Biofísica

SBE Magazine

Jan - Apr 2018
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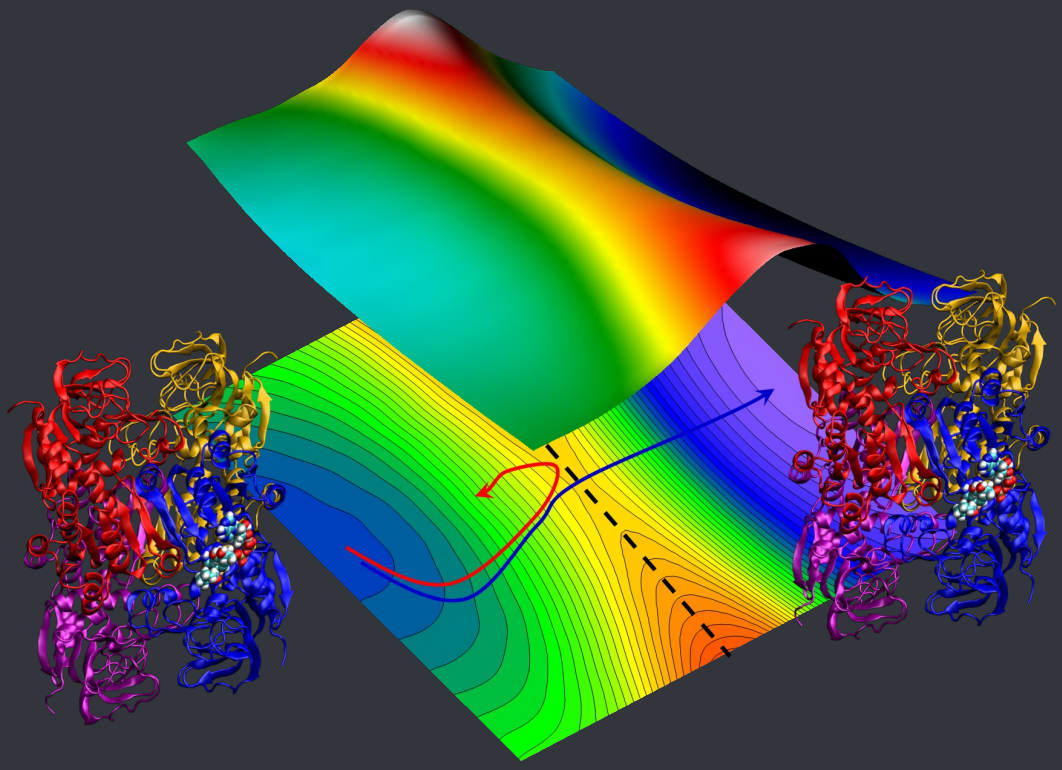

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SBE - Sociedad de Biofísica de España

ISSN 2445-43111

ISSN 2445-4311

CONTACT

SBE - Sociedad de Biofísica de España

Secretaria SBE, IQFR-CSIC,

C/Serrano 119, 28006 Madrid

Email: sbe_secretaria@sbe.es

WEB: http://www.sbe.es

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EDITORIAL / ANALYSIS

Science and post-truth

Jesús Salgado[1], Jorge Alegre-Cebollada[2], Xavier Daura[3], Teresa Giráldez[4]

[1]ICMol, UV, Valencia, [2]CNIC, Madrid, [3]ICREA, IBB-UAB, Barcelona, [4]CIBICAN, Universidad de La Laguna, Tenerife.

We live in a technological era, characterized by extensive, easy and quick access to information. Years ago, as we contemplated the rise of this *new age*, a common opinion was that it would contribute to spread knowledge to all layers of society, reinforcing democracy, equality, freedom and justice. Back in 2012 there was a positive general opinion about how internet was transforming our lives, as it was "changing, for the better, the relationship between governments and citizens and increasing the involvement of people in political debate" [1]. At that time we had increasing number of examples in the international scene about the prominent role of social networks in the flourishing of democracy in Tunisia, Egypt, Syria and other North Africa and middle East countries. But only a few years later the debate has made a sharp turn, and it now emphasizes fears and dangers of the potential of modern information technologies to blur reality and even manipulate, massively, people's opinion, while often serving to obscure interests. Unexpected results on US elections and UK Brexit referendum in 2016 consolidated the compound word *post-truth*, which was named Oxford Dictionaries' word of the year [2]. The post-truth concept had been introduced more than a decade before by Ralph Keyes [3] (previous to that, influential assays about the modern use of deceiving / persuading language were published in the 1980s [4, 5]). Meanwhile, we got used to other terms, like*fake news* and *alternative facts*, each of them with a particular connotation but all with roots in the same phenomenon.

Should Science and the scientists care about all that? According to the definition given by theOxford Dictionary, post-truth "denotes to circumstances in which objective facts are less influential than appeals to emotion and personal belief". Nothing can be more opposing to Science than the defeat of objective facts by some kind of *alternative* facts. It is easy to foresee that the post-truth era could turn into dark times for Science. Not in vain, implications of post-truth for Science are already being very actively discussed [6–10].

Nothing can be more opposing to Science than the defeat of objective facts by some kind of alternative facts

Post-truth means that there is a strong chance for triumph of weakly based (and even completely baseless) facts. Although this may sound unfeasible, it may indeed have deep connections with human nature. Back in the 1980s the use of inaccurate, and even *deceptive speech*, had been described as an intrinsic communication characteristic of mankind. On the other hand, idealized (mis-) conceptions, myths, fantasies, supra-natural explanations or conspiracy theories are probably as old as human culture and their intended use in order to manipulate people, with religious, political, economic or other interests, has been common in history. Thus, we might think that post-truth is in fact nothing new and that Science is well accustomed to coexist with it and well prepared to resist it. However, today's easy access to, and generalized use of extremely efficient tools for global and immediate dissemination of all kinds of information is unprecedented. Needless to say, the positive potential of these modern technologies for the progress and benefit of society, including Science, is unquestionable, but this does not prevent, as it happened before with other technological advances and discoveries, that they may be abused and misused.

> **The immediacy and brevity of messages in social network media facilitates judgment by motivated reasoning, with emotions dominating over facts**

It is, for example, preoccupying to learn, from words of one of the pioneers of social networks, that these platforms were intentionally tailored to exploit vulnerabilities in human psychology [**11**]. This ability *by design* of the social networks, which responds to their economic interests (trying to attract your time and attention as much as possible) constitutes a powerful *first level* of control of the communication process. Eventually, it may be used for the interest of persuaders, whose goal is spreading specific information. Here, the danger is that this *second level* may use the rules of so called persuasive communication, in which honesty is not the default position [**4**]. Finally, at a *third level*, the cycle completes from the side of the individuals who receive the information and re-opens again, multiple times, as these individuals resend the information, potentially propagating endlessly and exponentially. What happens at this third level is crucial to make this a very efficient communication process. The immediacy and brevity of messages in social network media facilitates judgment by motivated reasoning where, especially at short term, emotions dominate over facts [**12**, **13**]. The success is based on the good fit of the whole process with the characteristics of the modern information technologies, as well as the *satisfaction* of all actors involved: Individuals get rewarded by reaffirming their preexisting opinions and most believed ideas and simultaneously contribute to the initial persuader's interest by redistributing the information across their own networks, which in turn expands the number of users and consolidates their engagement. Meanwhile, in people's mind the flowing information enjoys a high level of credibility since it goes within the same framework (the same dominant social networks) used by trustworthy sources of information.

> **In the post-truth era, we can no longer assume that people recognize the authority of Science as provider and guardian of knowledge and reference for truth**

For what most directly may concern Science, an important negative face of post-truth is the vigorous propagation of visionary ideas commonly qualified as pseudo-science, often accompanied by attacks to regular sciences. Best known cases are related to medicine, like anti-vaccine movements, homeopathy or neuro-emotion therapy, which should be taken seriously since their spread relays on discrediting standard medicine and may end up putting the health of incautious followers at risk. Other important examples are different types of denialism that neglect mainstream scientific theories, like refusal to accept global warming, denial of evolution (by creationist and intelligent design theories) or pre-scientific conceptions of the universe (like advocacy of a flat earth and denial of moon landings). As scientists, we may be tempted to neglect this as anecdotic and stick to the idea that most people recognize the authority of Science as the provider and guardian of a corpus of standard knowledge that is the reference for truth. But in the post-truth era this can no longer be assumed. Thus, we are starting seeing pseudo-sciences making their way into University programs, professional societies and mass media, while denialism manages to influence the decisions of important governments. More than isolated episodes, this seems a real threat that concerns Science as a whole since it blurs the frontiers between scientific knowledge and beliefs, creates confusion in society and undermines the arguments and position of Science in its claim for continuing support. How should Science react to that?

Kathleen Higgins wrote recently in Nature [6] that

> *Scientists and philosophers should speak up when scientific findings are ignored by those in power or treated as mere matters of faith. Scientists must keep reminding society of the importance of the social mission of science – to provide the best information possible as the basis for public policy. And they should publicly affirm the intellectual virtues that they so effectively model: critical thinking, sustained inquiry and revision of beliefs on the basis of evidence.*

This statement calls for a novel task of Science that we should be prepared to fulfill. An obstacle for that mission can arise if scientists are taken as part of *the establishment* that, in the political and social sphere, has become widely discredited. We also have to be aware that recent claims of irreproducibility [14] or news pinpointing problems with plagiarism in academia [15] and weaknesses of peer-review [16] all contribute to erode the image of Science. Thus, our first objective should be to reconstruct and reinforce a solid reputation for Science, in a process that should be open and self-critical and also constructive and adaptable. Second, Science should be the solid pillar where people's thoughts can rest whenever they need to contrast information, acting as a visibly clear and recognizable source of trustworthy knowledge. This should allow room for discrepancy, criticism and skepticism, but not for pure and irrational denialism. And third, Science actors

Our first objective should be to reconstruct and reinforce a solid reputation for Science

(scientists and institutions) should get involved in the communication of scientific knowledge to society, assuming the responsibility and authority of being experts in a particular field, while adapting their language so that it can be understood by the public. To this end, we should be present where the debates are and where people get informed; i.e., we should disseminate Science using modern information technologies (from wikimedia to social networks). However, we should also be vigilant and keep away from the post-truth traps; in particular, never use persuasive communication while promoting our scientific or professional interests, as well as avoide creating false expectations or giving closed views which demotivate criticism.

Science has been a prominent actor of the technological era. It should now master it for the best of human kind.

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Biofísica Magazine

BEYOND BIOPHYSICS

Diseño de fármacos y búsqueda de nuevas dianas

Federico Gago, *Universidad de Alcalá (España)*

La industria farmacéutica, las instituciones académicas y los centros de investigación cuentan con dos aproximaciones principales para el descubrimiento de nuevos fármacos: (i) los conocidos como cribados fenotípicos, que no son otra cosa sino los ensayos tradicionales de medida de una actividad biológica y la posible observación de un cambio (positivo o negativo) en presencia de una determinada molécula candidata, y (ii) la identificación o creación de nuevas moléculas basada en el conocimiento de la estructura tridimensional de una macromolécula biológica que se utiliza como *diana*, sobre la cual actuará el fármaco. La imparable expansión de ambas estrategias en las últimas décadas ha sido propiciada de manera muy notable por impresionantes avances en el área de la biofísica, si bien las fronteras entre distintas disciplinas van difuminándose con el tiempo y se van imponiendo, afortunadamente, los conceptos de interdisciplinariedad y multidisciplinariedad. La propia biofísica, interesada en responder a preguntas fundamentales sobre las bases físicas de la vida, utiliza principios y métodos provenientes de la física fundamental y la biología celular pero también de la química, las matemáticas, la (bio)ingeniería y la computación, entre otras.

El descubrimiento de fármacos se ha beneficiado de las aportaciones de numerosas técnicas biofísicas desde prácticamente sus comienzos. Solo tenemos que pensar en los primeros experimentos de fisiología animal en los que se evocaban contracciones musculares o secreciones glandulares mediante estimulación eléctrica controlada. Fue cuestión de tiempo el que se observaran los mismos efectos, o su bloqueo, mediante la administración de alcaloides naturales y otras sustancias químicas sintéticas. El desarrollo de la instrumentación necesaria, incluyendo estimuladores, osciloscopios y polígrafos, fue fundamental para el progreso de la fisiología y la farmacología. La concesión del Premio Nobel en Fisiología o Medicina en 1991 a Erwin Neher y Bert Sakmann, de forma conjunta, *por sus descubrimientos relativos a la función de canales iónicos individuales en células* supuso un reconocimiento a la sinergia entre la biofísica y la biología celular, que nos ha llevado a una mejor comprensión de ciertas enfermedades (*canalopatías*) y ha proporcionado una herramienta (la amperometría en parche, o *patch clamp*) fundamental para el estudio de muchos fármacos. Otras metodologías biofísicas que resultan clave en las modernas plataformas de descubrimiento de fármacos son la espectroscopía de resonancia de plasmones superficiales – SPR, la calorimetría de titulación isotérmica – ITC, la espectrometría de masas tras ionización por electroespray – ESI-MS y la calorimetría diferencial de barrido – DSC. Los notables incrementos en velocidad, sensibilidad y aplicabilidad de las medidas han hecho posible una mejor comprensión de las uniones fármaco-receptor, en términos no solo de las afinidades clásicas, derivadas del cálculo de los valores de K_D, sino también de las elusivas constantes cinéticas de velocidad de asociación (k_{on}) y velocidad de disociación (k_{off}). Más aún, han facilitado el estudio de los componentes entálpicos y entrópicos de la unión, que no siempre se pueden entender en su totalidad, especialmente a la vista de las frecuentes compensaciones entre ambos. Esta información mecanística y termodinámica de alta resolución ha permitido comprobar que numerosos fármacos de última generación presentan tiempos de residencia particularmente prolongados y también que pequeñas diferencias en la composición de fármacos estrechamente emparentados pueden tener un efecto más grande del

El desarrollo de instrumentación fue fundamental para el progreso de la fisiología y la farmacología

anticipado sobre la cinética y la energética de la unión. Paralelamente, hemos asistido a una proliferación de técnicas de miniaturización, automatización y robotización que han hecho posible la realización rutinaria de cribados farmacológicos de altas prestaciones – HTS y uHTS en formatos de placas de 96, 384 ó 1536 micropocillos. Mediante su empleo, hoy en día es posible evaluar centenares o miles de moléculas de forma simultánea y en breves plazos de tiempo, especialmente en las empresas farmacéuticas.

Desde el punto de vista estructural, lo que ha progresado de forma casi inimaginable con relación a épocas pasadas es el conocimiento extraordinariamente detallado de los componentes moleculares de los seres vivos y su compleja organización y regulación. Con técnicas biofísicas, como la cristalografía de rayos X, la espectroscopía de RMN y la criomicroscopía electrónica, somos capaces de resolver las estructuras tridimensionales de muchas dianas farmacológicas con detalle atómico y apreciar de forma visual los huecos o espacios donde se unen las moléculas activas, ya sean sitios *ortostéricos* o *alostéricos*. En la actualidad podemos visualizar ensamblados macromoleculares que antes eran impensables (ribosomas bacterianos y eucarióticos completos fabricando cadenas polipeptídicas, polimerasas de ADN o ARN trabajando sobre sus plantillas de ácidos nucleicos y bloqueadas por lesiones o fármacos, complejos de proteínas reparadoras de ADN, etc). El uso extendido de estas metodologías ha dado lugar a una auténtica revolución en muchas áreas de la biología porque, junto con otras técnicas que utilizan moléculas fluorescentes, están permitiendo ver lo que antes era invisible al ojo humano y modelar de forma precisa estructuras biológicas muy sofisticadas, como son las vesículas intracelulares que contienen los neurotransmisores, los botones sinápticos de las neuronas o las partículas víricas.

En relación con la identificación de nuevas dianas farmacológicas, la aplicación de un número creciente de herramientas bioinformáticas, genéticas y proteómicas proporciona nuevos conocimientos de forma constante, no solo sobre el ser humano sino también sobre organismos patógenos. Esta información se puede convertir en estructuras atómicas con la ayuda de herramientas de modelado molecular y simulación, que han adquirido una madurez considerable en las últimas décadas y permiten profundizar en los fenómenos de reconocimiento molecular. Progresos constantes en el desarrollo de los campos de fuerzas, los algoritmos de dinámica molecular, los métodos híbridos QM/MM (que permiten tratar una parte del sistema mediante química cuántica – QM mientras el resto del sistema se simula mediante mecánica molecular – MM), así como en la computación distribuida y la implementación de códigos sobre procesadores gráficos – GPU han supuesto una confianza aumentada en estos métodos estrictamente teóricos y una aceleración masiva de los cálculos que permite alcanzar una escala de tiempos cada vez más próxima a la de los experimentos reales. Simultáneamente, la disponibilidad de colecciones enormes de moléculas (*quimiotecas*) y fragmentos moleculares hacen asequible a muchos investigadores la exploración, mediante algoritmos de acoplamiento (*docking*) automatizado, de posibles modos de unión a dianas seleccionadas. De este modo, el cribado *virtual* (o *in silico*) se puede utilizar para identificar y priorizar listas de moléculas candidatas para su posterior estudio experimental, y también para generar ideas que conduzcan al diseño de nuevas entidades químicas con potencial farmacológico.

> **La información que proporcionan estudios bioinformáticos, genéticos y proteómicos se puede convertir en estructuras atómicas con la ayuda de herramientas de modelado molecular y simulación**

En resumen, el panorama actual de la biofísica es muy esperanzador, especialmente para las generaciones más jóvenes, que disponen de una plétora de metodologías experimentales y teóricas, con una sólida base fisicoquímica, aplicables al estudio de las funciones de los seres vivos y con un potencial enorme en biomedicina. Los nuevos descubrimientos siempre generan nuevos interrogantes, por lo que me atrevo a vaticinar que no les quedará tiempo para el aburrimiento y que encontrarán su trabajo sumamente gratificante. No obstante, sería deseable que la educación de los futuros universitarios siguiera las recomendaciones de mi admirado Edward O. Wilson en su magnífico libro *Consilience: The unity of knowledge* y que las autoridades académicas reflexionaran seriamente sobre el manifiesto *La utilidad de lo inútil*, del profesor italiano Nuccio Ordine.

Federico Gago
Farmamol Lab, Departamento de Ciencias Biomédicas,
Universidad de Alcalá, Alcalá de Henares (Spain).
E-mail: federico.gago@uah.es

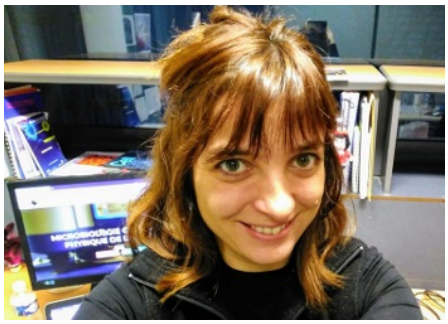
Biofísica Magazine

COOL BIOPHYSICS

High-Speed Atomic Force Microscopy

Probing the dynamics of biomolecules

Lorena Redondo-Morata, *INSERM, Marseille (France)*



Atomic Force Microscopy (AFM)-based studies constitute today a fairly established methodology to observe the structure of biomolecules and to measure their mechanical properties. However, biomolecules are *dynamic* in nature; hence, to understand how they work we need to increase the *spatiotemporal resolution* of conventional AFM. In the last decade, High-Speed AFM (HS-AFM) was developed and successfully applied to several cellular machineries, either cytoplasmic or bound to membranes. The molecular movies obtained by this method provide insights otherwise not accessible by other means to date. The technique itself, alone or combined with other techniques, is in continuous development and its relevance is foreseen to expand in the near future.

How it developed

In 2010, the team of Toshio Ando in Kanazawa University (Japan), filmed individual myosin molecules *walking* on an actin filament [1], operating their AFM instrument at a speed about 1000 times faster than the conventional instruments of that time (**Video 1**). Besides the visual impact and scientific value of those movies, these experiments illustrated that HS-AFM could obtain concomitantly structural and dynamic data, providing insights unmatched by any other method. But to understand how the development of HS-AFM was reached, let's walk first briefly through the history of the Scanning Probe Microscopy family.

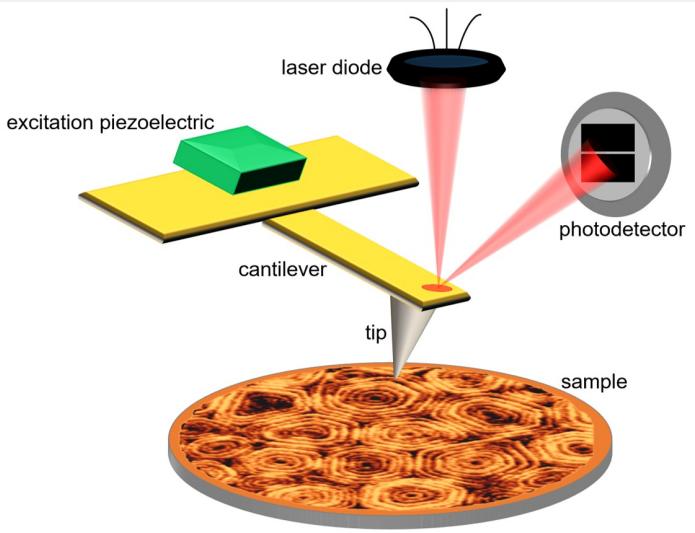


Figure 1. Schematic representation of an AFM instrument operated in tapping-mode
Thanks to a piezoactuator, the AFM cantilever is excited at its resonance frequency. The deflection of the oscillating cantilever is measured by a photodetector which collects the reflection of a laser beam focused at the back of the AFM cantilever.

Scanning Tunneling Microscopy – STM was invented in 1981 [2]. It was a conceptual revolution, because it bypassed the diffraction limit and exhibited a stunning atomic resolution –with higher sensitivity and lower energy consumption than the electron microscope. Five years later, Gerd Binnig and Heinrich Rohrer were awarded the Nobel Prize in Physics for the invention of the STM. As STM measures the tunneling current between a metallic tip and the sample surface, it requires this surface to be conductive. Therefore, it was not particularly suitable for biological samples –despite some circumvents, like covering the sample with a carbon or metal film. By 1986, the requirement about conductivity was overcome when Gerd Binning, Calvin Quate and Cristopher Gerber developed a variation of the STM: *Atomic Force Microscopy, AFM* [3]. The

AFM tip, which resembles a nanometer-sharp needle of a "record player" attached to a (micro)cantilever, *feels* the sample surface while scanning it using piezoelectric elements. An optical system is used to monitor the cantilever deflection (or force), thanks to a laser beam reflected on the back of the cantilever and detected by a photodiode. The change in deflection due to surface protrusions while the tip scans the sample is translated into electrical signals, thanks to a feedback mechanism. The AFM provides submolecular resolution of the topography of any type of surface, and can operate in aqueous environment on a wide variety of biological samples, from single molecules, such as DNA or proteins, to macromolecular assemblies, cells or tissues.

And yet, it moves

The frame rate of conventional AFM of one image every few minutes is not sufficient to visualize most dynamic processes of biological molecules, which take place in the majority of cases at sub-second time scales. Unlike other structural techniques that rely on ensemble averaging, such as X-ray crystallography, NMR or electron microscopy, single-molecule optical microscopy techniques are particularly well suited for the study of the dynamics of molecules. However, these latter methods rely on detection of fluorescent markers attached to proteins or lipids, which means that the resolution is limited to ~200 nm due to diffraction of light and to a few tens of nm thanks to super-resolution techniques. Besides, some other current techniques are pushing the limits in temporal resolution. This is the case, for example, of time-resolved serial femtosecond crystallography with X-ray free electron laser [4], although it is only pertinent to certain types of samples.

> **The frame rate limitation of conventional AFM was only practical**

In this scenario, AFM was a good candidate to occupy a niche in the myriad of biophysical techniques that tackle the dynamic visualization of molecules. The frame rate limitation of conventional AFM was not theoretical, but only practical. In the 1990s, two labs independently started efforts to achieve high speed AFM: Paul Hansma's group [5] in Santa Barbara (CA, USA) and Toshio Ando's group. The latter obtained a prototype in 2001 [6] which was practically developed for routine studies of biological samples in 2008 [7]. Currently, its functionality is being expanded, by applying different imaging modes, but mostly in combination with other techniques, such as fluorescence microscopy [8].

Optimization of the imaging rate

> **HS-AFM has successfully filmed a wide variety of samples, including proteins in action, membranes and cells**

For the study of biological samples, it is common to use AFM modes that have an intermittent tip-sample contact. Among them, the most often used is tapping-mode, in which the AFM cantilever is excited at its resonance frequency. The resulting *oscillating tip* is intermittently contacting -tapping- the surface, giving rise to a damped oscillation amplitude. The topography of the surface is reconstructed by monitoring the amplitude of the oscillating cantilever (**Fig. 1**). While scanning in the X-Y direction, the amplitude of the cantilever oscillation is kept constant thanks to a feedback control. HS-AFM is nowadays almost exclusively operated in tapping-mode to minimize the force or amount of energy caused by the tip-sample contact, at maximum rates of *5-10 frames per second* (fps) [9]. See for example the rotation and diffusion of the outer membrane protein F (OmpF) inserted in a lipid membrane (**Video 2**). In the video, acquired at ~2 fps, one can follow the organization of the trimeric structure of these channels in near-native conditions [10]. The technical developments which allow high-speed rates are based on the miniaturization of the moving components of the AFM (cantilever and scanner) to increase their velocity by 1000 times and thus be able to achieve reaction responses of microseconds. Below, I briefly detail the most important elements that allow the AFM to be operated at a video-rate:

1. Small cantilevers: The cantilever dimensions were reduced to 7 µm long, 2 µm wide and 90 nm thick (with respect to conventional cantilevers, 60-200 µm long, 100-170 µm wide and 400-800 nm thick). This point is crucial: the reduction in mass of these small microfabricated cantilevers allows for higher resonance frequencies and shorter response times (~1 µs). In order to get high-resolution imaging, long amorphous carbon deposits are grown on the cantilever, which serve as a tip once etched.
2. Fast scanners: The z-piezo actuator is subjected to high-frequency displacements during high-speed imaging,

hence it tends to generate mechanical vibrations. Thus, a dummy piezo is placed in the opposite direction and displaced simultaneously with the same length in order to counterbalance the impulsive force and therefore minimize the vibrations. Furthermore, each z-scanner is calibrated and the spurious frequencies are filtered out. The x- and y- piezo actuators are also smaller than in conventional AFM. Their center of masses are kept stationary using flexures to hold them and by attaching a balance weight to the counter side. They are also embedded in a silicon elastomer to passively damp vibrations.

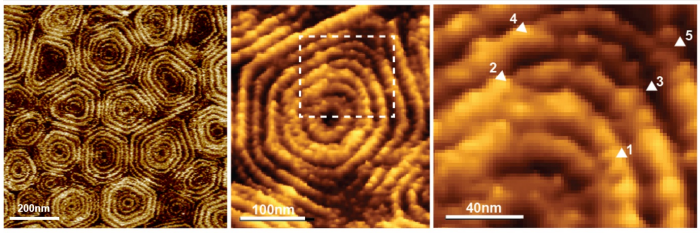


Figure 2. High-resolution AFM topographic image of a membrane area containing Snf7 patches. A large number of patches are shown in the panel on the *left* and one of them is enlarged in the *center* panel. The square drawn in this enlargement was zoomed and is shown on the *right*, where it reveals splits and variability of Snf7 structures. *Reproduced* from: Chiaruttini et al. *Cell* 2015, 163: 866 [13], CC BY NC ND 2015.

3. Fast amplitude detectors: The cantilever oscillation amplitude is measured and output by a Fourier method at every cycle of the oscillation.
4. Adaptive feedback: During fast imaging, the tip tends to "detach" completely from the surface at the downhill regions, an effect known as *parachuting*. To address this, a dynamic controller was developed, consisting in a Proportional-Integral-Derivative (PID) feedback controller that increases automatically the gain when downhill regions are scanned.

Still, we have to keep in mind that AFM is a surface technique, so the molecules of interest need to be adsorbed or be immobilized in a substrate. This, in turn, may restrict the natural interaction between molecules. Thus, for each system to be studied by HS-AFM, the conditions of sample, medium and substrate need to be optimized. Even so, molecules diffusing very fast on the surface can not be imaged by means of HS-AFM. Nevertheless, HS-AFM has successfully filmed a wide variety of samples, mostly proteins in action, but also membranes and cells, which has provided important insights about these systems. To review recent reports of dynamic imaging by HS-AFM see [**11**, **12**].

Sample case: HS-AFM imaging of membrane remodeling processes

HS-AFM has been recently fruitful to study membrane remodeling processes, particularly *fission* machineries. We studied the ESCRT-III (Endosomal Sorting Complex Required for Transport) system [**13**]. ESCRT-III is needed for lipid membrane remodeling in many cellular processes, from abscission to viral budding and the formation of late endosomes. However, how ESCRT-III polymerization generates membrane curvature remains debated. We showed that Snf7, the main component of ESCRT-III, polymerized into spirals at the surface of supported lipid bilayers (**Fig. 2**).

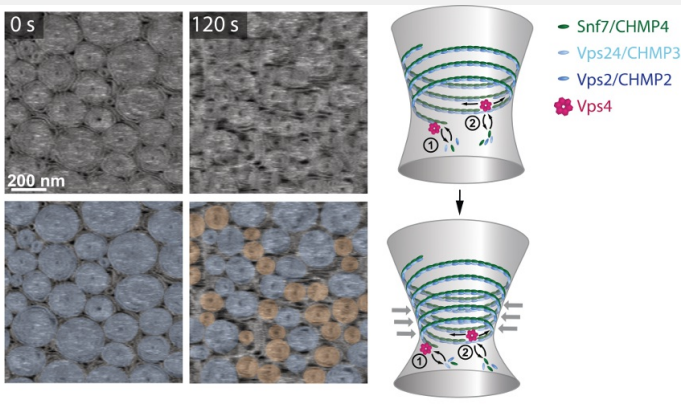


Figure 3. Vps4 induces a dynamic reorganization of ESCRT-III assemblies HS-AFM imaging of ESCRT-III polymers on supported lipid membranes, followed by the addition of Vps4 and ATP. The overlays highlight pre-formed spirals (*blue*) or newly formed spirals (*orange*). Our model suggests that Vps4 mediates continuous subunit turnover in ESCRT-III assemblies during growth and constriction. *Reproduced by permission* from Springer Nature: Mierzwa et al. *Nat Cell Biol* 2017, 19: 787 [15], *Copyright* 2017.

> **The spring-like activity of ESCRT-III could be the driving force for mediate membrane remodeling**

We were able to record HS-AFM movies of the Snf7 complex formation and its dynamics from filament to the maturated circular assembly around the membrane constriction site. We observed interfilament dynamics that provides a basis for a mechanistic explanation of how this protein machinery creates tension for membrane fission (**Video 3**). Furthermore, we showed that Snf7 assemblies compress the inner diameter during maturation, which constitutes a direct evidence of force generation during the

assembly process. When we disrupted the spirals with the AFM cantilever, the broken polymers spontaneously rearranged forming smaller rings, suggesting a preferred curvature of the Snd7 polymer of ~25 nm. We reasoned that Snf7 spirals could function as spiral springs. From measurements of the polymerization energy and the rigidity of Snf7 filaments, we concluded that they were deformed while growing in a confined area.

Furthermore, our dynamic data also suggest that the elastic expansion of compressed Snf7 spirals could stretch the lipids they are bound to, generating an area difference between the membrane leaflets and thus inducing curvature [13, 14]. This spring-like activity can be the driving force by which ESCRT-III could mediate membrane remodeling, which is a new property in this field.

In our most recent work, we studied the molecular role of Vps4, an ATPase that it is known to drive the disassembly of persisting filaments of ESCRT-III [15]. We observed that in the presence of Vps4, ESCRT-III polymers disassemble partially, remaining the most-inner part of the ring-like structure refractory to the action of the enzyme. Surprisingly, in the presence of a soluble Snf7 pool, ESCRT-III assemblies shrink under the action of Vps4, liberating free space in the membrane were new ESCRT-III assemblies are growing simultaneously (**Fig. 3** and **Video 4**). This results in a high exchange and lateral mobility of ESCRT-III assemblies on membranes. The dynamic exchange provides an explanation for how ESCRT-III filaments gradually adapt their shape during membrane constriction, which has broad implications in diverse cellular processes, differing in size, shape and duration –such as plasma membrane repair, cytokinesis or viral budding.

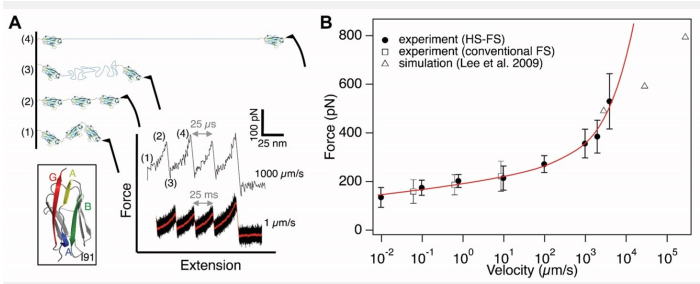


Figure 4. HS-FS of titin unfolding. (**a**) Schematic process of titin forced unfolding showing the relevant steps: (**1**) relaxed polyprotein, (**2**) polyprotein stretching, (**3**) unfolding of one domain and (**4**) unfolded domain stretching. Two examples of force extension curves revealing three unfolding peaks at 1 μm/s (*bottom*) and 1000 μm/s (*top*) are also shown. (**b**) Most probable force versus retraction velocity of titin unfolding using HS-FS (●), conventional AFM (□) and MD simulations (△). The red line is the fit of a model describing the response of the unfolding energy landscape. *Reproduced by permission* from John Wiley and Sons: Eghiaian et al. *FEBS Lett* 2014, 588: 3631 [12], *Copyright* 2014.

Beyond imaging: from molecular to cellular mechanics

The flexibility of the AFM cantilever also allows applying picoNewton forces to the sample. When the AFM is operated in force spectroscopy mode, the tip approaches and retracts from the surface with controlled force and velocity. This operation mode allows probing the mechanical properties of single molecules, membranes and living cells. Félix Rico *et al*. adapted the HS-AFM system to perform force spectroscopy measurements on single titin domains, which was unfolded at high velocities with microsecond time resolution [16]. Remarkably, the speed of these HS-AFM measurements -up to ~4 mm/s- reached that of molecular dynamics simulations, bridging the gap between the experiment and computational approaches and providing further insights into the mechanical behavior of biomolecules (**Fig. 4**). Most recently, the HS-AFM system was further adapted to study the microrheology of living cells over a wide dynamic range of frequencies [17].

Conclusions: progress and perspectives of the HS-AFM technique

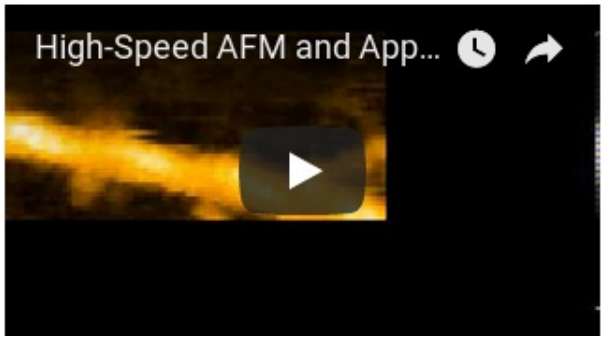
The possibilities of HS-AFM are still emerging and expanding. Some of the latest efforts are dedicated to observe dynamic and morphological changes in live cells, which imply the development of fast-wide area scanners and very long electron-beam deposited tips [18]. However, much of the future of HS-AFM seems to rely on its coupling with other techniques. The company RIBM in Japan has developed a tip-scan (not sample-stage scan) HS-AFM in order to correlate it with light microscopy. Fukuda *et al*. already have coupled it to a total internal reflection microscope [19] but the combination to other super-resolution optical microscopies remains to be explored. The team of Toshio Ando is working to combine HS-AFM with optical tweezers to visualize proteins under the application of an external force. Other advances will focus on the optimization of HS-AFM for different imaging modes; for example, to image in so-called

multimodal (exciting the cantilever at two or more resonance frequencies) or realize a high-speed mechanical mapping (a force curve in every pixel of the image). Such current and future developments could have a broad impact in biophysics, as they will likely allow further exploring the mechano-transduction pathways in cells and help opening new fields of discovery in basic and applied biological research.

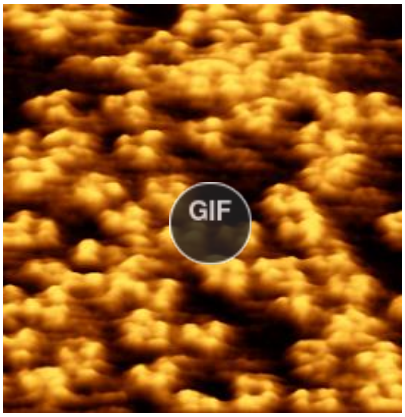
N.B.: I want to finish by noting that a significant amount of researchers pushing the HS-AFM methodology in European biophysics were, like myself (currently in Lille, France), formed in Spain. This is the case of my colleagues Félix Rico and Ignacio Casuso (in Marseille, France), Adai Colom (Aurélien Roux's lab in Geneva, Switzerland), Laura Picas (Montpellier, France) and Ignacio Munguira (Wouter Roos' team in Groningen, Netherlands).

Lorena Redondo-Morata
Force Microscopy for Biophysics Lab,
Institut de la Santé et la Recherche Médicale – Inserm U1006,
Aix-Marseille Université – AMU, Marseille (France).
Current address:
Cellular Microbiology and Physics of Infection Lab,
Institut de la Santé et la Recherche Médicale – Inserm U1019,
Institut Pasteur Lille, Marseille (France).
E-mail: lorena.redondo@inserm.fr

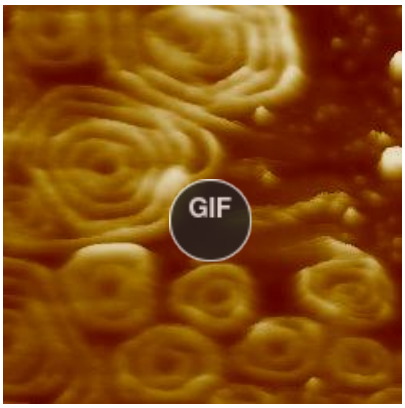
Movies



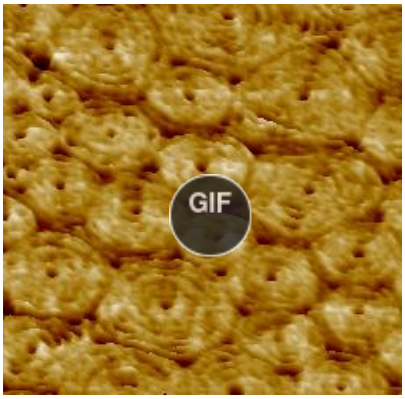
Video 1. Processive movement of myosin V under ATP hydrolysis, captured at 7 fps. Scan range, 130 nm × 65 nm. *Reproduced by permission* from Annual Reviews: Ando, Uchihashi & Kodera. *Annu Rev Biophys* 2013, 42: 393 [20], *Standard YouTube License* 2013.



Video 2. Diffusion of the bacterial outer membrane protein F (OmpF) on the membrane. The image size is 7.5 nm and was acquired at ~2 fps. *Reproduced by permission* from Springer Nature: Casuso et al. *Nat Nanotechnol* 2012, 7: 525 [10], *Copyright* 2012. Courtesy of Ignacio Casuso.



Video 3. Birth of new Snf7 spiral assemblies on a lipid bilayer. The frame size is 350 nm and was acquired at 1.2 fps. *Reproduced* from: Chiaruttini et al. *Cell* 2015, 163: 866 [13], CC BY NC ND 2015.



Video 4. Vps4 under ATP hydrolysis causes a non-equilibrium growing and shrinking behavior of concentric rings and spirals in 2D. The movie shows a constant turnover of subunits between the solution and the filaments. The frame size is 800 nm and the imaging speed 1 fps. *Reproduced by permission* from Springer Nature: Mierzwa et al. *Nat Cell Biol* 2017, 19: 787 [15], *Copyright* 2017.

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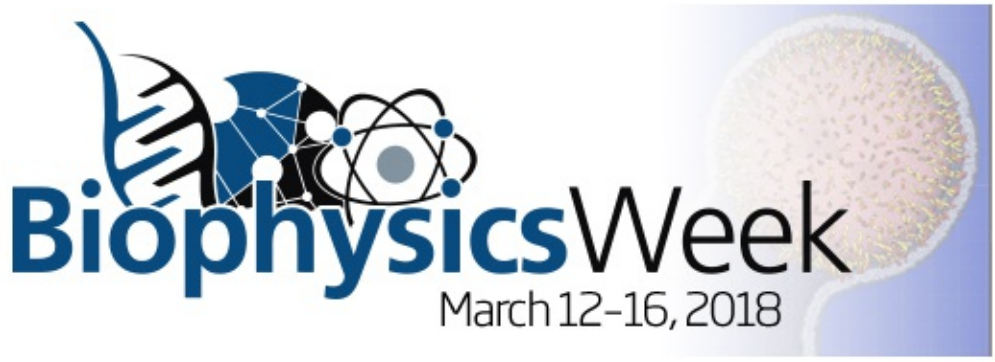
Biofísica Magazine

EVENTS / NEWS

BiophysicsWeek in Spain



Three members of the SBE will participate in one of the **BiophysicsWeek** initiatives (March 12-16, 2018), organized by the Biophysical Society to promote Biophysics all over the world.

Our three Biophysics Ambassadors are Teresa Giráldez (University of La Laguna), Carlo Manzo (University of Vic) and Jesús Pérez-Gil (Complutense University of Madrid). The events they are organizing will take place next Friday, March 16. Here you have some information about them:

The Biophysicist and the Pea

Organizer: Teresa Giráldez, University of La Laguna. La Laguna, Tenerife.

> *We will use games to introduce the most important findings of Biophysics to elementary school students.*

Scheduled time: Friday March 16th.

Bioday & Biophy...zza! / Quantitative Sciences: their role beyond academic research

Organizers: the QuBI lab and students & supervisors of Biology and Biotechnology at UVic.

> *One morning dedicated to bio-students to help them orient their career. The programe includes a talk by a professional from the industry about the role of quantitative studies of life and their valuable outside Academia, as well as round tables and flash presentations form researchers of UVic-UCC.*

Sponsors:

- UST – Facultat de Ciències i Tecnologia (UVic)
- UVIC – Vicerectorat de Recerca i transferència tecnològica

Place: Universitat de Vic – Campus Torre dels Frares. C/ de la Laura, 13 – 08500, Vic.
Scheduled time: Friday March 16th, 9:00 – 13:00.
Website: http://mon.uvic.cat/qubilab/**biophysweek**

Biophyzza Party / Women in Biophysics, Women in Science

Organizer: Jesús Pérez-Gil.

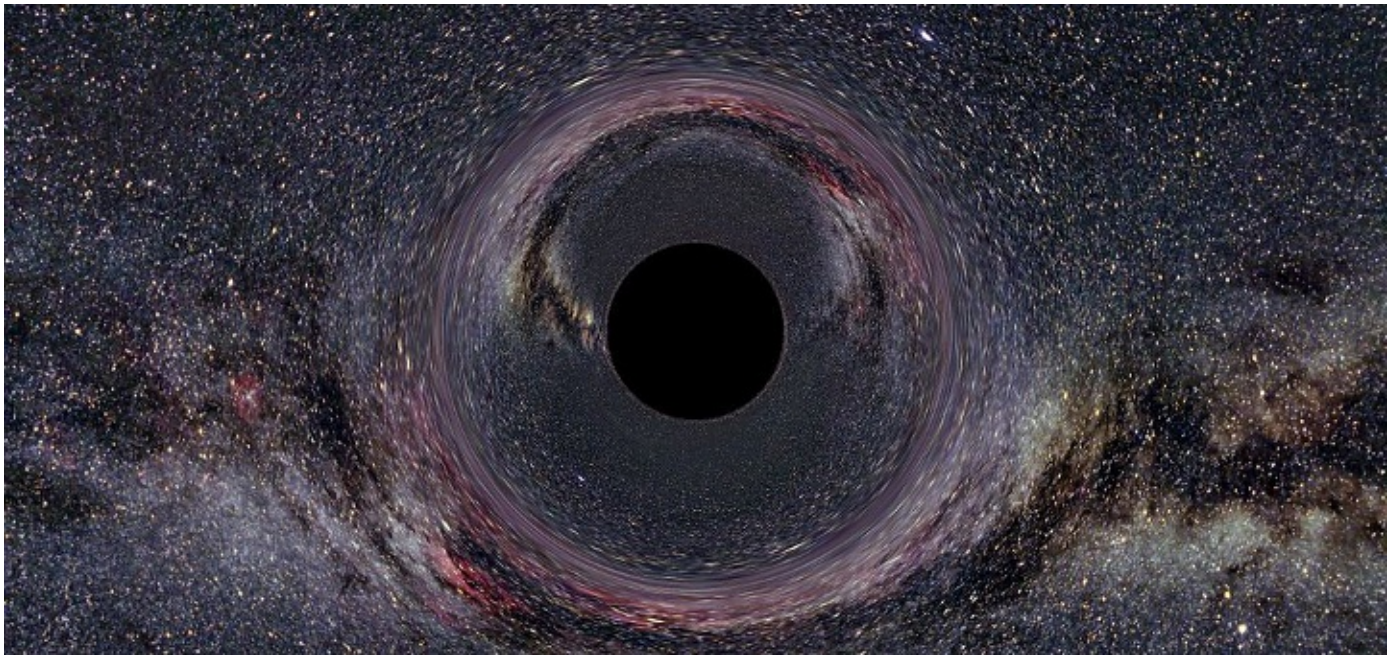
> *After last year's success, we are organizing the second edition of our Biophyzza Party! This year, high school students will also participate. They will highlight the contribution of well recognized women biophysicists, and will present motivating interviews with women biophysicists from all over the world. We will also have a Round Table of women biophysicists, from current students to Full Professors with a life of dedication, to debate about the participation of women in science and research as viewed over the years and the experience*

Place: Faculty of Biology, Complutense University of Madrid. Madrid.
Scheduled time: Friday March 16th, 17:00 – 21:00.
Website: https://**biophyzza2018**.wordpress.com/

Biofísica Magazine

NEWS

SBE adheres to the defence of Stephen Hawking after falsehoods and offences published in a blog backed by the ABC newspaper



Shortly after the dead of the distinguished physicist Stephen Hawking (Oxford, Jan. 8th 1942 – Cambridge Mar. 14th 2018), a libel was published in a blog backed by the Spanish newspaper ABC. The text ignores Hawking's prestige and broadly acknowledged scientific value. Instead, with clear political and religious motivations, mocks his theories and ideas as well as his successful efforts to popularize Science.

The Spanish Royal Physics Society – RSEF has promptly reacted to that infamous text by witting a letter to the Director of ABC, asking him to counteract the attacks on Hawking's honorability by publishing the letter, along with a link to the RSEF news, from where readers can find a selection of obituaries underlying the enormous personality of Stephen Hawking.

The Spanish Confederation of Scientific Societies – COSCE and the Biophysical Society of – SBE adhere to the letter written by the RSEF. The text, in Spanish, can be downloaded from http://rsef.es/images/Fisica/CartaDirectoABC.pdf.

Biofísica Magazine

AWARDS / NEWS

F. Javier Luque winner of the Bruker prize 2018

The Executive Council of SBE has awarded the 2018 *"Manuel Rico" – Bruker* prize to:

F. Javier Luque, *University of Barcelona (Barcelona, Spain)*,

> *For his exceptional scientific trajectory in the study of biomolecular systems and design of novel bioactive compounds, using a diverse array of theoretical and computational approaches, from quantum chemistry to classical simulations and molecular modeling.*

ABOUT DR. F. JAVIER LUQUE

Full Professor in Physical Chemistry at the University of Barcelona (Barcelona, Spain).

Scientific Trajectory

Dr. F. Javier Luque is Full Professor in Physical Chemistry at the University of Barcelona. He obtained his PhD degree in Chemistry at the University Autonoma de Barcelona in 1989. He spent research periods at the Swiss Federal Institute of Technology, University of Pisa and University of Nancy. In 2002 he was awarded the Catalan Distinction for the Promotion of University Research for Young Scientists, and the ICREA Academia award in 2012. He is leading the Computational Biology and Drug Design group in the Institute of Biomedicine, and is also member of the Institute of Theoretical and Computational Chemistry at the University of Barcelona.

The main focus of his research is the study of biomolecular systems using the theoretical and computational methods of quantum chemistry, classical simulations and molecular modeling. Special emphasis is made on the structure-dynamics-function relationships in proteins, the molecular determinants of biomolecular association and the design of novel bioactive compounds, specifically in drug discovery.

More information

Please, visit the website of the Computational biology and drug design group at the University of Barcelona.

ABOUT THE *"MANUEL RICO" – BRUKER* PRIZE

> *Awarded in memory of Professor Manuel Rico, who was a leading biophysicist, member of the SBE, and a Research Professor at the Institute of Chemical Physics 'Rocasolano', CSIC (Madrid). He was a pioneer using NMR technologies to study protein structure, stability, dynamics and interactions.*

Sponsored by

Bruker Española S.A.

Addressed to

Biophysicist who develope their main activity in Spain. **Preference** is given to members of the SBE working on Structure/Function problems from a Biophisics perspective.

Award

3000 € and a talk delivered by the awardee during a special session of the 6th Iberian / 10th Iberoamerican Biophysics Congress (Castellón, Spain June 20 – 22, 2018).

Past winners of this prize

- 2017: Alicia Alonso (Leioa-Bizkaia) and María García-Parajo (Barcelona).
- 2016: Xavier Gomis-Rüth (Barcelona).
- 2015: Juan A. Hermoso (Madrid).
- 2014: Óscar Llorca (Madrid).
- 2013: José Manuel Sánchez Ruiz (Granada) and Félix Ritort (Barcelona).
- 2012: Antonio V. Ferrer Montiel (Elche) and Marta Bruix (Madrid).
- 2011: Ignacio Fita (Barcelona).
- 2010: Modesto Orozco (Barcelona) and José Luis Rodríguez Arrondo (Bilbao).
- 2008: José García de la Torre (Murcia).
- 2006: Jesús Pérez Gil (Madrid).
- 2004: Javier Sancho (Zaragoza).
- 2002: José María Valpuesta (Madrid).
- 2000: Miquel Pons (Barcelona).
- 1998: Rafael Picorel (Zaragoza).

More information

Please, visit the SBE website.

Biofísica Magazine

AWARDS / NEWS

Pere Roca-Cusachs winner of the SBE-40 prize 2018

The Executive Council of SBE has awarded the 2018 *"Enrique Pérez-Payá" – SBE-40* prize to:

Pere Roca-Cusachs, *IBEC and University of Barcelona (Barcelona, Spain)*,

> *For his outstanding contributions to uncover the physical basis of cellular responses to mechanical signals.*

ABOUT DR. PERE ROCA-CUSACHS

Group leader at the Institute for Bioengineering of Catalonia – IBEC and Associate professor at the University of Barcelona (Barcelona, Spain).

Scientific Trajectory

Dr. Pere Roca-Cusachs obtained his PhD in cellular biophysics in 2007 from the Medical School at the University of Barcelona. He then worked in the lab of Prof. Michael Sheetz (Department of Biological Sciences, Columbia University) as a post-doctoral researcher until 2011. In 2011, he joined the University of Barcelona, where he is now an associate professor. In 2012, he obtained a joint position as group leader at the Institute for bioengineering of Catalonia (IBEC).

The research of his group focuses on unraveling the physical and molecular mechanisms by which cells detect and respond to mechanical signals. His contributions include the discovery of mechanisms explaining transcription

factor mechanosensitivity (Elosegui-Artola et al., Cell 2017) or cell sensing of extracellular matrix properties such as mechanical rigidity (Elosegui-Artola et al., Nat. Cell Biol. 2016) and ligand distribution (Oria et al., Nature 2017). He is currently the coordinator of an EU-funded Future and Emerging Technologies (FET) project dedicated to understanding the mechanical control of biological function. He is a recipient of the EMBO Young Investigator award, and the 2017 City of Barcelona award to the life sciences.

More information

Please, visit the website of the Cellular and molecular mechanobiology group at IBEC.

ABOUT THE *"ENRIQUE PÉREZ-PAYÁ" – SBE-40* PRIZE

> *Awarded in memory of Dr. Enrique Pérez-Payá, SBE member who contributed to the development, translation and internationalization of Biophysics in Spain. He worked on peptide-membrane interactions and apoptosis and was a pioneer in the use of combinatorial chemistry to expand the chemical space for basic research and to develop peptide-based therapeutics. He was also an entrepreneur and always supportive of young biophysicists.*

Sponsored by

BCN Peptides and Prima – Derm.

Addressed to

Biophysicist with age limit of 40 (in the year of publication of the call) who develope their main activity in Spain. **Preference** is given to members of SBE and to achievements from the last 10 years.

Award

1500 € and a talk delivered by the awardee during a special session of the 6th Iberian / 10th Iberoamerican Biophysics Congress (Castellón, Spain June 20 – 22, 2018).

Past winners of this prize

- 2017: Carlo Manzo (Vic-Barcelona) and Emilio J. Cocinero (Leioa-Bizkaia).
- 2016: Raúl Pérez-Jiménez (San Sebastián).
- 2015: Irene Diaz Moreno (Sevilla).
- 2014: Fernando Moreno (Madrid).
- 2013: Xavier Salvatella (Barcelona).
- 2012: José Manuel Gómez Vilar (Leioa-Bizkaia).
- 2011: Teresa Giráldez (La Laguna).
- 2010: Pau Bernardó (Barcelona).

More information

Please, visit the SBE website.

Biofísica Magazine

AWARDS / NEWS

Joan Camunas-Soler winner of the SBE-33 prize 2018

The Executive Council of SBE has awarded the 2018 *AntalGenics – SBE-33* prize to:

Joan Camunas-Soler, *Stanford University (CA, USA)*,

> *For his studies on binding reactions between nucleic acids and small ligands using single-molecule and non-equilibrium physics approaches and the development of new methods based on optical tweezers to measure the selectivity, thermodynamics and kinetics.*

ABOUT DR. JOAN CAMUNAS-SOLER

Postdoctoral Scholar at the Department of Bioengineering and Applied Physics. Stanford University (Stanford, CA, USA).

Scientific Trajectory

Dr. Camunas-Soler obtained his B.Sc. in Physics in the University of Barcelona and M. Sc. in Biophysics in the Royal Institute of Technology (KTH) in Stockholm. In 2015, he obtained his PhD under the supervision of Prof. Felix Ritort in the University of Barcelona, where he combined single-molecule methods and non-equilibrium physics to study binding reactions between nucleic acids and small ligands. In this work, he contributed to the formulation and experimental validation of non-equilibrium laws governing the dynamics of biomolecular systems. He also developed new experimental methods using optical tweezers to measure the selectivity, thermodynamics and

kinetics of small anticancer agents that target DNA. His doctoral work has been recognized through several awards such as the 'XXI Premi Claustre de Doctors' from University of Barcelona.

As a postdoctoral scholar in Stephen Quake lab (Stanford University), he is extending his field of expertise to the physics of larger biological systems, such as the cell and the genome. He is currently developing novel tools to dissect the relationship between the biophysical properties of cells and their genetic content. In particular he is combining electrophysiological measurements (patch-clamp) with single-cell RNA sequencing, to link the transcriptome of a cell to its functional response as observed from its electrical activity. He is currently using this set-up to characterize the functional response of human pancreatic cells and determine the genetic signatures explaining cellular dysfunction in diabetes. He combines this work with projects aiming to detect nucleic acids in blood as a tool for non-invasive diagnostics.

More information

Please, visit the website of the Stanford | Quake Lab at the Department of Bioengineering and Applied Physics. Stanford University.

ABOUT THE *ANTALGENICS – SBE-33* PRIZE

> *Recognizes the work of outstanding young Biophysicists, independently of the country where their work has been done.*

Sponsored by

AntalGenics.

Addressed to

Outstanding young Biophysicists with age limit of 33 (in the year of publication of the call), independently of the country where their work has been done. **Preference** is given to members of the SBE.

Award

1000 € and a talk delivered by the awardee during a special session of the 6th Iberian / 10th Iberoamerican Biophysics Congress (Castellón, Spain June 20 – 22, 2018).

Past winners of this prize

- 2017: María Queralt-Martín (Bethesda, USA) and Álvaro Inglés (Klosterneuburg, Austria).
- 2016: Lorena Redondo-Morata (Marseille, France).
- 2015: Cecilia Artola (Madrid, Spain).
- 2014: Jorge Alegre-Cebollada (Madrid, Spain).
- 2013: Anna Shnyrova (Bilbao, Spain).
- 2012: Sergi García Manyes (London, UK).

More information

Please, visit the SBE website.

Biofísica Magazine

AWARDS / NEWS

Imagin'Action winner 2018: Ancestral Nano Flowers, by Leyre Barandiaran Larrea

> *Combining phylogenetic and informatics tools we resurrect a laccase from up to 3000 million years. This Enzyme has been immobilized as organic-inorganic (copper- sulphate-protein) Nano flower.*

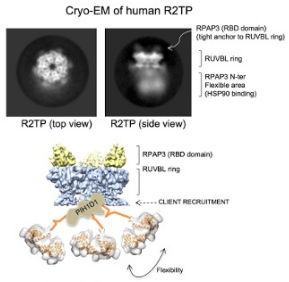
Pictures were obtained with a scanning electron microscope.

The image will be displayed in the main hall at the location of the 6th Iberian / 10th Iberoamerican Biophysics Congress (Castellón June 20 – 22, 2018). The prize consist on a free inscription to the meeting, plus a sum of money to cover travel expenses.

Biofísica Magazine

HIGHLIGHTED PUBLICATIONS: JANUARY - APRIL 2018

Papers of the month by SBE members



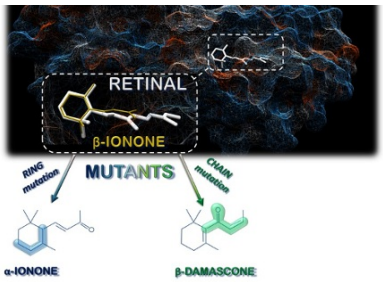
Martino...Llorca {*Nat Commun* 9: 1501}

HIGHLIGHTS 2018 | APR.

RPAP3 provides a flexible scaffold for coupling HSP90 to the human R2TP co-chaperone complex

Martino F, Pal M, Muñoz-Hernández H, Rodríguez CF, Núñez-Ramírez R, Gil-Carton D, Degliesposti G, Skehel JM, Roe SM, Prodromou C, Pearl LH, Llorca O

Nat Commun **2018** (Apr), 9: 1501



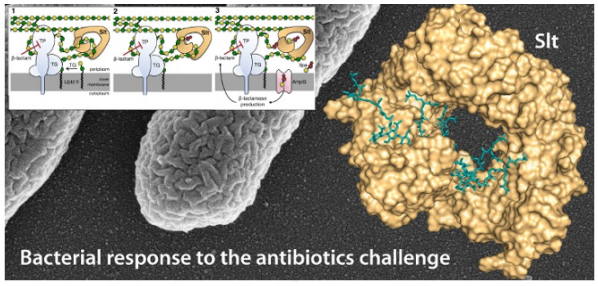
Uriarte...Cocinero {*J Phys Chem Lett* 9: 1497}

HIGHLIGHTS 2018 | APR.

Shapes, Dynamics, and Stability of upbeta-Ionone and Its Two Mutants Evidenced by High-Resolution Spectroscopy in the Gas Phase

Uriarte I, Melandri S, Maris A, Calabrese C, Cocinero EJ

J Phys Chem Lett **2018** (Apr), 9: 1497



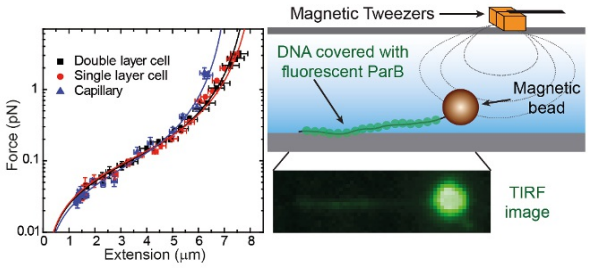
Lee...Hermoso, Mobashery {*Proc Natl Acad Sci USA* 115: 4393}

HIGHLIGHTS 2018 | APR.

Exolytic and endolytic turnover of peptidoglycan by lytic transglycosylase Slt ofPseudomonas aeruginosa

Lee M, Batuecas MT, Tomoshige S, Domínguez-Gil T, Mahasenan KV, Dik DA, Hesek D, Millán C, Usón I, Lastochkin E, Hermoso JA, Mobashery S

Proc Natl Acad Sci USA **2018** (Apr), 115: 4393



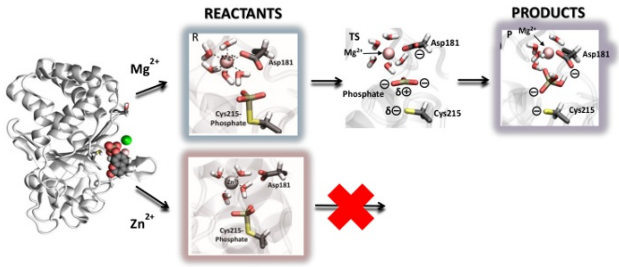
Madariaga-Marcos...Moreno-Herrero {*Nanoscale* 10: 4579}

HIGHLIGHTS 2018 | MAR.

Force determination in lateral magnetic tweezers combined with TIRF microscopy

Madariaga-Marcos J, Hormeño S, Pastrana CL, Fisher GLM, Dillingham MS, Moreno-Herrero F

Nanoscale **2018** (Mar), 10: 4579



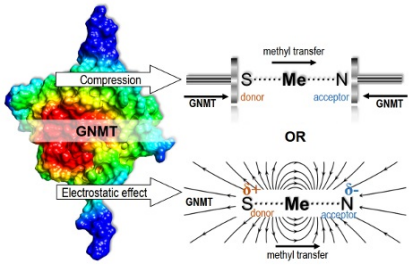
Bellomo...Domene {*J Am Chem Soc* 140: 4446}

HIGHLIGHTS 2018 | MAR.

Role of Zinc and Magnesium Ions in the Modulation of Phosphoryl Transfer in Protein Tyrosine Phosphatase 1B

Bellomo E, Abro A, Hogstrand C, Maret W, Domene C

J Am Chem Soc **2018** (Mar), 140: 4446



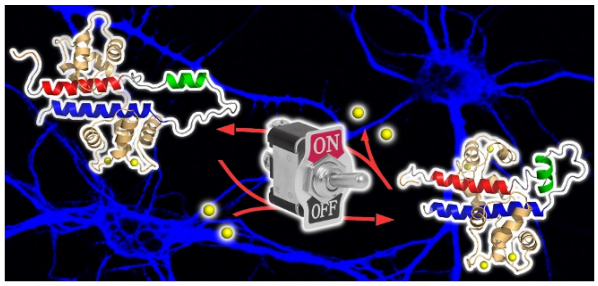
Swiderek...Moliner {*J Am Chem Soc* 140: 4327}

HIGHLIGHTS 2018 | MAR.

Insights on the Origin of Catalysis on Glycine N-Methyltransferase from Computational Modeling

Świderek K, Tuñón I, Williams IH, Moliner V

J Am Chem Soc **2018** (Mar), 140: 4327



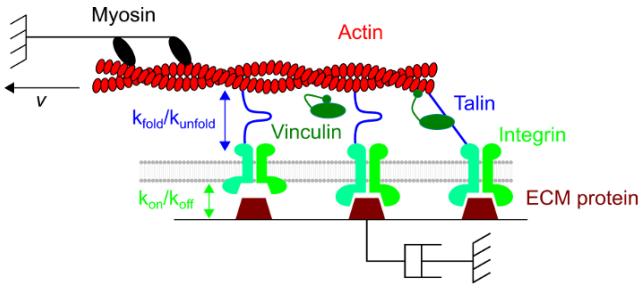
Bernardo-Seisdedos...Millet {*Proc Natl Acad Sci USA* 115: 2395}

HIGHLIGHTS 2018 | MAR.

Structural basis and energy landscape for the Ca2mathplusgating and calmodulation of the Kv7.2 Kmathpluschannel

Bernardo-Seisdedos G, Nuñez E, Gomis-Perez C, Malo C, Villarroel Á, Millet O

Proc Natl Acad Sci USA **2018** (Mar), 115: 2395



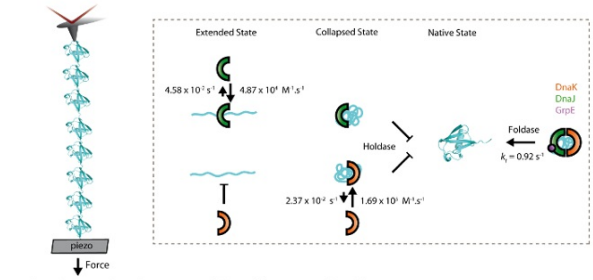
Bennett...Roca-Cusachs, Salmeron-Sanchez {*Proc Natl Acad Sci USA* 115: 1192}

HIGHLIGHTS 2018 | FEB.

Molecular clutch drives cell response to surface viscosity

Bennett M, Cantini M, Reboud J, Cooper JM, Roca-Cusachs P, Salmeron-Sanchez M

Proc Natl Acad Sci USA **2018** (Feb), 115: 1192



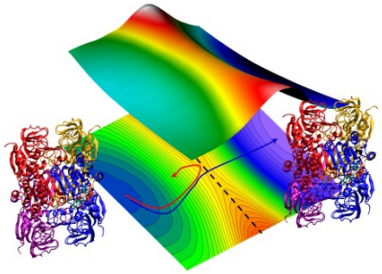
Perales-Calvo...Garcia-Manyes {*Sci Adv* 4: eaaq0243}

HIGHLIGHTS 2018 | FEB.

The force-dependent mechanism of DnaK-mediated mechanical folding

Perales-Calvo J, Giganti D, Stirnemann G, Garcia-Manyes S

Sci Adv **2018** (Feb), 4: eaaq0243



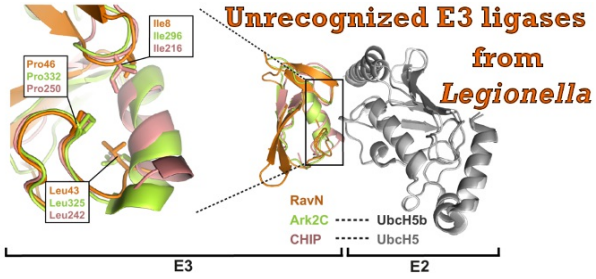
Behiry...Moliner, Allemann {*Angew Chem Int Ed Engl* 57: 3128}

HIGHLIGHTS 2018 | FEB.

Isotope Substitution of Promiscuous Alcohol Dehydrogenase Reveals the Origin of Substrate Preference in the Transition State

Behiry EM, Ruiz-Pernia JJ, Luk L, Tuñón I, Moliner V, Allemann RK

Angew Chem Int Ed **2018** (Feb), 57: 3128



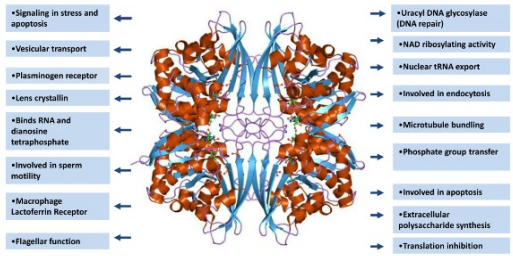
Lin...Hierro, Machner {*PLoS Pathog* 14: e1006897}

HIGHLIGHTS 2018 | FEB.

RavN is a member of a previously unrecognized group of Legionella pneumophila E3 ubiquitin ligases

Lin Y-H, Lucas M, Evans TR, Abascal-Palacios G, Doms AG, Beauchene NA, Rojas AL, Hierro A, Machner MP

PLoS Pathog **2018** (Feb), 14: e1006897



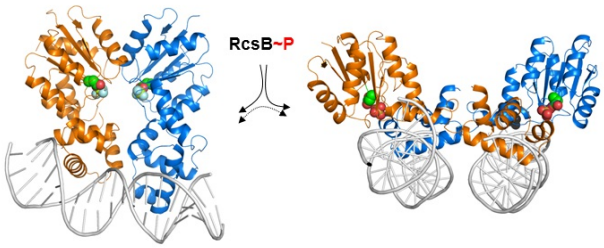
Franco-Serrano...Querol, Cedano {*Nucleic Acids Res* 46: D645}

HIGHLIGHTS 2017 | JAN.

MultitaskProtDB-II: an update of a database of multitasking/moonlighting proteins

Franco-Serrano L, Hernández S, Calvo A, Severi MA, Ferragut G, Pérez-Pons J, Piñol J, Pich Ò, Mozo-Villarias Á, Amela I, Querol E, Cedano J

Nucleic Acids Res **2017** (Jan), 46: D645



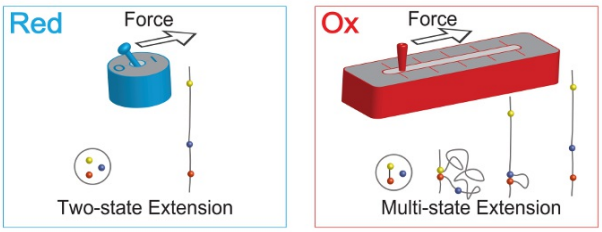
Casino...Marina {*Nucleic Acids Res* 46: 456}

HIGHLIGHTS 2017 | JAN.

Conformational dynamism for DNA interaction in the Salmonella RcsB response regulator

Casino P, Miguel-Romero L, Huesa J, García P, Portillo FG-d, Marina A

Nucleic Acids Res **2017** (Jan), 46: 456



Giganti...Alegre-Cebollada {*Nat Commun* 9: 185}

HIGHLIGHTS 2018 | JAN.

Disulfide isomerization reactions in titin immunoglobulin domains enable a mode of protein elasticity

Giganti D, Yan K, Badilla CL, Fernandez JM, Alegre-Cebollada J

Nat Commun **2018** (Jan), 9: