Biophysics of disordered nuclear receptors and their DNA binding regulation

Heling, L.W.H.J.

List of publications

Publications during PhD at Universiteit Leiden

Heling, L. W. H. J., Banijamali, S. E., Satarifard, V. & Mashaghi, A. Programmed Polymer Folding. in *Topological Polymer Chemistry: Concepts and Practices* (eds. Tezuka, Y. Deguchi, T.) 159-176 (Springer, 2022).

Sheikhhassani, V., Scalvini, B., Ng, J., **Heling, L.W.H.J.**, Ayache, Y., Evers, T.M.J., Estébanez-Perpiñá, E., McEwan, I.J., Mashaghi, A. Topological dynamics of an intrinsically disordered N-terminal domain of the human androgen receptor. *Protein Science* **31**, (2022).

Scalvini, B., **Heling, L.W.H.J.**, Sheikhhassani, V., Sunderlikova, V., Tans, S.J., Mashaghi, A. Cytosolic Interactome Protects Against Protein Unfolding in a Single Molecule Experiment. *Adv Biol* **7**, (2023).

Scalvini, B., Sheikhhassani, V., van de Brug, N., **Heling, L.W.H.J.**, Schmit, J.D., Mashaghi, A. Circuit Topology Approach for the Comparative Analysis of Intrinsically Disordered Proteins. *J. Chem. Inf. Model* **63**, (2023).

Wruck, F., Avellaneda, M.J., Naqvi, M.M., Koers, E.J., Till, K., Gross, L., Moayed, F., Roland, A., **Heling, L.W.H.J.**, Mashaghi, A., Tans, S.J. Probing Single Chaperone Substrates. in *Biophysics of Molecular Chaperones: Function, Mechanisms and Client Protein Interactions* (eds. Hiller, S., Liu, M. & He, L.) 278-318 (Royal Society of Chemistry, 2023).

Heling, L.W.H.J., van der Veen, J., Rofe, A., West, E., Jiménez-Panizo, A., Alegre-Martí, A., Sheikhhassani, V., Ng, J., Schmidt, T., Estébanez-Perpiñá, E., McEwan, I.J., Mashaghi, A. Polyglutamine expansion induced dynamic misfolding of androgen receptor. *Protein Science* **34**, (2025).

Heling, L.W.H.J., van der Veen, J., Rofe, A., West, E., Jiménez-Panizo, A., Alegre-Martí, A., Sheikhhassani, V., Ng, J., Schmidt, T., Estébanez-Perpiñá, E., McEwan, I.J., Mashaghi, A. Deciphering the allosteric control of androgen receptor DNA binding by its disordered N-terminal domain. *Mol. Cell Endocrinol.* **608**, (2025).

Heling, L.W.H.J., Kovač, K, de Vries, C.J.M., Mashaghi, A. Modulation of Nur77–DNA interactions by the Glucocorticoid Receptor. *Biochem. J.* **483**, (2026).

Other publications

Heling, L. W. H. J., Geeves, M. A. & Kad, N. M. MyBP-C: one protein to govern them all. *J. Muscle Res. Cell Motil.* **41**, (2020).

Pilagov, M., **Heling, L. W. H. J.**, Walklate, J., Geeves, M. A. & Kad, N. M. Single-molecule imaging reveals how mavacamten and PKA modulate ATP turnover in skeletal muscle myofibrils. *J. Gen.Physiol.***155**, (2023).

Curriculum Vitae

Laurens Wilhelmus Hubrecht Joseph Heling was born on the 13th of June 1994 in Zoetermeer, the Netherlands. After finishing secondary school at the Erasmus College in 2014, he pursued a Bachelor of Science in Biomedical Sciences (with Honours) at the University of Kent in Canterbury, United Kingdom. While his initial interest was to pursue a career in medicine, his time as part of the University's team for the international genetically engineered machine (iGEM) competition, introduced him to fundamental molecular biochemical research. The team, which aimed to develop a CRISPR Cas13 based cellular mRNA tracking device, was awarded a bronze medal as well as the best poster award at the Giant Jamboree in Boston.

Upon completion of his BSc, Laurens pursued a Master of Science by Research in Biochemistry in the labs of Professor Michael Geeves and Professor Neil Kad. Here he studied the role of myosin binding protein C in the regulation of muscle contraction. He co-developed a novel assay to study single myosin molecules within a myofibrillar lattice in real time using super-resolution microscopy techniques. After his MSc, he relocated to Budapest, Hungary, early 2020, joining the lab of Professor András Malnasi-Csimedia at Eötvös Loránd Tudományegyetem (ELTE) to study the effects of novel myosin inhibitors on molecular and cellular processes.

In March 2021 he joined the laboratory of dr. Alireza Mashaghi at the Leiden Academic Centre for Drug Research, Universiteit Leiden to start his PhD research, which is summarised in this thesis. During his PhD, Laurens worked closely together with biochemists, molecular biologists, mathematicians and physicists on an interdisciplinary effort to characterise structural and functional dynamics of nuclear receptors. He attended several international conferences and presented his work at the 2025 LACDR Spring Symposium. Aside from his doctoral research, Laurens has been involved with the iGEM organisation in the capacity of veteran judge at the competition.

In June 2025, Laurens joined the lab of dr. Jurian Schuijers at the Centre of Molecular Medicine, UMC Utrecht, as a postdoctoral researcher. His current research focuses on elucidating the fundamental mechanisms of biomolecular condensates in transcriptional signalling.

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fluorescence microscopy proved so contagious that I pursued it in three chapters of this thesis. Words cannot define the impact of my time in your lab; I am incredibly thankful for the opportunities that sprouted from this and our professional friendship.

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