DESCRIPTIF DU SUJET ET ARGUMENTAIRE DU DIRECTEUR DE THESE

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Intitulé du sujet de thèse *:*

(ENG) **Statistical mechanics for macromolecular structures of nanotechnology**

(FRA) **Mécanique statistique pour les structures macromoléculaires de la nanotechnologie**

Acronyme :

STAMENA (STAtistical MEchanics for macromolecular structures of Nanotechnology)

Résumé du sujet de thèse *(Décrire en français les objectifs visés en 1500 caractères maximum)*

(FRA) L'un des plus grands défis de la nanotechnologie est d'intégrer des structures macromoléculaires artificielles ou des machines moléculaires, c'est-à-dire des molécules capables de présenter un mouvement mécanique contrôlé ou des transformations configurationnelles, dans des microsystèmes. Ici, les variations mécaniques nanoscopiques peuvent être amplifiées afin d'obtenir les comportements et les fonctions micro et mésoscopiques souhaités. Cependant, il reste extrêmement difficile d'amplifier le mouvement des macromolécules aux échelles méso et macroscopiques, à l'instar de ce que font les cellules musculaires par une action synchronisée des filaments de myosine et d'actine hiérarchiquement organisés. En ce sens, l'une des idées à suivre est celle du biomimétisme, où les mécanismes biologiques sont compris et reproduits dans des situations nanotechnologiques. Néanmoins, l'un des problèmes à résoudre est celui des fluctuations thermiques, qui affectent considérablement le comportement des structures macromoléculaires à l'échelle nanométrique. Pour cette raison, nous proposons dans ce projet de doctorat l'utilisation de la mécanique statistique pour étudier l'intégration possible des macromolécules dans les structures nanotechnologiques. Nous aborderons, par exemple, les liaisons sacrificielles utilisées pour augmenter la résistance des microstructures artificielles ou les polymères supramoléculaires, qui permettent de créer deux ou plusieurs molécules reliées de façon permanente par la topologie. Ces derniers sont parfaitement adaptés pour développer l'idée de machines moléculaires intégrées à des dispositifs.

(ENG) One of the greatest challenges of nanotechnology is to integrate artificial macromolecular structures or molecular machines, i.e. molecules that are capable of exhibiting controlled mechanical motion or configurational transformations, into microsystems where nanoscopic mechanical variations can be amplified in order to achieve desired micro- and mesoscopic behaviors and functions. However, it remains extremely challenging to amplify the movement of macromolecules at the meso- and macroscopic scales, similar to what muscle cells do through synchronized action in hierarchically organized myosin and actin filaments. In this sense, one of the ideas to follow is that of biomimetism, where biological mechanisms are understood and reproduced in nanotechnological situations. Nevertheless, one of the problems that needs to be addressed is that of thermal fluctuations, which greatly affect the behavior of macromolecular structures at the nanoscale. For this reason, we propose in this Phd project the use of statistical mechanics to study the possible integration of macromolecules into nanotechnology structures. We will address, for example, sacrificial bonds used to increase the toughness of artificial microstructures or supramoleculecular polymers, which allows the creation of two or more molecules permanently connected via topology. They are perfectly suited for developing the idea of devices-integrated molecular machines.

DESCRIPTIF DU SUJET *(en 3 pages minimum)*

1) Le sujet de recherche choisi et son contexte scientifique et économique :

The behavior of macromolecules and their complex conformational transitions (changes in their geometrical structure under external stimuli) play a very important role in several artificial and biological mechanical systems. On one hand, concerning artificial systems, we can mention the peeling of a film from a substrate [1], the waves propagation in bistable lattices [2], the energy harvesting through multistable chains [3], the plasticity and the hysteresis in phase transitions and martensitic transformations of solids [4], the cracks and dislocations nucleation and propagation in materials and alloys [5] and the friction at the nanoscale [6].
On the other hand, micro-mechanical biological phenomena include the conformational transitions in polymeric and biopolymeric chains [7], the attached and detached states of fibrils in cell adhesion [8], the unzipping of macromolecular hairpins [9], the myosin and actin filaments behavior in skeletal muscles [10], the denaturation or degradation of nucleic acids, polypeptide chains or other macromolecules of biological origin [11] and the macromolecular friction [12]. Moreover, it is also interesting to remark that friction is also at the basis of understanding the plastic phenomena in solid materials,

being able to control the nucleation of dislocations and fractures and to regulate the shear transformations and the ductile-to-brittle failure transition.
The study of these situations is at the base of the macromolecular understanding, crucial to promote the integration of macromolecular structures into nanotechnological devices. The studies of the biological systems are useful to apply the biomimetic approach, where the extremely smart solutions of nature can be reproduced in artificial devices.
In all the above physical systems, we eventually find a multi-basin energy landscape and the state of the system can be in stable or meta-stable configurations, identified by the wells of the energy function. As a matter of fact, these systems are constituted by a large number of units characterized by well-defined physical states. The transitions between these states or, equivalently, the exploration of the energy landscape govern the macroscopic behavior of the whole system and, in particular, its static and dynamic features. There are two important different classes of microinstabilities. **In some cases, the intrinsic micro-instabilities may describe bistable units with transitions between one ground state and one metastable state** (e.g. for the conformational folded-to-unfolded transitions in macromolecules or martensitic phase changes in metallic alloys or also friction). These states represent different, yet mechanically resistant conformations. This case can be represented in a one-dimensional setting by introducing an effective two-well potential energy *U*, as schematized in Fig. 1(a). We observe that the choice of a simple one-dimensional system is aimed at a simple presentation of the idea. In other words, *x* represents an effective order parameter adopted to describe the transition between the different wells, whereas all other variables can be considered to be minimized out. **Alternatively, the micro-instabilities can explain transitions between unbroken and broken states of the breakable units of the system** (e.g. in the unzipping of hairpins, denaturation of macromolecules, fibrillar biological adhesion, peeling of films and cracks propagation). This process can be reversible, partly reversible or irreversible according to the specific physical phenomenon. The one-dimensional energy considered in this second case is shown in Fig. 1(b). Here, the unbroken configuration corresponds to a potential well and the broken configuration corresponds to constant energy and zero force.

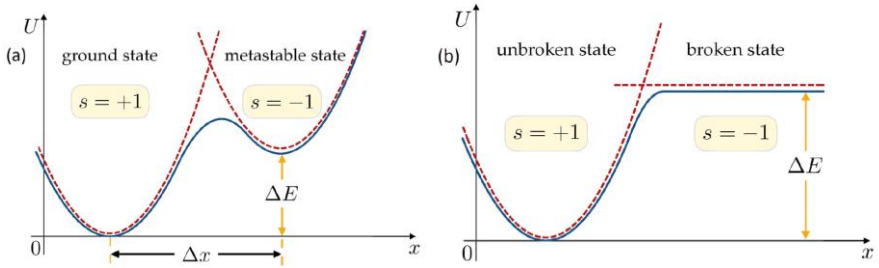

Fig.1. Two different classes of microinstabilities: bistability between a folded (ground) state and an unfolded (metastable) state in panel (a), and link transition between attached (unbroken) and detached (broken) state in panel (b).

In Fig.2 one can find the classification of most of previously mentioned examples following the classification given in Fig.1. Moreover, the different situations have been subdivided between biophysics and materials science, for the sake of clarity. It is interesting to note that there is a parallel between all the problems in biophysics and materials science. This similarity is at the basis of the development of mathematical models that are applicable indistinctly to both areas of research, as discussed in the following. **In fact, the main goal of this project is to develop models between physics and mechanics that are able to study state transitions in some of these biological and technological situations in order to better understand the effects of temperature and external mechanical actions on their behavior, and to ultimately promote the integration of macromolecules into devices.**

The transitions between the states in all previous systems are indeed strongly influenced by the thermal fluctuations, which can modify the probability of being in a given state or the passage rate between the neighboring energy wells. Therefore, the correct framework in which we can develop the theoretical modeling of these phenomena is the classical statistical mechanics. In particular, the systems exhibiting switching mechanisms between different energy basins can be studied by means of the spin variables approach. The first theoretical approaches based on this method have been developed to model the biomechanical response of skeletal muscles. Since these pioneering investigations, this technique has been generalized to study different multi-stable systems [13], macromolecular chains [14], and adhesion problems [15].
This approach is based on the introduction of a series of discrete variables (similar to the spins used to deal with magnetic systems), which are able to identify the state associated with a given system unit (see the variable *s* in Fig.1). For example, the bistable potential energy of Fig. 1(a) (continuous line) can be approximated by a biparabolic function (dashed lines) with the switching among the wells described by the spin variable. It means that, depending on the value of these discrete variables, the energy function may change its shape and, in particular, the position and the depth of its wells. The introduction of the spin variables frequently simplifies the calculation of the partition function and, consequently, the analysis of the corresponding averaged thermodynamic quantities.

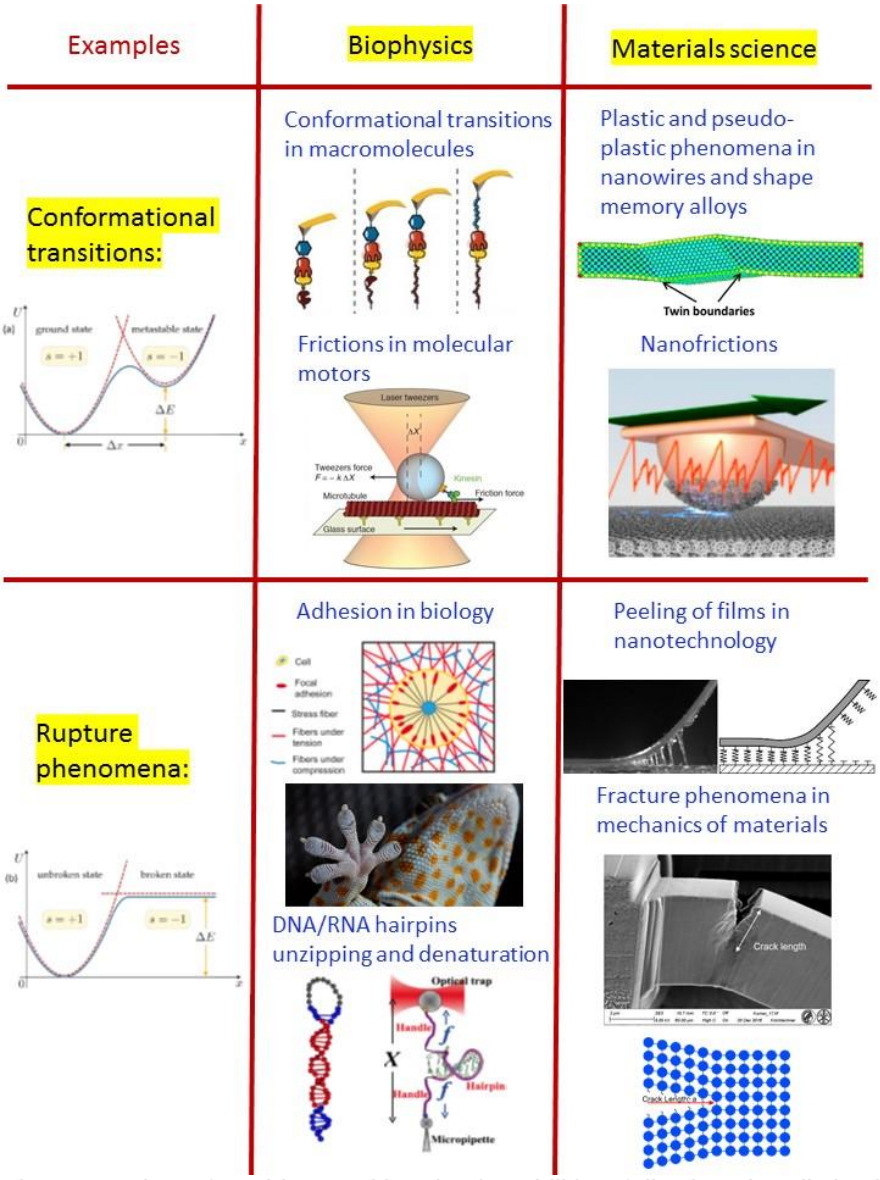

Fig.2. Classification of the examples of problems with microinstabilities following the distinction made in Fig.1 and subdivided between biophysics and materials science.

This theoretical device is able to give mathematical results in closed form, very useful to advance the understanding of the underlying mechanics and physics. It is important to remark that, as discussed in detail in Refs. [13-15], the evaluation of the partition function based on the spin approach assumes that for both configurations all possible deformations (values of *x* in Fig. 1) can be attained by the system. This corresponds to the assumption of a multivalued energy function (see superposition of dashed lines in Fig. 1). As shown numerically in Refs. [13-15], with typical experimental temperatures, the effect of this approximation can be considered (statistically) negligible since these artificial configurations (superposition of dashed curves) have an energy sensibly higher than real configurations (continuous lines). This technique has been largely exploited to investigate bistable systems with transitions between ground and metastable states, with important application to the nanomechanics of macromolecules. Concerning the systems with transitions between unbroken and broken states, only some configurations have been investigated within the framework of the statistical mechanics and many open problems have been identified. **In this context, concerning the present PhD project, we will work on some structures and problems useful to foster the integrations of macromolecules into nanotechnology. In particular, we will apply the spin variable approach to the following situations: 1) sacrificial bonds used to improve the toughness of polymeric system and other microstructures with important applications in micro and nanomechanics; 2) macromolecules obtained through the paradigm of the supramolecular chemistry, where different molecules are linked by topological structures rather than chemical bonds, with applications to the development of molecular machines in nanotechnology; 3) molecular friction, which is a very important physical phenomenon at the nanoscale, crucial for the operations of nanotechnological devices.**
The whole PhD activity is coherent and complementary with the project ESR-EquipEx+ NANOFUTUR in which IEMN is strongly involved, especially in the Sections (3) TERAHERTZ TECHNOLOGIES, (4) NANO BIO TECHNOLOGIES, (5) SENSORS IOT AND MICRO ENERGY, and (6) NANO MANIPULATION NANO ASSEMBLY.

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2) L'état du sujet dans le laboratoire d'accueil.

Directeur de thèse: Stefano Giordano was born in Genoa, Italy, on October 14, 1971. He received the "Laurea" degree in electronic engineering (summa cum laude) from the University of Genoa, Italy, in 1996, and the Ph.D. degree in materials science from the University of Trento, Italy, in 2000. He subsequently joined the Department of Physics of the University of Cagliari, Italy. Since October 2010, he has been CNRS Senior Researcher at the Institute of Electronics, Microelectronics and Nanotechnology (IEMN), Villeneuve d'Ascq, France. He is working within the AIMAN team, which is part of the International Associated Laboratory (LIA) LEMAC/LICS on Critical and Supercritical Phenomena in Functional Electronics, Acoustics and Fluidics. His research interests include homogenization methods for heterogeneous materials and structures, multiphysics and multiscale modeling of the thermo-magneto-electro-elastic response of multiferroic materials and spintronic structures, and statistical mechanics of small systems with applications to biological and artificial macromolecules, force spectroscopy, phase transitions, adhesion, friction and fracture. He has authored or co-authored over 100 papers in leading journals on these topics, five invited chapters in edited books and one textbook.

Codirecteur de thèse: Giuseppe Puglisi is full professor of Mathematical Physics at the Politecnico di Bari. After graduating as a Structural Engineer at Politecnico di Bari he took his PhD in Materials and Structural Engineering at the Trento University with a thesis on smart materials at the AME Dept. of the University of Minnesota. After several periods as visiting researcher in prestigious European and American universities, he became researcher and then associate professor of Continuum Mechanics and Structural Engineering at Politecnico di Bari. He is member of the Society of Natural Philosophy (SNP), of the International Society for the Interaction of Mechanics and Mathematics (ISIMM), and of the Italian Group of Mathematical Physics (GNFM). He authored more than fifty articles in leading journals in the fields and he has been invited in several prestigious conference, in some of them as a keynote speaker. He has been principal investigator in two MIUR national projects. He is Editor for Frontiers: Mechanics of Materials and Frontiers: Soft Matter. He has been guest Editor of the Special issue: "Soft Matter: a nonlinear continuum mechanics perspective" of the International Journal of Nonlinear Mechanics, Elsevier. He has been invited by the Royal Society of London to write a review on his research activity on soft matter (joint with G. Saccomandi). His research topics are in Continuum and Materials Mechanics with particular interests in soft rubberlike and biological materials and active and smart materials.

Encadrant: Romain Peretti graduated from Institut d'optique graduate school (Orsay France) in 2005 and got his PhD degree in physics from the University of Lyon (France) in 2008. He then worked as postdoc fellow at "Ecole centrale Lyon" (France) and "Eidgenössische Technische Hochschule Zürich", ETHZ (Switzerland). In 2016, he was awarded an international chair of excellence from region "Hauts de France" to build a new activity at IEMN Terahertz biophotonics leading to the position of CNRS Senior researcher in 2018. Here he is working in the terahertz photonics team to implement Terahertz spectroscopy on macromolecules. His research involved micro and nano fabrication of samples to concentrate the Terahertz light on the macromolecular samples and time-domain spectroscopy experiments to measure their vibrational signature in the terahertz range. He has authored or co-authored over 70 papers in leading journals on these topics and holds two patents.

The research topic concerning statistical mechanics and nanomechanics of macromolecules, of central importance for the international scientific community, is widely studied within the **AIMAN-FILM group at IEMN**, where the PhD thesis will be developed (see References below and results described in http://giordanostefano.it/). It is important to underline that the theoretical background of the proponent has been crucial in the collaboration between the AIMAN-FILM group and the **Physics group at IEMN** on the subject concerning the degradation of DNA bundles under irradiation. This collaboration also involved the partners "**Centre Hospitalier Régional Universitaire de Lille**" (for the irradiation techniques), the structure "**SMMiL-E**" in Lille (for the DNA characterization), and "**LIMMS-CNRS-IIS UMI 2820 (Japan)**" (for the MEMS construction). The collaboration achieved important results, now published in high-ranked international journals (see References). In particular, the statistical mechanics of nanotechnological systems can be studied by means of the "spin variables approach", a technique elaborated and developed by the PhD advisor of the present proposal (see References). Moreover, it is worth noticing that these methodologies have been largely used in the Phd thesis of Manon Benedito (2017-2020), supported by the "**Région Hauts-de-France**" (50%) and by "**Centrale Lille**" (50%), and supervised by the same advisor. In this PhD thesis, important results concerning the response of proteins and other macromolecules of biological interest have been achieved and published (see References). In addition, the PhD thesis of Andrea Cannizzo (2020-2023) supported by the "**Région Hauts-de-France**" (50%) and by "**Centrale Lille**" (50%) is supervised by the same advisor under

the framework of a PhD supervision agreement with the Polytechnic of Bari in Italy. The thesis concerns the problems of adhesion and fracture in nanostructures and is performed through the same techniques. A first important result has been achieved for the statistical mechanics of adhesion (see References). Therefore, this new research line will be efficiently pursued and sustained by means of a new PhD student, which is crucial to allow for the continuity of the activities. The advisor has a strong expertise in tutoring Phd students and all previous experiences led to important results published in highly ranked international journals. A description of the activity based on statistical mechanics can be found in a recent (July 8th, 2021) internal seminar at IEMN entitled “Modeling mechanical micro-instabilities in biophysics and materials science” (slides available in pdf format at the link http://dx.doi.org/10.13140/RG.2.2.12939.62248 and live recording at the following one https://www.youtube.com/watch?v=A_U_vsUBK34).

2) Les objectifs visés, les résultats escomptés.

The aim of this project is to investigate the potential of macromolecules in the development of nanotechnology devices, with applications from nanoelectronics to healthcare. Indeed, the behavioral properties of macromolecules can be exploited to induce desired performances to matter. The central point is to be able to create a direct link from the nanoscopic evolutions of a macromolecule to the mesoscopic behavior of a material or device. One of the lines that can be exploited, which in particular will be analyzed in the course of this thesis, is the use of macromolecular systems with microinstabilities and conformational transitions, as discussed in the previous section. In fact, the possibility of having transitions for example in the length of a macromolecule, can generate an amplification from nanoscale to mesoscale of great importance for applications. Also, the possibility of increasing the fracture resistance at the nanoscopic level can amplify the observed toughness at a larger scale. These phenomena induced by macromolecules and able to tightly link two very different spatial scales can generate the design of nanotechnological devices with exceptional properties. At the base of this technological revolution, there must be a refined knowledge of microinstability phenomena in macromolecular structures. The spin variable technique has been largely exploited to investigate bistable systems with transitions between ground and metastable states, with important application to the nanomechanics of macromolecules. Concerning the systems with transitions between unbroken and broken states, only some configurations have been investigated within the framework of the statistical mechanics and many open problems have been identified. Among them, the following three situations will be studied in the context of this thesis:

Sacrificial bonds

A phenomenon that will be studied is the mechanism of sacrificial bonds in macromolecules or polymers. **This is a classic example where we study biological structures to synthetize materials or systems that have functions that mimic biological processes**. Sacrificial bonds in molecules and composites have been found to greatly increase the fracture toughness of biomaterials by providing a reversible, molecular-scale energy-dissipation mechanism [16,17]. This type of links is involved in complex hierarchical structures, such as bone, tendons, ligament, nacre, and mussels. Sacrificial bonds are defined as bonds that break before the main structural link (often the molecular backbone) is broken (see Fig.6a). These bonds are frequently reversible and weaker than the covalent bonds of molecular backbones. **When a material is stretched, a large amount of energy is dissipated through the reversible rupture of sacrificial bonds and the release of hidden lengths, thereby ensuring high toughness and integrity**.

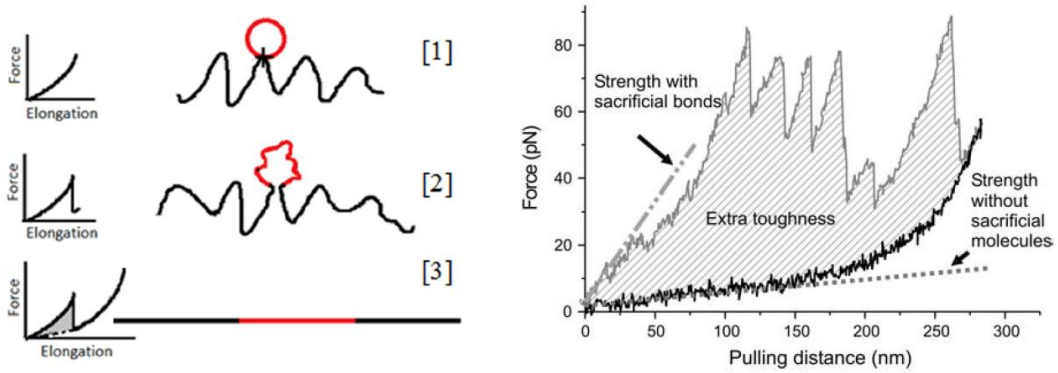

Fig. 3. (Left) Schematic drawing of the basic principles of the sacrificial bond mechanism [16]. [1] Before a sacrificial bond is broken, only the black length of the molecule contributes to the force with which the molecule resists stretching. The red length of the molecule is hidden from the force by the sacrificial bond. [2] When the bond fracture threshold is reached, the bond breaks and the whole length of the polymer (black plus red) contributes to its entropy. The force supported by the polymer molecule abruptly drops in response to this sudden increase in entropy. [3] As the polymer molecule is further stretched the force supported by it increases. The grey area represents the extra work done in stretching a polymer with sacrificial bonds relative to a polymer of the same length but without them. (Right) Sacrificial molecules increase the stiffness and the toughness of a material [17]. The initial slope of the pulling curve is a measure for the stiffness of a material. In the case with sacrificial molecules (upper curve) this slope is steeper (dash-dotted line) than the slope (dotted line) in the case without sacrificial molecules (lower curve). The extra energy that is dissipated through the sacrificial molecules (shaded area in the curve) is a measure for the increase in toughness of the material.

The biomimetic approach aims at reproducing these properties of natural materials using engineered and scalable components and processes. The understanding of the mechanism of sacrificial bonds is therefore of crucial interest. However, this phenomenon, governing interactions at the molecular level of different natural structures, is not yet fully explained. Our modeling activity can be used to investigate this mechanism, which can enhance the toughness (see Fig.6b) and the strength of the polymeric system and can allow for better resistance to crack initiation and propagation as well as better performance under dynamic loading. It is important to emphasize that no theory exists yet for such a mechanism. We can apply the spin variable approach by identifying the intact and broken states of the sacrificial bonds. This allows for the elaboration of a complete thermodynamic theory of the sacrificial bonds mechanism including the effect of the thermal fluctuations. In particular, we can develop the theory for both the Helmholtz (hard device, prescribed extension) and the Gibbs (soft device, applied force) statistical ensembles. As a result, we can quantify the toughness intensification by measuring the increase of the area under the response on the stress-strain plane. The properties obtained through this novel approach can be used in designing nanosystems with improved mechanical features and to foster the integration of these mechanisms in nanotechnology devices.

Supramolecular structures

Another promising class of polymer structures for nanotechnology is introduced by the so-called supramoleculecular chemistry, which allows the creation of two or more molecules permanently connected via topology. In these molecules, alongside the traditional chemical bonds there are exotic mechanical bonds, which link atoms together by what might be loosely called topological linkages. The first research in this field was developed by Jean-Pierre Sauvage (2016 Nobel Prize in Chemistry) for creating molecules able to mimic the functions of machines by changing their conformation in response to an external signal. Among the simplest of these are catenanes (interlocking rings) [18], and rotaxanes (wheel and axel molecules) [19] (see Fig.4). **These daisy chains actuate individually on a nanometer length scale and can produce a micrometer length change when integrated in large numbers, being perfectly adapted for nanotechnology integration (amplification of the mechanical variation from nano- to mesoscale) [20].** Despite significant and almost magical progress in their synthesis [21], the physics and material properties of these systems remains almost entirely unexplored when compared to their chemically-bonded cousins. Again, our mathematical approaches can be adopted to study the mechanics of these new systems. In particular, our statistical mechanics methods can be applied to obtain the 1D, 2D and 3D force-extension response of chains of catananes and rotaxanes (in both Helmholtz and Gibbs ensembles). Importantly, this analysis is able to explicitly show the link between topology and statistics, which is very interesting from both the theoretical and the practical point of view. To cite a specific application, in order to generate stable and ordered 1D, 2D and 3D nanoparticle structures, nanotechnology can be combined with supramolecular chemistry to control the self-assembly of functionalized nanoparticles. As nanoparticles are now widely used in medicine, this approach may open the door to so-called supramolecular nanomedicine, where supramolecular chemistry, nanotechnology and healthcare are properly combined. In addition, this kind of macromolecules can be used to create sacrificial bonds, as discussed in the previous point. Moreover, supramolecular structures are particularly adapted to design sensors and actuators in nanotechnology since exhibit a significant response (often bistable) to different external stimuli including pH, force, light and so forth. Concerning the light interaction, recent findings show that (strong) coupling light to molecular vibrational states changes their material properties at the macro scale [22]. These results were only performed in the mid infrared coupling light with vibrational bonds. At lower energy, in the TeraHertz range, the vibrations are delocalized on many bonds spreading on the nano scale and relate to the structure and therefore to the function of the macromolecule. Strong coupling of THz vibrational mode to electromagnetic one could lead to modification of their function. The theoretical tools to describe these effects only emerge at the molecular scale and are fully missing at the meso scale making this study important for both theoretical and applied grounds.

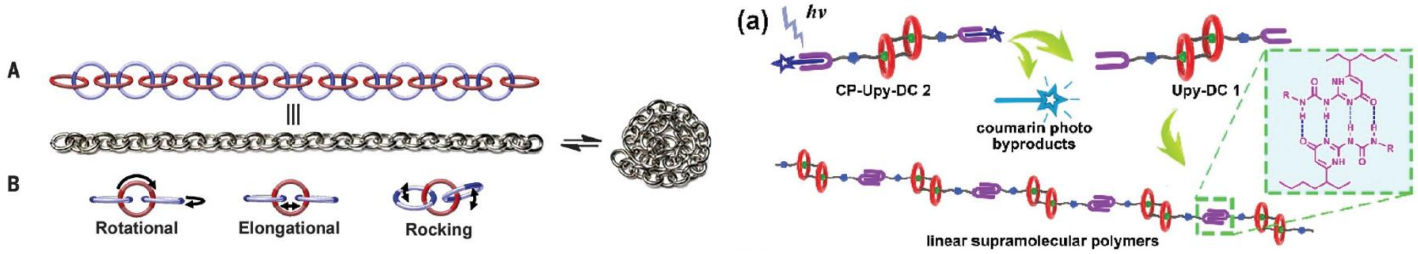

Fig. 4. (Left) Structure and conformational mobility of and synthetic approach to poly[n]catenanes. (A) Schematic representation of the poly[n]catenane architecture, which can be thought of as the molecular equivalent of a robust and flexible metal chain [18]. (B) Common conformational motions observed in catenanes. (Right) Graphical representation for the phototriggered supramolecular polymerization of a [c2] daisy chain rotaxane [19].

Molecular friction

Another important phenomenon in nanotechnology, strongly influenced by the temperature and characterized by transitions between energy wells, is molecular friction or nanofriction. It rules the physics of small contacts in nanoscience and nanotechnology [23] and the sliding of macromolecules in biological and soft structures [24,25]. The nature of friction at the nanoscale has begun to be studied systematically with the advent of the atomic force microscope, and the development of efficient molecular dynamics simulations. These approaches to nanotribology have enabled the experimental and numerical observation of the characteristic stick-slip motion of the slider atoms, which interact with the

periodically corrugated potential energy representing the atoms of the substrate. **This result allowed the validation of an older conceptual model, which is usually referred to as the Prandtl-Tomlinson model [26]. This is the most efficient model currently known for describing nanoscale friction and, for this reason, has been largely investigated and compared with experimental and numerical results.** It consists in a single point mass moving on a one-dimensional sinusoidal potential pulled by a linear spring characterized by its elastic constant. **The most natural generalization of the Prandtl-Tomlinson model considers a one-dimensional elastic chain of interacting atoms or particles moving on the sinusoidal potential mimicking the substrate. This scheme is known as Frenkel-Kontorova model and perfectly describes the mutual sliding of two interfaces or macromolecules [27].**

In order to have a comprehensive view of the effect of temperature on the friction phenomenon, we can develop theories of friction, based on statistical mechanics. To do this, we can implement the spin variable approach useful to deal with nonconvex potential energies. We will introduce a simple model concerning the one-dimensional stick-slip behavior of a single particle in contact with a substrate described by a periodic potential energy. **In particular, we propose a modification of the classical Prandtl-Tomlinson model, able to consider the effect of thermal fluctuations on the friction behavior**. The characteristic sinusoidal profile of the Prandtl-Tomlinson substrate potential can be substituted by a periodic sequence of quadratic wells with elastic constant k_0 and spacing d (see Fig.5a). In order to identify the well occupied by the particle, we have to introduce a new discrete variable n within the phase space of the system, which represents the number corresponding to the concerned substrate site. Moreover, we can also consider a one-dimensional chain composed of N particles linked by linear springs with elastic constant k_m and equilibrium length s. This chain interacts with a substrate lattice composed by a sequence of pinning sites with stiffness k_0 and spaced by a uniform distance d (see Fig.5b). **This arrangement corresponds to the Frenkel-Kontorova model, where a competition between the intrinsic chain spacing s and the substrate lattice spacing d is introduced.** At the same time, the elastic potential energy of the moving chain competes with the pinning potential energy of the substrate. This model allows the study of structural lubricity and thermolubricity between solids or macromolecules.

We can say that our proposed methods to take into account the temperature effect in friction phenomena can be adopted for studying the molecular friction in the macromolecular structures of the nanotechnology. Other perspectives approached within the PhD can concern: the generalization of this approach to the two-dimensional case, to a more complex corrugated substrate having for example two energy levels for the intercalated wells, to a corrugated soft substrate with elastically moving wells, to the interplay between adhesion and friction with application to bio-systems, to the kinetic or dynamic case by means of the Langevin and/or Fokker-Planck methodologies, and so forth.

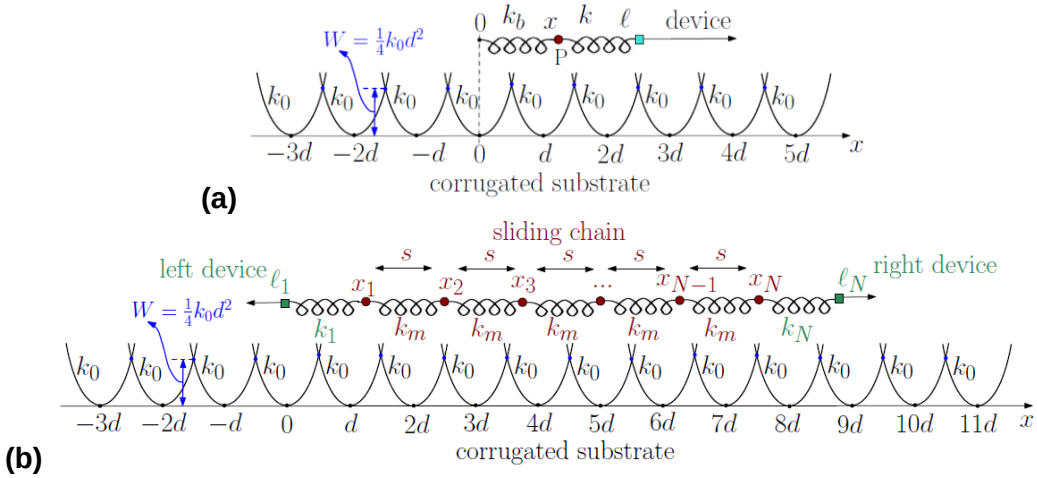

Fig.5. (a) Scheme of the modified Prandtl-Tomlinson model, where the sinusoidal substrate profile is substituted by a sequence of quadratic potentials with stiffness k_0 and placed at positions jd for any integer j. The energy barrier W characterizes the corrugated substrate. The particle at point P is linked by a first linear spring (constant k_b) to the origin of the x-axis, and by a second linear spring (constant k) to the position l, representing the sliding device. (b) Scheme of the modified Frenkel-Kontorova model, where the sinusoidal substrate profile is substituted by a sequence of quadratic potentials with stiffness k_0 and placed at positions jd. The mass-spring chain (elastic constant k_m, equilibrium length s), placed at $x_1,\ldots,x_N$, is linked by a first linear spring (constant k_1) to the position l_1 (left device), and by a second linear spring (constant k_N) to the position l_N (right device).

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3) *Le programme de travail avec les livrables et l'échéancier prévisionnel.*

First PhD year:
-Study of the literature concerning micro-instabilities in macromolecules and mechanical systems.
-Study of the statistical mechanics at equilibrium and non-equilibrium.
-Study of the spin variable approach useful to develop models of micro-instability.
-Study of the literature on sacrificial bonds in bio-systems.
-Implementation of a one-dimensional model first model of the toughness amplification with sacrificial bonds.
-Analysis of both Helmholtz and Gibbs ensembles.
-Comparison with experimental results and observation of points to improve.
-Development of a fully three-dimensional model of chains with sacrificial bonds.
-Deliverable: Software code implementing the model.
-Numerical implementation of previous model and application to real macromolecules.
-Redaction of an article on the modeling activity of sacrificial bonds.
-Application to nanotechnology devices.

Second PhD year:
-Study of the literature on supramolecular chemistry.
-Study of specific chains composed for example by catenanes and rotaxanes.
-Study of the classical freely jointed chain (FJC) model and the worm like chain (WLC) model for the force-extension behavior of polymers.
-Observation of the non-applicability of these theories to the exotic behavior of daisy chains.
-Development of new model adapted to these macromolecules.
-Implementation of the model in 1D, 2D and 3D geometries.
-Analysis of the model under Helmholtz and Gibbs ensembles.
-Deliverable: Software code implementing the models.
-Comparison with experimental results of the literature.
-Application to nanotechnology devices.
-Redaction of a paper on models of daisy chains.

Third PhD year:
-Study of molecular friction or nanofriction.
-Study of the Prandtl-Tomlinson model.
-Study of the Frenkel-Kontorova model.
-Study of the techniques of friction reduction (structural superlubricity, and the thermolubricity).
-Development of the statistical mechanics of the Prandtl-Tomlinson model.
-Development of the statistical mechanics of the Frenkel-Kontorova model.
-Implementation of the two models.
-Deliverable: Software code of the two models.
-Application to nanotechnology devices.
-Redaction of an article on molecular friction.
-Redaction of the thesis manuscript

4) *Les collaborations prévues* *(préciser le cadre, la nature des collaborations, l'ancrage régional, national, international, la transdisciplinarité éventuellement)**.***

University of Bari, Italy: Dr. **Giuseppe Florio ("coencadrant"), Department of Mathematics, Mechanics and Management (DMMM) of the Polytechnic of Bari,** and **Giuseppe Puglisi ("co-directeur")**, **Department of Civil Engineering Sciences and Architecture (DICAR) of the Polytechnic of Bari** are experts of mathematical, biophysical and nanomechanical problems studied by means of the methods of statistical physics. This international collaboration is already active (the PhD thesis of Andrea Cannizzo under a double-degree agreement is ongoing) and this PhD thesis is very useful to reinforce and continue the undertaken research activity. In particular, the international character of the collaboration will be exploited in the near future to create a group of partners working on the same subject, coordinated to participate in European projects or other international calls. In addition, a continuing cooperation agreement will be signed with Ecole Centrale de Lille. **Importantly, a double-degree Ph.D. agreement ("cotutelle") will be signed for this PhD program and the partners will surely fund this thesis at 50%, as indicated in the attached engagement letter.**

Within IEMN: **internal collaboration with Romain Peretti ("coencadrant", CNRS Researcher, Photonics Terahertz group),** expert in Optics/Nanophotonics in the THz for light matter interactions, Time Domain Spectroscopy (TDS), vibrational spectroscopy of large molecules and molecular complex, and optical trapping. This collaboration will allow for the experimental characterization of some macromolecules of interest for developing nano-sensors based on supramolecular chemistry.

The collaborations envisaged provide evidence of the **transdisciplinary** character of the proposed subject: indeed, for the success of the project, we have to combine statistical mathematical methods, theoretical physics methods, biological competence, material science skills and experimental measurements to achieve the desired results concerning the integration processes of macromolecules (via the biomimetic paradigm) in nanotechnology devices.

6) Une liste de 10 publications maximum portant directement sur le sujet en soulignant celles du laboratoire.

[1] Grégoire Perret, Thomas Lacornerie, Fabio Manca, Stefano **Giordano**, Momoko Kumemura, Nicolas Lafitte, Laurent Jalabert, Mehmet C. Tarhan, Eric F. Lartigau, Fabrizio Cleri, Hiroyuki Fujita and Dominique Collard, Real-time mechanical characterization of DNA degradation under therapeutic X-rays and its theoretical modeling, Nature Microsystems & Nanoengineering 2, 16062 (2016).
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[5] M. Benedito and **S. Giordano**, Thermodynamics of small systems with conformational transitions: the case of two-state freely jointed chains with extensible units, Journal of Chemical Physics 149, 054901 (2018).
[6] M. Benedito and **S. Giordano**, Isotensional and isometric force-extension response of chains with bistable units and Ising interactions, Physical Review E (**Editors' Suggestion**) 98, 052146 (2018).
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[8] L. Bellino, G. Florio, **S. Giordano**, and **G. Puglisi**, On the competition between interface energy and temperature in phase transition phenomena, Applications in Engineering Science, 2020, Vol. 2, 100009,
[9] G. Florio, **G. Puglisi**, and **S. Giordano**, Role of temperature in the decohesion of an elastic chain tethered to a substrate by onsite breakable links, Physical Review Research 2, 033227 (2020).
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ARGUMENTAIRE DU DIRECTEUR DE THESE

En quoi le sujet répond à l'un au moins des critères de priorisation de la Région ? *cf. Délibération de lancement de l'appel à projets Allocations n° 2021.02022 du 23 novembre 2021* https://delibinternet.hautsdefrance.fr/

Pour ce que concernent les stratégies affichées par l'I-SITE Université Lille Nord-Europe, les deux axes qui bénéficieront de cette recherche sont :

a) **Santé de précision : vers une approche personnalisée de la prévention et des traitements** *:* des connaissances théoriques approfondies sur la réponse nano-mécanique des macromolécules d'origine biologique sont au cœur de la compréhension des différents mécanismes biologiques. Tout cela peut avoir des répercussions importantes sur les stratégies thérapeutiques et diagnostiques.

b) **Science pour une planète en mutation : Troisième Révolution Industrielle et agricole, transition énergétique :** Les similitudes théoriques entre la micro-instabilité biophysique et celles observées en science des matériaux nous permettent d'utiliser les mêmes méthodes dans des problèmes très différents. En particulier, l'idée de biomimétisme peut être appliquée à la conception de dispositifs nanotechnologiques avec des macromolécules complexes et une variété d'applications allant des capteurs aux actionneurs en passant par la nano-médecine.

En quoi le sujet participe à la structuration de la recherche en Région ? *Indiquer si le sujet contribue ou non à un programme régional en cours ou envisagé, notamment un projet déposé au CPER 2021-2017, si le sujet est lié à l'arrivée d'un chercheur en région, à la création d'une nouvelle équipe, à un rapprochement d'équipes, à un projet collaboratif etc…*

Le projet contribue à la structuration de la recherche au niveau régional pour une raison principale: il favorise le rapprochement de deux groupes internes de l'**IEMN** (le groupe **AIMAN-FILM**, auquel appartient le promoteur du projet, et

le groupe **PHOTONICS-THz** qui concerne les dispositifs fonctionnant dans la gamme des térahertz). Grâce à la collaboration internationale avec l'**Université de Bari**, il sera possible d'avoir les candidatures des étudiants de l'**Université Polytechnique de Bari**, une école de renommée internationale.

En quoi le sujet s'inscrit dans les priorités du cofinanceur sollicité ?

La thèse est cofinancée par le « Politecnico di Bari », Italie, et le cofinancement a déjà été acquis selon la lettre d'engagement ci-jointe (un accord de cotutelle sera établi et signé). Le doctorant sera inscrit à l'Ecole Centrale de Lille. L'une des deux missions de l'**Ecole Centrale de Lille** est la recherche. L'activité proposée dans ce projet de thèse s'inscrit parfaitement dans la ligne de recherche « Nanotechnologie ». Il est aussi un projet clef inclus dans le programme scientifique du **Laboratoire International Associé LIA LICS** fortement soutenu par l'Ecole Centrale de Lille. Le directeur de thèse Stefano GIORDANO étant membre du LIA LICS et enseignant vacataire à l'Ecole Centrale de Lille, est en contact direct avec l'établissement d'inscription.

Pour les sujets en lien avec un partenariat public-privé ou un partenariat entre plusieurs laboratoires publics, quelles sont les modalités du partenariat ? *nature, moyens, propriété, partage et diffusion des résultats, encadrement et localisation du doctorant…*

Le projet n'est pas en lien avec un partenariat public-privé ou un partenariat entre plusieurs laboratoires publics.

En quoi le sujet pourrait être valorisé dans un cadre national, européen, international ?*conférences, publications*

La synergie entre la santé et les nanotechnologies est un sujet très porteur pour le futur de la science et pour les retombés directs dans le suivi thérapeutique, la production de nanomatériaux structurées avec propriétés ciblées et l'ingénierie de structures composites. Donc, les résultats de cette thèse peuvent avoir des retombées applicatives à niveau national comme international dans le domaine de la santé et des nanotechnologies. Les résultats obtenus seront publiés dans des conférences nationales et internationales et dans les revues internationales les plus prestigieuses, comme ce fut le cas pour les deux précédentes thèses financées par la région.

Quelles sont les perspectives de valorisation, de transfert et d'innovation sur le territoire des Hauts-de-France ?
Le projet contribue-t-il à la Stratégie Recherche Innovation de la région (S3) ? Si oui, pour quel Domaine d'Activité Stratégique ? D'une façon plus générale, quelles sont les retombées socio-économiques pour le territoire régional ?
https://delibinternet.hautsdefrance.fr/Docs/CommissionPermanente/2021/02/04/DELIBERATION/2021.00280_annexe.PDF

L'IEMN est fortement impliqué dans la Stratégie Recherche Innovation de la région (S3) pour la recherche scientifique en général et in particulier pour les plateformes académiques et le transfert de technologie. Les nanotechnologies développées à l'IEMN et étudiées dans ce projet de thèse sont utiles en particulier pour la piste de spécialisation « Santé de précision et maladies civilisationnelles ». L'intégration de fonctions macromoléculaires complexes dans les nanotechnologies peut générer des nouvelles ruptures technologiques dans les années qui viennent.

Le sujet peut-il ou non contribuer à la Troisième Révolution Industrielle (TRI) ? cf
Référentiel sur la TRI enseignement supérieur et recherche https://rev3.fr/enseignement-superieur-recherche/;
Les Hauts-de-France pionniers d'une économie durable et connectée
https://rev3.fr/wp-content/uploads/sites/7/2020/09/REV3_2020_BROCHURE_A4-23.pdf
Feuille de route Hydrogène https://www.hautsdefrance.fr/hydrogene-filiere-davenir/
Feuille de route Economie circulaire
https://delibinternet.hautsdefrance.fr/Docs/CommissionPermanente/2020/11/19/DELIBERATION/2020.02126_annexe.PDF

Les fondations de la troisième révolution industrielle doivent être basées sur l'innovation, elle-même basée sur la recherche fondamentale. Cette proposition de thèse concerne des aspects de recherche fondamentale liés à la biochimie, la biophysique, la science des matériaux et les nanosciences avec des effets applicatifs importants par exemple sur la santé, les nanotechnologies et les matériaux et nanomatériaux. L'idée qui soutient ce concept est qu'une véritable révolution industrielle moderne ne peut avoir lieu qu'avec le développement de solutions et d'idées innovantes qui ne peuvent provenir que de nouveaux paradigmes théoriques scientifiques. Comme déjà évoqué plus haut, les bénéfices de ce projet de thèse pour le contexte socio-économique, et en particulier pour la troisième révolution industrielle, doivent être imaginés à long terme pour laisser le temps à la recherche fondamentale d'atteindre le stade de maturation avec effets économiques sur le territoire (en particulier, pour les matériaux et/ou nanomatériaux et pour l'économie liée à la santé).

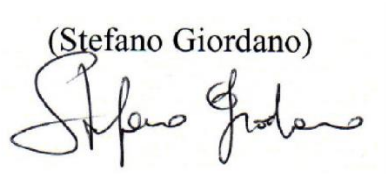
Le sujet peut-il contribuer à développer la bioéconomie en région ? *cf. master plan délibération n° 2018.1233 bioéconomie*
https://www.hautsdefrance.fr/categorie/dossiers/bioeconomie/

Le projet n'est pas directement lié à la bioéconomie mais porte sur des outils théoriques de recherche fondamentale qui peuvent contribuer à la compréhension des propriétés des macromolécules impliquées dans le remplacement des énergies fossiles avec des énergies dites "vertes".

Le sujet peut-il contribuer à développer l'intelligence artificielle ?
https://www.hautsdefrance.fr/humain-lambition-des-hauts-de-france-pour-une-intelligence-artificielle-au-service-des-habitants/

Le projet n'est pas directement lié à l'intelligence artificielle, mais par contre l'intelligence artificielle peut être utilisée dans un état avancé du projet pour aider à développer de nouveaux matériaux avec les propriétés souhaitées. En fait, la recherche de nouveaux matériaux s'appuie souvent sur le biomimétisme : on identifie un matériel biologique aux caractéristiques intéressantes et on étudie la microstructure pour comprendre comment naissent ses caractéristiques spéciales. Cela permet de la reproduire en créant des matériaux artificiels. On peut aussi imaginer de renverser cette logique. D'abord on peut spécifier les propriétés qu'on désire et après un logiciel va générer par calcul basé sur l'intelligence artificielle les microstructures idéales pour coller aux spécifications.

Fait à Villeneuve d'Ascq, le 6-12-2021



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LICS - Laboratoire International des phénomènes Critiques et Supercritiques

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