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MNIBS

Multiscale Modelling of Nanostructured Interfaces for Biological Sensors

NMP-NSF-1 EU-NSF

Coordinated activities in computational materials research

Publishable Final Activity Report

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1 Project execution

The unusual properties of liquid cyrstals have been known and very profitably exploited for more than half a century. Yet they still seem to keep useful surprises in store: the realization that liquid crystalline materials can be applied to detect the presence of peptides, proteins and toxins is very new. The first experiments on liquid crystal-based biosensors are only a few years old. Understanding how these sensors can, under favourable conditions, detect individual molecules is still a work in progress, which requires a combined, multi-level approach.

The development of such a multi-level, hierachical modelling technique was the primary objective of MNIBS. In addition to its intrinsic scientific value, a thorough understanding of the mechanisms of the extreme sensitivity of liquid crystals to certain biological molecules would make it possible to design sensors tailored to specific proteins or viruses.

The most striking, and most useful, feature of liquid crystals in the context of biosensors is their ability to “amplify” a signal at the molecular level. The arrival of a single protein molecule at the exposed surface of a liquid crystal has been observed to trigger a re-organization of the liquid crystal around the protein.

This remarkable amplification effect that takes place in liquid crystal sensors is triggered by an event at the molecular level (a few nanometers) and spontaneously develops macroscopic size (a few milimeters). It is thus not surprising that the techniques used to model the ordering transtion of liquid crystal molecules around the protein cannot be applied to the spreading of ordering to macroscopic size. Conversely, those continuum models that are the most natural framework to describe macroscopic behaviour have no molecular resolution. There is thus no single, all-encompassing technique that can tackle the amplification problem

MNIBS has addressed this apparent impasse by means of a hierarchical strategy, in which different techniques, each ideally suited to a particular length and time scale, are combined in a thermodynamically consistent way.

MNIBS was jointly funded by the EC and the NSF. Contractors on the EC side were the Universidad Politecnica de Madrid (UPM), the National Technical University Athens (NTUA) and the Eidgenössische Technische Hochschule Zürich (ETH). A new contractor joined the Consortium on January 1st 2007: the Universidad Autónoma de México, funded

also by the EC under its call FP6-2006-TTC-TU-Priority-3. US contractors were the University of Wisconsin-Madison (UW), Northwestern University (NW) and Purdue University (PU).

An outstanding success of MNIBS was the fruitful collaboration of groups from the EC, USA, and Mexico. Thanks to the joint character of the Call, EC and US groups received independent but coordinated financial support. A TTC project enabled the Mexican group to join the project after its first year. Given the variety of modelling techniques used in MNIBS, it was a prerequisite to include in the Consortium the leading experts in the fields, which not always reside in EC member countries. The joint Call scheme has proved to be a very flexible tool for enabling collaboration beyond the borders of the EC.

All participants in MNIBS have contributed highly specialized expertise in areas as diverse as atomistic molecular modelling, mesoscopic, stochastic techniques, dynamic mean field and single-molecule theory, and continuum mechanics. Overall thermodynamic consistency was given high priority. A group specializing in non-equilibrium thermodynamics was charged with the task of guaranteeing that information transfer across the different spatial and temporal scales complied with thermodynamic consistency.

In this respect, one of the most prominent successes of MINBS was the effective integration of all modelling techniques into a multiscale tool that went all the way from the molecular to the macroscopic level:

- at the microscopic (atomistic) level, the dynamic behaviour of both the liquid cruystal and the biological molecule have been studied in great detail. Phase transitions, analyte dynamics, and diffusive behaviour could be fully characterized and quantitatively described.

- at the mesoscopic level, a series of coarse-grained representations were developed based on widely differing methodologies, all of which have proved to be capable of describing LC-analyte interaction based on a few parameters extracted from the microscopic level simulations.

- at the macroscopic level, three independent and parallel routes (continuum mechanical, micro-macro, and Lattice Bolzmann) to the design of actual liquid

crystal sensors have been pursued. All three have been developed to the point of practical utility.

The successful meshing of the three description levels into a practical simulation and design tool by means of a thermodynamically consistent formalism was a very satisfactory confirmation of the ideas advanced in the proposal phase. As a result of the convergence of all the modelling techniques developed or applied in MNIBS, a first principles simulation and design of LC-based, single-molecule sensors for proteins and toxins is now possible.

Several of the techniques developed in the project represent the current state-of-the-art in the simulation of soft condensed matter at the micro-, meso-, and macroscopic levels. These advances are reflected in over 40 publications in top level journals, including several Physical Review Letters, Soft Matter, Journal of Physical Chemistry B, etc.

MNIBS also made a significant contribution to dissemination and outreach through successful contacts with a number of industrial and academic partners. In view of the successful achievement of all objectives, and thanks to a contract extension granted by the EC, such dissemination activities were given greater priority than originally planned.

The predictive power of the modelling hierarchy developed in MNIBS has also attracted the attention of companies keen on the large scale manufacturing of liquid crystal sensors by low cost processes such as inkjet printing. These collaborations born from MNIBS have resulted in long-lasting collaborations with industrial partners (both SMEs and large multinationals), and in the diffusion of MNIBS-related methods in industrial areas where they had been unknown up to now.

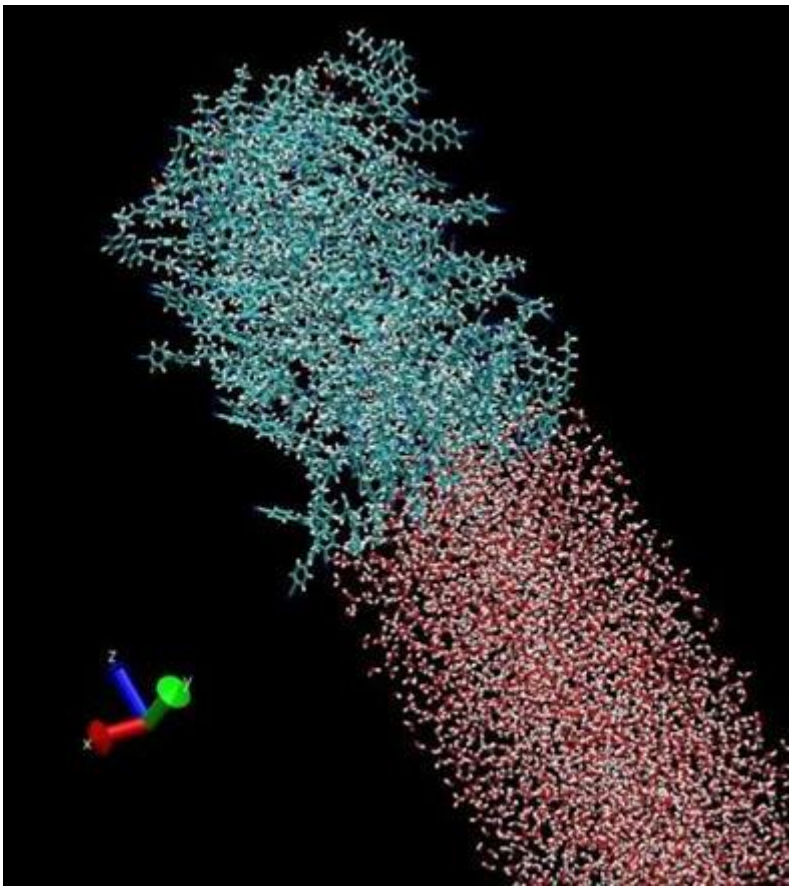

Figure 1 The figure illustrates the systems addressed by MNIBS: Molecular Dynamics snapshot of the water / liquid crystal interface (the system contains 256 molecules of 4'-pentyl-4-cyanobiphenyl (5CB) and 3456 water molecules.

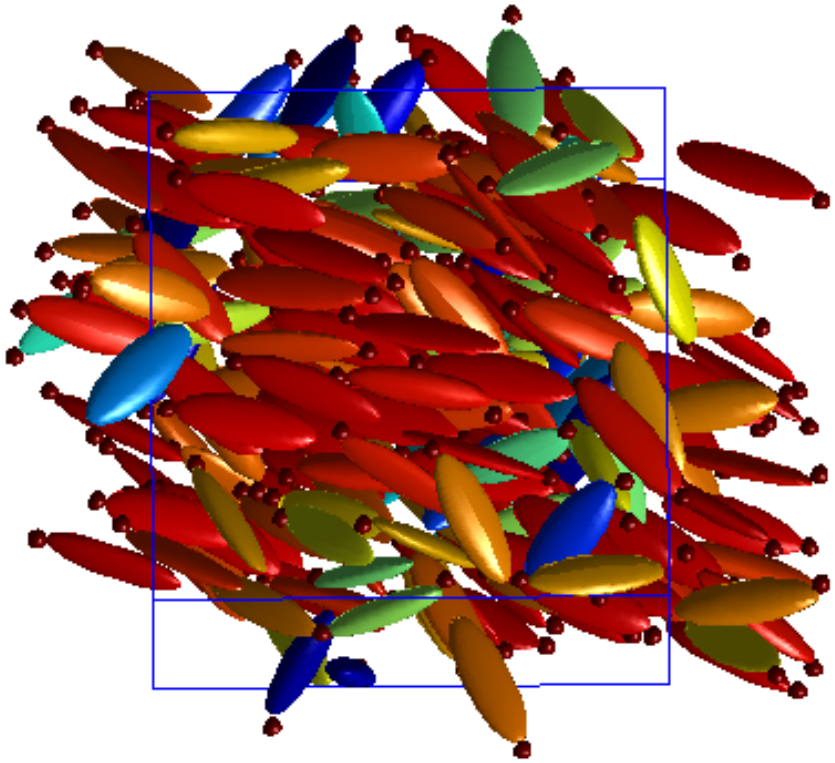

Figure 2 Coarse-grained representation of the nematic configuration of the liquid crystal (mesogen) 4'-pentyl-4-cyanobiphenyl (also known as 5CB). It shows a typical nematic configuration of a coarse grained molecular description of a low molecular weight mesogen. Colour is keyed according to orientation with respect to the director: it ranges from transversally oriented (blue), to high, parallel alignment (red). The coarse-grained model was constructed based on atomistically detailed simulations, and a coarse-grained force field was validated.

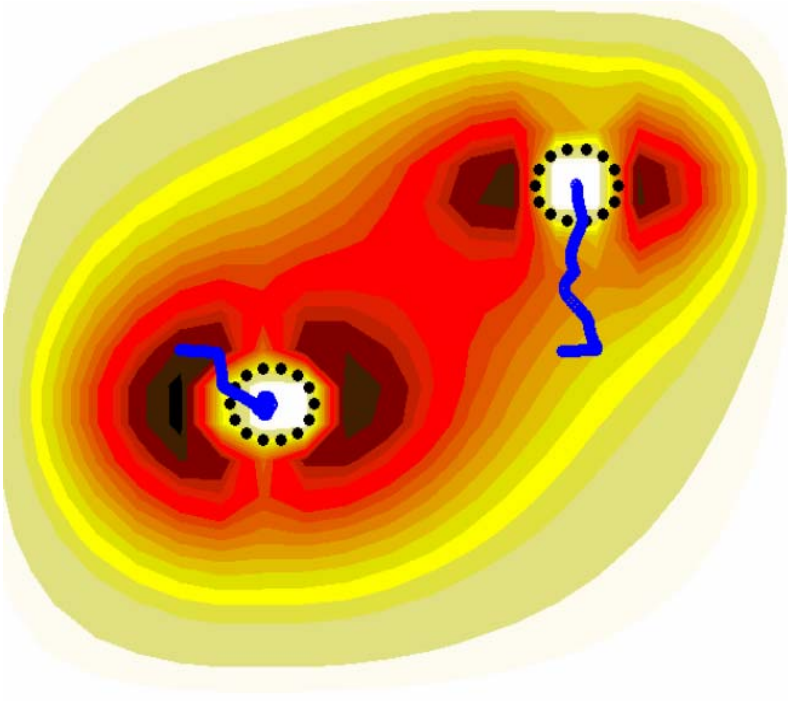

Figure 3 The figure below is a coarse-grained representation of a liquid-crystal sensor for toxins: sensor particles (outlined in black) immersed in a nematic LC-sensor are subject to elastic interaction forces due to defects in the LC (red). As a consequence, the particles move along the paths shown in blue.

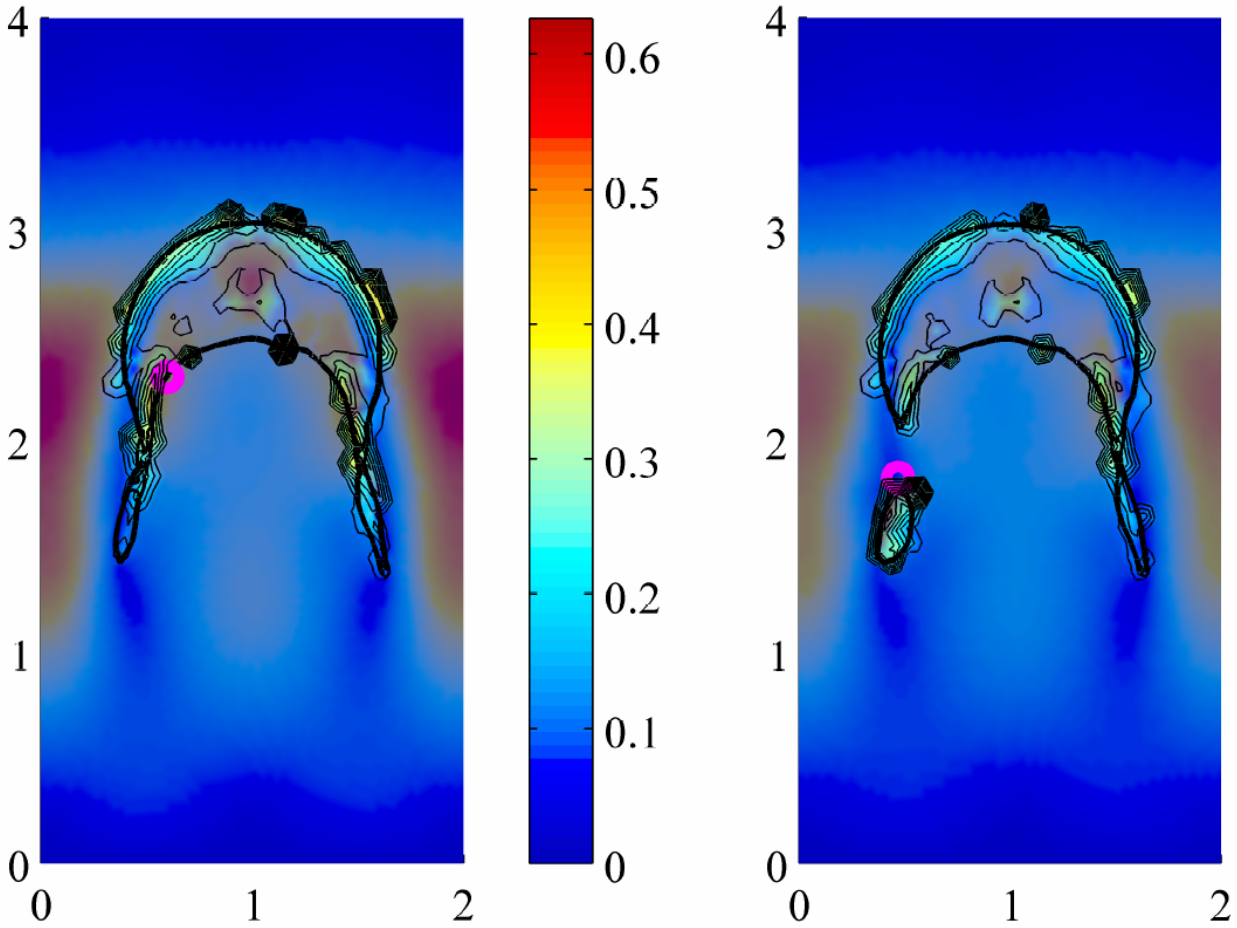

Figure 4 Effect of the adsorption of a protein molecule (magenta circle) on the breakage of a liquid crystal droplet in a single-molecule sensor. On the right, the protein is assumed not to interact in any way with the LC. On the right, the interaction of the protein and the LC has been taken into account. The ordering effect of the protein on the LC causes a rearrangement in the stress field of the LC droplet sufficient to induce the breakage of the latter. Events such as this breakage (and others not shown) are easily detectable by macroscopic means, and path the way to inexpensive, highly sensitive sensors for proteins and toxins.

Project Logo:

MNIBS

2 Dissemination and use

- Result description: Methodology and simulation codes for hierarchical or multilevel modelling of polymeric materials. (product(s) envisaged, functional description, main advantages, innovations).

- Possible market applications: simulation of polymeric materials in the area of polyolefin and polycondensate synthesis and application, or in industries where polymeric materials or additives are used.

- Stage of development: already in industrial use.

- Collaboration offered to industrial partners with an interest in micromechanical modelling of polymeric materials.

- Collaborator details: industrial partner with strong R&D capabilities, in the area of production, formulation or application or polymeric materials (mainly non-crosslinked).

- Intellectual property rights granted or published: none.

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