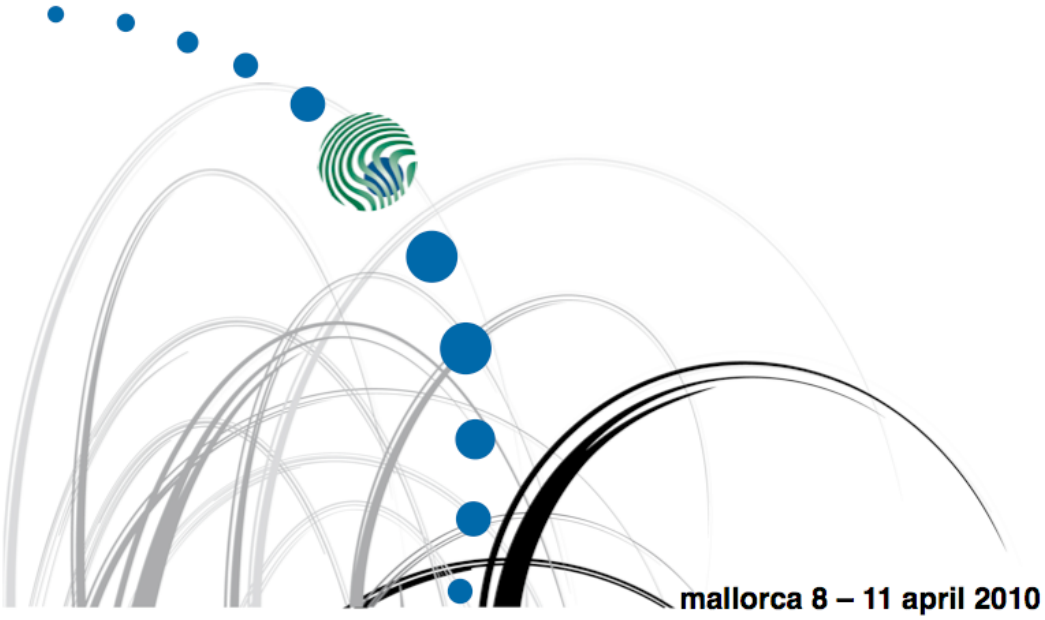
mechanics of large molecular assemblies

from single molecules to cell shape



Scientific Report

Summary

This workshop explored cell biological, biophysical and theoretical aspects of the dynamics of molecular assemblies. A particular focus was to understand the link between the behavior on cellular length- and time-scales and the dynamics at the single-molecule level. The workshop succeeded in bringing together experimentalists and theorists, and connected biological work aimed at understanding cellular behavior with theoretical approaches aimed at providing coarse-grained descriptions of the underlying physical mechanisms.

Many PhD students and PosDocs participated in the workshop, and they gave short talks about their work. The format allowed participants to give detailed talks, which prompted many fruitful scientific discussions that have even lead to incentives for formal collaborations.

Scientific content

The conference started Thursday morning with a session at the IFISC in the Son Lledo Auditorium at the UIB campus. **Emilio Hernandez-Garcia** welcomed the participants and opened the workshop with a scientific summary of the IFISC activities. **Jacques Prost** presented the first scientific talk and discussed novel hydrodynamic approaches for describing tissue dynamics. **Anthony Hyman** explored the biological principles that underlie cell division in *Caenorhabditis elegans* embryos. He was followed by two short talks from **Stephan Grill** and **Ewa Paluch**, who presented the ongoing activities in their respective laboratories.

The rest of the workshop took place at the Hotel Rural San Monnaber and explored two main topics: DNA motors, focusing on mechanical aspects of polymerase function; and mechanics of the cell actomyosin cortex. Both experimental and theoretical approaches to these problems were presented, triggering particularly lively and fruitful discussions between theorists and experimentalists.

1. DNA motors

Borja Ibarra showed fascinating single molecule work on DNA replication. **Marcus Jahnel** discussed the experimental apparatus that is used in such experiments, by measuring the non-harmonic potential in an optical trap. **Edgar Rolan** shifted the discussion towards theory, by illustrating how such a device could be used to construct a microscopic Szilard engine. Finally, **Abigail Klopper** presented theoretical investigations of DNA sequence variation on pausing of RNA polymerase.

2. The actomyosin cortex

The workshop covered a variety of aspects of the actomyosin cortex: speakers with a biology background presented new results on the molecular regulation of the cortex mechanical properties, biophysicists presented various techniques and approaches to study cortex mechanics, particularly insisting on the importance of theory to bridge the physical properties and the cortical cellular behaviors. Finally, novel findings on the function of the cortex in various processes, including cell division, adhesion, polarization and migration were presented.

Molecular regulation of cortex mechanics
Maté Biro, presented new tools using blebs (cortex-driven membrane protrusions) as a model system to analyze cortex assembly. **Andrew Clark** gave insights into experimental approaches that elucidate the role of various myosins in the generation of

cortical tension. **Mirjam Mayer** discussed the general relationship between tension and flow of cellular cortices. **Sundar Naganathan** further discussed a strategic approach towards identifying the function of all *C. elegans* actin binding proteins in the context of large-scale cortical flow. **Sebastian Fürthenauer** shifted the focus towards theoretical approaches, by discussing general principles that give rise to chiral movements in active polar fluids such as the cortex. **Ernesto Nicola** presented how molecular assemblies can give rise to patterns that are much larger than the assemblies, by presenting a mass-conserved reaction-diffusion mechanism for cellular polarization. **Justin Bois** brought the mechanics back into the interacting macromolecular assemblies, by discussing how mechanics and biochemistry can interact to give rise to novel types of biological patterns, such as those observed in the cortex during *C. elegans* polarization.

Role of the actomyosin cortex in cell and developmental biology
Carrie Cowan presented genetic and physical mechanisms that lead to the establishment of cortex polarity *C. elegans.* **Jakub Sedzinski** discussed the role of the cortex in cell division and gave insight into the mechanisms of cleavage furrow stabilization by cortical instabilities. **Martin Bergert** discussed the differences between blebs (cortex-driven protrusions) and lamellipodia during cell migration in culture. **Alba Diz-Munoz** addressed a similar question *in vivo* and presented experimental work on the role of membrane-to-cortex adhesion for protrusion formation in germ layer progenitor cells in zebrafish. Considering cell migration from a theoretical perspective, **Nicholas Licata** gave insights into the diffusion interaction during chemotaxis. Finally, **Jean-Leon Maitre** and **Helene Berthomieux** shared a talk on experimental and theoretical considerations of the role of the cortex in cell-cell adhesion of zebrafish germ layer progenitors.

Finally, **Juan Parrondo** gave a “general culture” evening lecture on how to detect active processes from time-reversal asymmetries.

Impacts and results

The meeting was an outstanding success. It has brought together people that tackle similar problems but with different approaches and backgrounds. The main aim of the workshop was to bring together theorists and experimentalists to discuss a central and recurrent problem: the systematic bridging of length-and time-scales when moving from single-molecule to cellular behavior. A large fraction of speakers directly addressed this problem, but of particular interest where those speakers that worked on either one of the two ends (e.g. Borja Ibarra for single molecules, or Carrie Cowan and Sundar Naganathan for cell biology) – these talks in particular sparked great discussion on how to systematically analyze the data presented in light of a theoretical framework for

bridging scales. A surprisingly large number of talks touched on biological structures essentially behaving like fluids; this was particularly clear in Anthony Hymans talk, which was nicely contrasted by the kinds of rigorous theoretical treatments of active fluid behavior that Jacques Prost discussed. In summary, we have seen an increasing application of active polar gel theories in many of the talks; it was impressive to learn how many different types of biological problems can be interpreted within this approach. It is likely that a generalized framework of active behavior of biological matter will be based on the types of concepts that Jacques Prost so nicely introduced in his opening seminar.

Finally, it was particularly nice to see that a large number of discussions were sparked amongst the different participants, some of which have already evolved into collaborations. Clearly, this workshop has formed new and strengthened existing connections between the IFISC in Palma de Mallorca, Institute Curie in Paris, the Max-Planck-Institutes in Dresden, the IMP in Vienna and the IMDEA in Madrid.

On the other hand, it is clear that the fruitful interactions between Biology and Physics can only strengthen in the future, as Physics offers a specially attractive playground to understand living matter, helping to design new experiments, while Biology offers a manifold of problems where to test physical theories.

The program and other information about the workshop can be checked in the workshop's web page:
http://ifisc.uib-csic.es/mlma10/

Schedule

Thursday, April 8
Son Lledó Auditorium on the UIB campus

10:00	Opening
10:10	Emilio Hernández-Garcı́a
10:30	Jacques Prost
11:30	Coffee
12:00	Anthony Hyman
13:00	Stephan Grill
13:15	Ewa Paluch
13:30	Lunch at Son Lledó Cafeteria
15:15	Transfer to Hotel Rural Son Monnaber Nou
16:30	Informal scientific discussion
20:00	Dinner

Friday, April 9
Conference room Rural Son Monnaber Nou

10:00	Carrie Cowan
10:45	Martin Bergert
11:10	Sebastian Fürthauer
11:35	Coffee
12:10	Andrew Clark
12:35	Sundar Naganathan
13:00	Maté Biro
13:30	Lunch
14:30	Informal scientific discussion, hike to the mountains, etc.
19:30	Dinner
21:00	Juan Parrondo

Saturday, April 10
Conference room Rural Son Monnaber Nou

10:00	Borja Ibarra
10:45	Mirjam Mayer
11:10	Alba Diz-Munoz
11:35	Coffee
12:15	Jean-Leon Maitre & Helene Bertomieux
12:40	Ernesto Nicola

13:15 Lunch
15:00 Justin Bois
15:25 Jakub Sedzinski
15:50 Abigail Klopper
16:15 Coffee
17:00 Nicholas Licata
17:25 Marcus Jahnel & Martin Behrndt
17:50 Edgar Roldan
19:30 Dinner

Sunday, April 11
Conference room Rural Son Monnaber Nou

10:00 Discussion: Emerging concepts and approaches
12:00 Closing
12:15 Bag Lunch
13:00 Departure

Invited talks

Jacques Prost discussed a novel physical description of tissue growth dynamics in simple geometries, introducing the notion of homeostatic pressure. The model is based on dynamical equations, which exhibit fluid-like behavior on time scales long compared to cell division and apoptosis times, in the vicinity of homeostatic conditions. The model predicts that when two tissues compete for space, in the absence of chemical signaling, the one, which has the largest homeostatic pressure, always wins and expands at the expense of the other. One physiologically important implication is that in order for a micro-tumor to grow, the tumor must exceed a critical radius.

Anthony Hyman presented the cell biological and biophysical mechanisms that underlie cellular polarization, focusing on the nematode *Caenorhabditis elegans.* He started off by presenting a historical perspective, illustrating how the area of molecular biology has succeeded in providing us with parts lists, and we now need to understand how the observed types of complex behaviors emerge from the functions of the components that take part. He went on to discuss this problem in light of polarity establishment, by discussing one of the key downstream effectors of the polarity pathway, so-called P granules. Work from his lab has shown that they have surprising liquid-like properties, with features rather like colloidal liquids. His lab is now investigating whether liquid like properties have more general relevance to assembly of the cytoskeleton.

Carrie Cowan discussed the cell biological events that trigger the establishment of cellular polarity, again in the nematode *Caenorhabditis elegans.* Her lab is focusing on the interplay between the actin and the microtubule cytoskeleton in the process of the triggering event, which appears to stem from a signal that is derived from the centrosome. She went on to discuss the modes of mobility that are available to the early centrosome, to understand how it is that this structure can move towards the cortex for delivering a spatial signal. Her lab is now focusing on the different biological factors that contribute to the accurate chain of events in this regard.

Juan Parrondo presented novel schemes of detecting irreversibility. He illustrated how it can be unambiguously determined from the analysis of a time series of a measured variable weather or not the physical mechanisms that give rise to the observed dynamics are themselves reversible. He particularly emphasized similarities and differences of his approach to arguments that are based on the so-called Shannon Entropy. He also highlighted the potential biological implication, and it was fascinating to see that very fundamental questions remain when thinking about irreversibility in the movement of molecular motors, for example.

Borja Ibarra talked about the micromechanical events that govern elongation by DNA Polymerases. He presented single molecule data that shows how movement of DNA polymerase is effected by template tension. He then went on to use this data to build a model for the underlying events, and discussed how these events depend on tension and force. He succeeded in providing a first mechanochemical description of proofreading and elongation by DNA polymerases. Importantly, his talk was a beautiful illustration of the type of knowledge on is able to attain through state-of-the-art single molecule mechanical perturbation experiments.