Unraveling the molecular interactions of single nucleobases and amino acids within material openings

Peijia Wei, Chandan K. Das, Mayukh Kansari, Longlong Li, Maria Fyta

Computational Biotechnology, RWTH Aachen University, Worringerweg 3, 52072 Aachen, Germany

The specific interactions of single biomolecules, such as DNA, RNA, and peptides with a material can be tailored in order to give rise to novel biosensors. These are made of a material part in which a nanometer-sized pore is drilled and can electrophoretically thread charged (bio)molecules through in the presence of an electrolyte solution [1]. This molecular transport through the material pore can be detected by ionic and/or electronic current signals. Both types of currents, though different in nature, inherently include the analyte information, that is the length, type, and sequence. At the same time, these currents map the explicit interactions of the threaded (bio)molecule to the surface of the material. The exact chemical details of both the (bio)molecule and the material, as well as their relative orientation strongly influence the interactions of the two and define the transport properties of the molecule through the material opening [2]. In order to unravel these exact interactions and their effect on the measurable current signals, two separate types of materials are probed: (a) two-dimensional graphene and molybdenum-disulfide [3] and (b) a biomimetic graphite-based structure [4]. The molecular transport and its interplay with the electrolyte solution through these materials are unraveled using atomistic simulations. At the same time, the electronic tunneling current, which is enhanced by the molecular transport through the material opening is calculated using quantum transport simulations. Both the ionic and electronic currents that are calculated, as well as those measured in relevant experimental setups need to be analyzed by applying Machine Learning schemes [5] in order to provide the exact chemical information on the (bio)molecule threading the material pores. These schemes are being integrated in the novel nanopore sequencers as part of the next generation sequencing schemes.

[1] M. Fyta, *Chem.-Asian J.*, **2023**, 1*8*, e202200916.
[2] F.C. Maier, M. Fyta, *ChemPhysChem*, **2020**, *21*, 2068-2074.
[3] P. Wei, M. Kansari, M. Fyta, *Nanoscale*, **2025**, *17*, 3873-3883.
[4] C.K. Das, M. Fyta, *Small*, **2025**, *21*, 2407647.
[5] Á. Diaz-Carral, M. Rotegui, A. Koc, M. Ostertag M. Fyta, *NanoX*, **2024**, *5*, 025020.