NANO *BIO* SCIENCE: BACK TO THE RENAISSANCE MAN

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Physics and biology have been courting each other throughout the last century, and are celebrating their engagement in this century, a match arranged by Nano *Bio* Science. Molecular and Cell Biophysics are basically a modern conception of life sciences at the nanoscopic scale.

The revolution brought about by microelectronics had a great impact in its time and its influence still surprises us today. We have not yet reached such a critical moment in nanotechnology, but from a scientific point of view, both revolutions are rooted in very different ways. Microelectronics, though highly influential in society at large, is limited to a very small part of science: the area of electronics, which does not even make up an area of knowledge in the discipline of physics. Nanotechnology, on the contrary, is expanding in such a way that it tends to involve all scientific disciplines. This is why a scientist working in nanotechnology must of necessity have wide-ranging up-to-date general knowledge; apart of course from specialist knowledge of the problems he deals with.

The Renaissance man, as well as having the desire to recover all the knowledge of the classical and mediaeval world, sought to understand and interrelate it. Galileo, with his famous principle of relativity, engaged in an incredible endeavour for that time: to connect concepts in physics, the most highly developed natural science at that time. It was an age when the scientific mindset started to accept the idea of continuity in knowledge: everything must be related, even though at the moment we may not understand how. We scientists of today continue to subscribe to this idea. One example which reflects this mindset is quantum mechanics and classical mechanics. Many endeavours of theoretical scientists have been directed at relating both areas of physics, but so far they have proved insufficient. Another example of the objective which many physicists pursue today is to relate Einstein's theory of gravitation with quantum theory. Science today is highly specialised, which means that is it very difficult to have, for example, a highly detailed knowledge of both molecular biology and quantum physics. However, the boundaries are starting to blur, so that the scientist of today needs to return to the ideal of the Renaissance Man. We find the best example in Nano *bio* science, fostered in Spain at centres such as IMDEA-Nanoscience, where science, technology and interdisciplinarity shake “nano-hands”.

A first misconception under which we may labour when approaching nanoscience is to associate it with one or two disciplines of knowledge. Nanotechnology is a concept which, by being based on the word "technology", would appear to imply first and foremost the disciplines of physics and engineering. However, not only is technology not exclusively a matter for these two disciplines, but actually it is precisely in the *nano* ambit where this lack of exclusivity is most evident. Like nanoscience, nanotechnology is built on a highly interdisciplinary scenario (1). The former represents applied research, and the latter, the base of foundations most directly related with observation.

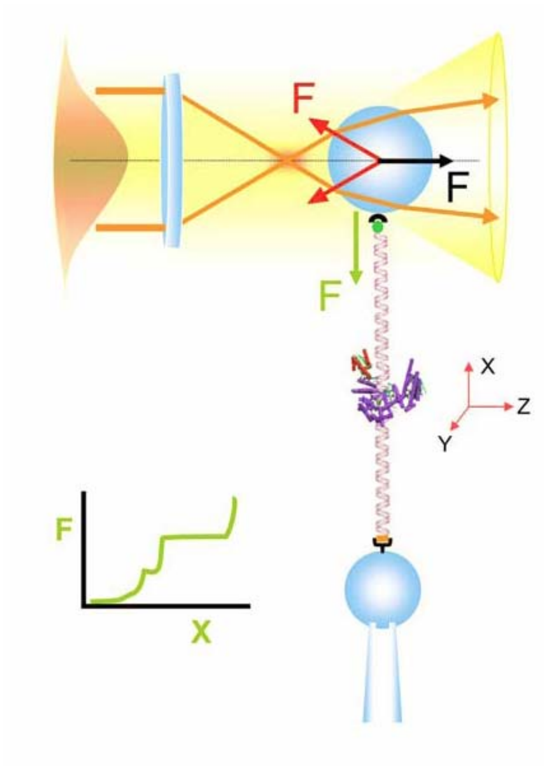

Fig. 1: *Diagram of the study of a molecular motor operating on DNA, for example a polymerase. Molecular motors are biological nanomachines which perform mechanical work typically consuming chemical energy and thermal energy from fluctuations. In the experiment shown, the DNA is engaged between two microspheres. The upper microsphere is held by Optical Tweezers, which make it possible to manipulate biological macromolecules by means of lasers, and measure in real time the ultra-small forces they develop, and also subsequent nanometric movements.*

Nanoscience is, from the point of view of physics, the study of all phenomena situated at a mesoscopic scale, which differs from the macroscopic in that it is not governed only by average behaviours and at the same time differs from the microscopic-quantum –which is not actually *micro* at all but *sub-nano*– as fluctuations are not an ingredient at the level of principle. At the mesoscopic scale, average behaviours exist but are greatly affected by fluctuations, which are deterministic in origin, and which make up an integral part of the behaviour of physical systems. From a biological point of view, nanoscience is situated at and below the cellular level. The fields of structural, molecular and genetic biology are clearly imbued with the objectives of the *nano* scale of science. Nanotechnology has been constituted as the executive and recombinant arm of all developments at nanometric level, and from this viewpoint, its future is practically yet to be written. Neither is biology only an ambit to which the applications of *nano* technology extend, nor does nanotechnology represent only the classical disciplines of knowledge filtered at the nanometric scale. Today it is at the *nano* scale that the space for scientific encounter arises with the greatest degree of interrelationship between disparate disciplines of knowledge. An example of this is the study of molecular biomachines, such as the one represented in figure 1.

The need to link, in the solution and framing of a problem, such different aspects of areas of physics, chemistry, engineering and computational sciences, goes beyond the improvement or design of more or less complex technologies and experimental techniques. In this connection, biology at molecular and cell level is not only benefiting from this new approach, but is itself providing a unique laboratory of phenomena at nanometric scale. One only has to think that the cell is a source –until only a few years ago an almost unnoticed source– of models for the development of nanotechnology, and these have been worked out under the efficient oversight of evolution.

Research in biology is becoming more quantitative, techniques are becoming gradually more sophisticated, and the discoveries that are being made stand increasingly at the crossroads of what were formerly considered to be separate disciplines. It is also surprising that basic research in the biology of that crossroads is having consequences and proposing applications that are relatively immediate in nanotechnology.

In the *Optical Nanomanipulation Laboratory* (see a detail in figure 2), at IMDEA-Nanoscience, we work in the field of Molecular and Cell Biophysics, furthering the study of the macromolecules that make up the machinery of cells. This laboratory attempts to increase our understanding of the molecules of life beyond the biochemical viewpoint. Looking at the cell from the perspective of physics one can see, on the one hand, that the cytoplasm is an overcrowded medium in which molecular structures such as motor proteins, chromosomes, ribosomes, nuclear pores, membrane channels, spindle apparatus and centromere, contractile ring, and so forth must operate in concert. Furthermore, one concludes that many of these structures are present in remarkably small numbers, each one working individually and subject to great fluctuations which in many cases form an integral part of their function.

Fig. 2: *Optical Nanomanipulation Lab at IMDEA-Nanoscience. Detail of the "Optical Tweezers" instrument, which measures the ultra-small forces developed by molecular motors.*

Biological molecules have traditionally been studied with bulk biochemical methods, where a large number of these are analysed simultaneously. These macroscopic experiments provide ensemble and time averages of the individual characteristics of each molecule. The set of deterministic properties and slow variation thus obtained result in an idealised image, that is, molecules with slow and well defined dynamics. Yet at the level of individual molecules, the picture is very different: one can find them in states that are far from the average behaviour of the population, and their instantaneous dynamics are rapid and highly random. At this level of detail, the macroscopic picture fails and a mesoscopic description becomes necessary.

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