The mechanical genome : inquiries into the mechanical function of genetic information

Tompitak, M.; Tompitak M.

STELLINGEN

behorende bij het proefschrift "the mechanical genome: inquiries into the mechanical function of genetic information"

I It is easy to find sequences for which the assumption that the intrinsic curvature of DNA molecules can be neglected breaks down.
Chapter 2.

II Nucleosomes are better viewed as a class of protein-DNA complexes, rather than a single one, because the DNA sequences involved impart physical properties with significant variation.
Chapter 3.

III The Markov-chain approximation for the sequence-dependent affinity of DNA for a given system vastly extends the reach of the Mutation Monte Carlo methodology.
Chapters 4, 5 and 6.

IV The mechanical properties of promoter regions divide organisms into classes with a remarkable universality that persists across the tree of life.
Chapter 6.

V Surprisingly, Rosanio *et al.* found DNA rings to have no strong global dinucleotide preferences, despite having clear local preferences. Not only is this a rather special scenario, but dinucleotide properties reported in the literature predict otherwise.
Rosanio et al. *Biopolymers* **103** 303 (2015).

VI Our understanding of nucleosomal sequence preferences is incomplete because the only experimental study ever to probe them using random DNA did not publish sequence ensembles or statistics derived therefrom.
Lowary and Widom *J. Mol. Biol.* **276** 19 (1998).

VII Many approaches to predicting nucleosome affinity use the same experimental methods for training and testing their models, possibly fitting models to experimental artifacts and overestimating their accuracy.
Kaplan et al. *Nature* **458** 362 (2009), ...

VIII Much data exists on nucleosome positioning in various organisms, but literature that attempts synthesis of what is known into a general, coherent picture is sparse.
Locke et al. *BMC Gen.* **14** 284 (2013), Valouev et al. *Nature* **474** 516 (2011), ...

IX Due to rising complexity and diminishing returns in the scientific endeavor, the feasibility of carrying forth into the 21st century, the fast pace of scientific progress that the 20th century exhibited, and which society has come to expect, is questionable.

X As a consequence of IX, the amount of progress that can be achieved within the limited time frame of a PhD project is shrinking, and the traditionally expected accomplishments required for obtaining the doctorate are becoming unrealistic.

Marco Tompitak
Leiden, October 11th, 2017