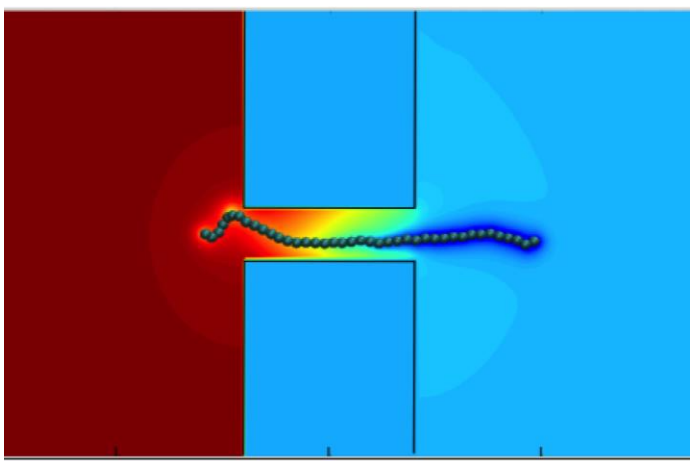
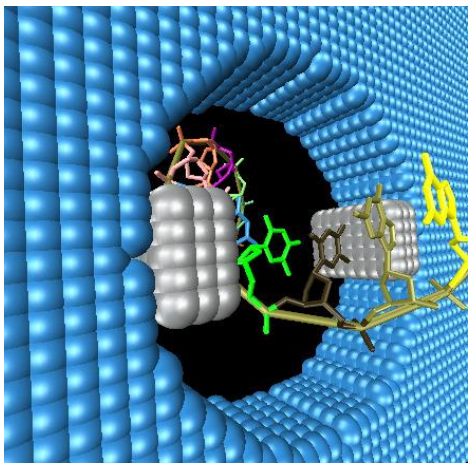
Computational Biotechnology Group
Selected Research Foci

DNA sensing and nanopores

DNA molecules can be electrophoretically threaded through nanometer sized pores in a process named *DNA translocation*. Such pores can be biological or drilled in solid-state materials. The passage of biomolecules, such as DNA, RNA, and proteins through a narrow pore can be monitored by the change in the ionic current through the pore, the change in the electronic conductance across the pore or through optical measurements provided that fluorescent tags are used. In any case, the concept of sensing biomolecules with nanopores has opened up a pathway towards ultra-fast and cheap DNA and peptide(modifications) sequencing potentially realizing medical applications related to personalized genome sequencing. Our group has been investigating different aspects of the translocation process, including the influence of the solvent, the interactions of DNA with the material, the physical scaling concepts underlying the process, the configurational details of the biomolecules, etc. All these studies are directed towards optimizing the threading of the biomolecules through the pore in order to increase the accuracy in sequencing the biomolecule.

(Left) The process of a biopolymer electrophoretically threading a pore in a material within a

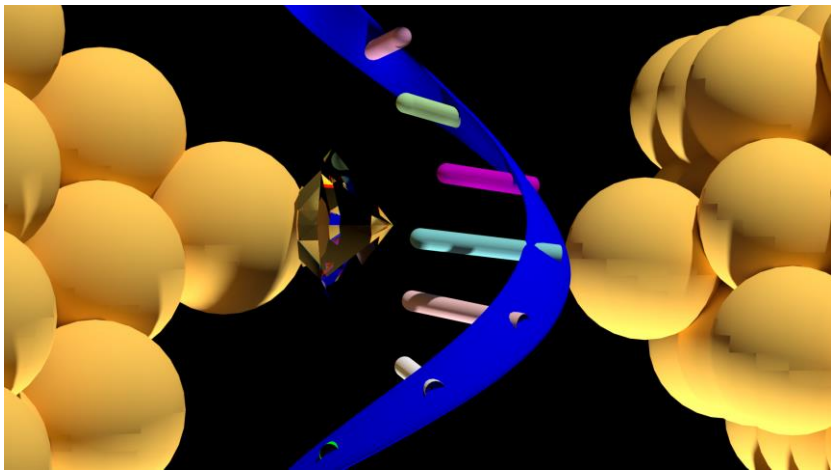




salt solution. (Right) A closer view into the nanopore, revealing the hole in the material

embedded with electrodes (gray). The colored rods represent DNA nucleotides forming single-stranded DNA.

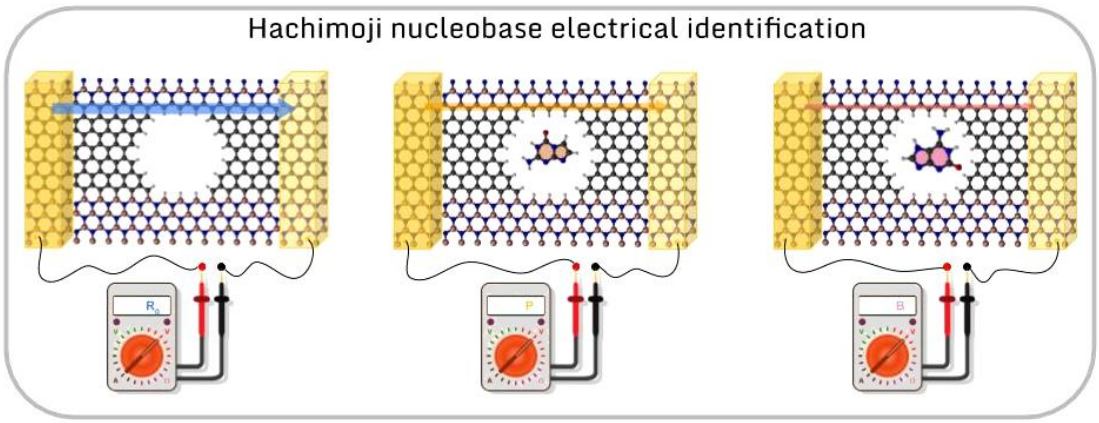
Specific modeling efforts have been directed in revealing the relevance of gold electrodes functionalized through tiny carbon nanoparticles in sensing DNA. These electrodes are embedded in nanopores drilled in materials in order to electrically sense DNA. The sensing mechanism strongly relies on the hydrogen bonding between DNA and the carbon nanoparticles.



Gold electrodes (right and left) functionalized with a tiny carbon nanoparticle (on the right) can sense a DNA strand passing through the nanogap formed by the electrodes (Courtesy of G. Sivaraman).

Synthetic DNA detection

The feasibility of synthesizing unnatural DNA/RNA has recently been demonstrated, giving rise to new perspectives and challenges in the emerging field of synthetic biology, DNA data storage, and even the search for extraterrestrial life in the universe. In line with this outstanding potential, solid-state nanopores have been extensively explored as promising candidates to pave the way for the next generation of label-free, fast, and low-cost DNA sequencing. In this work, we explore the sensitivity and selectivity of a graphene/*h*-BN based nanopore architecture towards detection and distinction of synthetic Hachimoji nucleobases.



The concept behind the electrical detection of synthetic Hachimoji DNA nucleobased placed in an opening of a 2D material (Courtesy: F.A. de Souza).

Machine Learning approaches

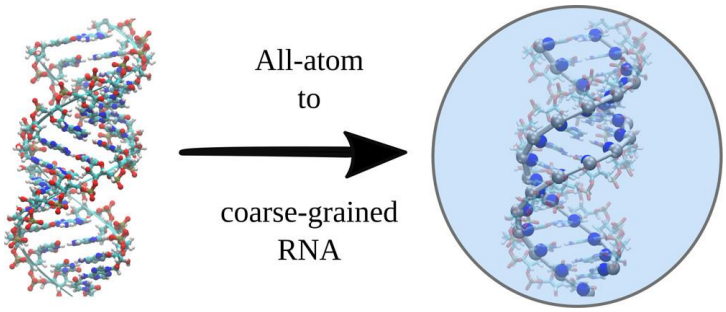
Different Machine-Learning schemes, both supervised and unsupervised are being utilized in two different areas, in order to (a) assist, extend and enhance the accuracy of computer simulations at certain spatio/temporal scales and (b) analyze and interpret experimental data for providing insight into hidden microscopic aspects in the experiments. Selected examples are for (a) the development of machine learned potentials and force fields and for complex materials and for (b) the extraction of knowledge from current traces obtained in nanopore experiments for DNA detection.

A sketch of the feature extraction from experimental ionic traces in DNA threading a nanopore. The features build images, which train Neural Networks in order to predict the sequence of DNA.

Development of biomolecular force-fields

The efficiency of modeling biophysical systems relies strongly on the appropriateness of the involved inter-atomic and inter-molecular interactions. However, employing the full level of

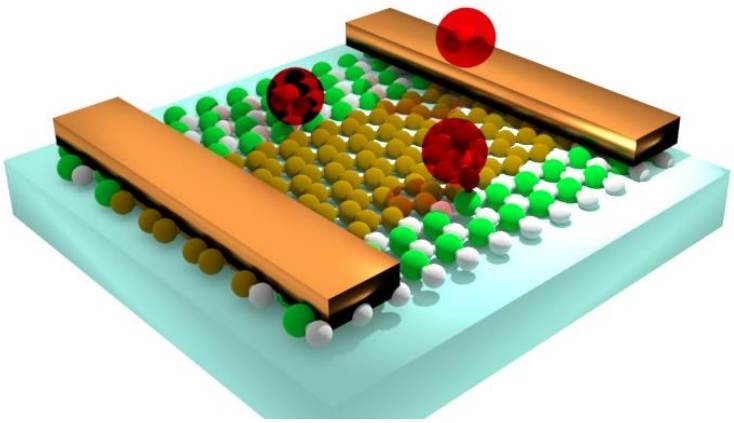
accuracy of these interactions strongly enhances the relevant computational demand. A workaround is to find concepts for enhancing the computational efficiency, without compromising the accuracy of the simulations. To this end, we have been developing coarse-grained potentials for DNA and RNA using as a start quite accurate quantum-mechanical calculations of their full atomic structure.



A sketch of the approach followed for developing coarse-grained potentials for DNA/RNA using their full structural details (Courtesy: S.Cruz-Leon).

2D materials for sensors

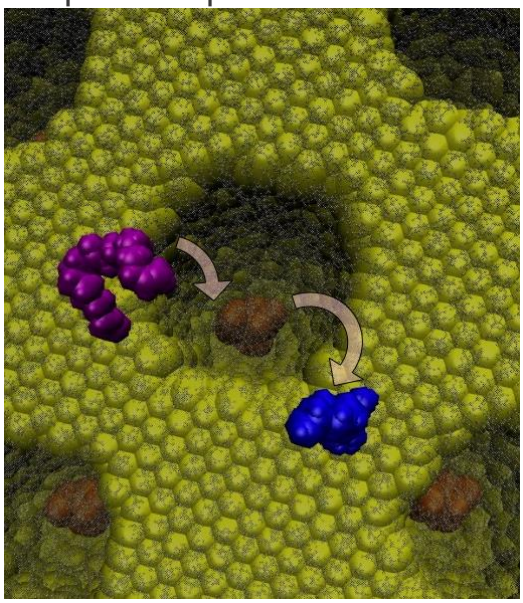
We scan different types of two-dimensional materials, ranging from graphene, hexagonal boron nitride, transition metal dichalcogenides, and their lateral combinations and assess their potential sensing gas or other types of molecules.



A sketch of a 2D-based device with embedded electrodes (gold rods) sensing the (bio)molecules (red) (Courtesy: R. Amorim).

Porous functional materials for catalytic applications

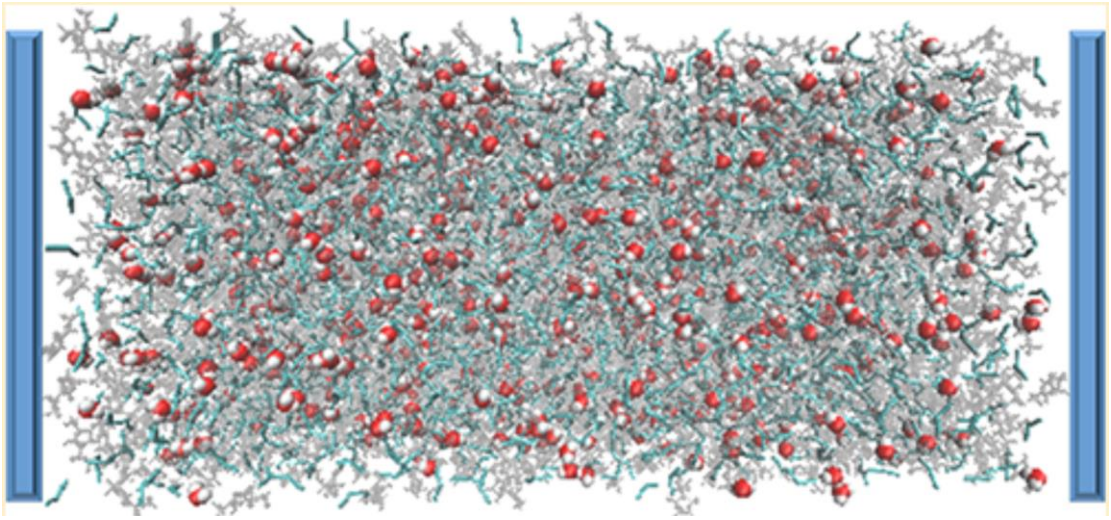
The possibility for a linker-free immobilization of catalytic molecules in a pore through the use of ionic liquid solutions is studied providing insight on the role of ionic liquids (ILs) on the confinement of catalysts in porous materials. Through computer simulations, a deeper understanding on the micro-details for a rational design of the catalyst immobilization and the relevant conditions in catalytic templates is provides.



Functionalized pores filled with an ionic-liquid solution provide a template for catalytic reactions (Courtesy: T. Kobayashi).

Salt and ionic liquid solutions

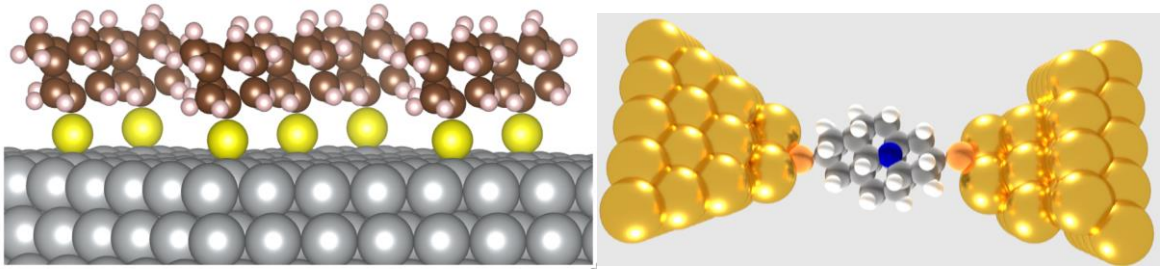
Salt and ionic liquid solutions are and can become very relevant to biophysical and biotechnological systems. We have been investigating in details the thermodynamic properties of such solutions and their specific solvent effects and interactions with other types of solutes in bulk and at interfaces.



An ionic liquid mixture placed between two interfaces (blue rods) (Courtesy: T. Kobayashi).

(Bio)functionalized materials

Integration of materials with (bio)molecules can give rise to templates with enhanced selected properties and functionalities. Such templates are hybrid materials with potential applications ranging from bio-sensors to templates for programmable self-assembly, and molecular devices. Our simulations provide insight into different length and time scales of these materials and their properties.



Sketches of functional materials: (Left) a surface (gray spheres) on which different molecules have been grafted. The latter can be further functionalized in order to tailor selected functionalities of the template. (Right) A molecular device (Courtesy: B. Adhikari).