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## **Freedom of additional signals on genes: on the combination of DNA mechanics, genetics and translation speed**

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## Propositions

- I Mechanical nucleosome signals are caused by various effects, which can only be understood by decomposing the signals.

*Chapters 2 and 5.*

- II  $k$ -shortest path algorithms enable the exploration of the entirety of sequence space at once.

*Chapters 3 and 4.*

- III Various layers of information on DNA (e.g. nucleosome positioning signals and translation speed) can be easily manipulated

*Chapters 3 and 4.*

- IV Genetics is not an all-deciding factor for the amino acid sequences that constitute a protein.

*Chapter 5.*

- V Eslami-Mossallam et al. use synonymous mutation Monte Carlo to modify mechanical information on top of genes. However, synonymous codons affect many types of information, which restrict the replacement of these codons, see Chamary et al. It would be interesting to incorporate these additional types of information to the Monte Carlo approach.

*Eslami-Mossallam et al. PLoS ONE, 11:e0156905, 2016.*

*Chamary et al. Nat Rev Genet 7, 98108, 2006*

- VI It is not true that the distribution of dinucleotides on a nucleosome may be explained through their relative energy cost to bend via base pair roll, as claimed by Segal et al. Their claim ignores a crucial nonlocal effect.

*Segal et al. Nature 442, 772-778, 2006*

- VII On average, one finds high GC signals near the promoter regions of housekeeping genes in human. Tillo et al. explain this by proposing that these signals allow regulatory sequences of specialized genes to be closed off for non-specialized cells. This is wrong, which illustrates that one has to be careful when looking at genome-wide averages. In fact, housekeeping genes (i.e. non-specialized genes) have high GC signals near their promoter regions, see for example the findings of Vavouri et al.

*Tillo et al. PLoS ONE, 5(2):e9129, 2010.*

*Vavouri and Lehner, PLoS Genet. 7, e1002036, 2011.*

- VIII It is remarkable that three out of the four most-produced crops are independently-cultivated cereal grains. Cereal grains have high GC content near the transcription start sites (TSSs). For human, Vavouri et al. show that GC content near the TSSs is related to the transfer of epigenetic information. Thus, strong epigenetic markers of cereal grains may very well be the cause of the prevalence of grain cultivars.

*Tubana et al., Soil Science, 181, 1. 2016*

*Vavouri and Lehner, PLoS Genet. 7, e1002036 (2011).*

- IX Distrust in academia is a huge problem, as is evident from public reaction to the corona crisis.