characterized by persistent inflammation, granuloma formation and fibrosis with low no-effect levels. Little is known about the regulation of the response to CNTs. To this end, we have profiled transcription start sites and enhancers in mouse lung tissues following CNT exposure using Cap Analysis Gene Expression Assay (CAGE). This revealed a massive transcriptome response, with over 100-fold expression increases for key promoters, and a large change in transcription of enhancer regions linked to similarly responding genes. The response included key genes involved in inflammation, phagocytosis, cell and proliferation. We found a clear correlation between the overall CNT response strength and the number of alternative promoters in a given gene, but not the number of proximal enhancers. Upregulated genes after CNT exposure, where only the most annotated upstream promoter was upregulated, were associated to inflammation. Also NFkB binding sites were over-represented among these promoters. Conversely, upregulated genes where the upregulation could be attributed to promoters within the gene were not in particular linked to inflammation, and these promoters had distinct DNA motif enrichment patterns, not including the NFkB binding sites. Interestingly, NFkB binding sites were not over-represented in upregulated enhancer regions.