

**The role of linker DNA in chromatin fibers** Brouwer, T.B.

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## PROPOSITIONS

#### accompanying the thesis

### The Role of Linker DNA in Chromatin Fibers

1. Every research group should have its own publicly available repository, including version control, for the development and organization of experimental protocols.

Chapter 2 of this thesis.

- 2. The biophysical community should aim for experimental standardization. Either by the use of robotized experimentation or the implementation of certain industry standards in equipment and experimental conditions. Chapters 2, 4, 5, and 6 of this thesis.
- 3. It is more insightful to compare trends within a series of biophysics experiments than to get lost in a discussion on the magnitude of the measured parameter.

Chapters 4, 5, and 6 of this thesis.

4. The eukaryotic DNA sequence has evolved to carry implicit mechanical folding information. It follows that mutations in non-coding parts of the genome can therefore affect epigenetic regulation – an effect perhaps overlooked by the scientific community.

Chapter 5 of this thesis, B. Eslami-Mossallam et al., **PLOS ONE** 11.6 e0156905 (2016), S. Todolli et al., **Biophys. J.** 112.3 416-426 (2017).

5. It requires years of training and a deep understanding of the data to confidently interpret a graph of only two parameters in order to derive the mechanical properties and higher-order structure of chromatin fibers. 6. Although chromatin research has advanced tremendously from *in vitro* studies of artificial chromatin, the real challenge lies in understanding native material.

N. Hermans et al., Sci. Rep. 7.1 1-9 (2017), O. Shukron et al., Trends Genet. 35.9 685-705 (2019).

- 7. The observation or absence of certain higher-order chromatin structures may simply be an artefact of the implemented experimental method. *F. Song et al.*, Science 344.6182 376-380 (2014).
- 8. The scientific community might have been looking in the wrong direction in its search for chromatin structure *in vivo*. For example, a regular pattern to nucleosome-phasing per gene may lead to local higher-order chromatin folding motifs, much like proteins.

S. Baldi et al., Nat. Struct. Mol. Biol. 27.2 109-118 (2020).

9. The concept of statistical significance should be treated carefully: *p*-values should not be used for the dismissal of possibly crucial effects – especially when measurements are difficult or destructive in nature.

V. Amrhein et al., Nature 305-307 (2019).

10. Scientific literature, due to its very nature, has limited effectiveness in sharing knowledge. Alternative methods, such as graphical summaries, instructional videos, or catchy guitar songs, should be recognized and explored by the scientific community.

Thomas B. Brouwer Leiden, 4-11-2020