CENTER FOR
COMPLEXITY
& BIOSYSTEMS
University of Milan

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NEWSLETTER

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Looking ahead

STEFANO ZAPPERI
CC&B Coordinator

The Center for Complexity and Biosystems is completing its third year of activity and is therefore the right time to look back at what has been done so far, planning also for future activities. We have an intense record of 81 publications in international journals, including prestigious titles such as PNAS and Nature Communication, 29 conference proceedings and 74 invited talks at conferences, universities and research centers. CC&B researchers have made important progress on several interesting scientific topics including the mechanics of cell, tissues and a broad range of materials from graphene to glasses; the use of big data to understand genetic regulation and deregulation in obesity and regeneration; the measure of centrality in complex networks, protein aggregation in neurodegenerative diseases, phenotypic switching of cancer stem cells and the biophysics of microtubules and chromatin. The CC&B has also fulfilled its outreach mission by organizing a series of events including two summer schools on Advanced in Complex Systems at the Lake Como School of Advances Study and three editions of the CC&B workshop. Furthermore, members of the CC&B have contributed to the organization of eleven workshops and conferences on complex systems, computer science and biophysics. CC&B organized a series of 42 seminars by distinguished scientists from all around the world, discussing topics at the frontiers between physics, biology and computer science. The CC&B is now well known even beyond academia and research, with more than 100 appearances on radio, TV, newspapers and web.

Beside scientific seminars, we organized talks on research and data integrity, training sessions on image analysis and journal clubs on the latest research developments. We firmly believe that the training of young researchers should not only focus on the required technical skills, but should also aim at a deep understanding of the fundamental importance of correct data handling, storing and sharing. Images and data should be treated with the greatest care and be available for further analysis by fellow scientists. To this end, the CC&B has acquired a data storage facility and maintains a git software repository where all the algorithms used to produce scientific papers are available to the research community.

For the coming three years, our goal will be to consolidate the profile of the CC&B as a key international player in the study of complex systems. This aim will be pursued by broadening our international collaboration network, currently involving 30 research institutions, inviting visiting researchers for extended stays at the CC&B and continuing our seminar, conference and outreach activities. The CC&B welcomes the entry of three new colleagues, Giacomo Aletti, Alessandra Micheletti and Giovanni Naldi, who will bring to the center their expertise in applied mathematics and statistics. The steering committee will be enriched by two new high profile international members: Eytan Domany, professor at the Department of Physics of Complex Systems of the Weizmann institute of Science, and Herbert Levine, director of the Center for Theoretical Biological Physics at Rice University. From the scientific point of view, the research goals of the CC&B will revolve on reconstructing gene regulatory networks in physiological and pathological conditions through computational modeling and data analysis, using methods of artificial intelligence such as deep learning to read genetic and transcriptomic data. We will continue our investigations at the frontier between physics and biology, tackling the role of mechanics in the behavior of cells and tissues, and in the design of new smart bio-inspired materials and meta-materials.

Evolution: Common genetic signature of animal regeneration

All animals capable of regenerating a lost body part, from an organ or a limb to the whole organism, share a common set of genes. This is the striking discovery of a team of researchers from the Center for Complexity and Biosystems (CC&B) of the University of Milan.

The capacity to replace damaged or lost parts following injury without scarring or loss of functionality is widespread among almost all animals, but with many major differences. Regeneration capabilities range from the replacement of organs, tissues, and limbs up to the complete regrowth of whole organisms from body fragments, and can vary during the life cycle and with age. In principle, every organism maintains some capability to regenerate. However, while invertebrates can regenerate complex structures and even the whole body, amphibians are the only vertebrates that can regenerate anatomically complete and fully functional tissues and organs. Mammals have the regenerative capacity to restore the function of the liver, but recover only the organ mass and not its anatomy.

"We looked at the genes involved in regeneration in different animals, in order to understand why mammals lost the ability to regrow amputated body parts", explains Maria Rita Fumagalli, postdoc researcher at CC&B and leading author of the study, published on Systems Biology and Applications.

Researchers from CC&B selected three well-known model organisms with high regeneration capacity, hydra, planaria and sea cucumber, and analysed their genome at different times after an injury, in order to see which genes activate and at which point of the regeneration process. They then compared their results with previous data from mouse liver regeneration. What they found is that different animals activate a similar set of genes during the early regeneration phase. This suggests that there is a remembrance of a primordial regeneration capacity that is common to all organisms, including mammals. On the other hand, genes involved during late regeneration are related to the characteristics of the specific tissue or organism considered.

CC&B researchers also investigated the genes involved in inflammatory response, which is not only a defense mechanism against external microbes, but also plays a crucial role during regeneration. Their analysis revealed that, in the early inflammatory response after injury in hydra, planaria and sea cucumber, there is an activation of genes related to immune system cells similar to the mammalian ones, like macrophages and neutrophils. Which means that, in mammals, the regenerative capacity lost during evolution might have been replaced by the presence of a complex immune response acting during tissue repair.

Altogether, this study helped uncover the presence of a set of genes whose expression and function are critical among all species during early regeneration, suggesting the importance of these genes for their survival.

"The discovery of this shared genetic signature is of great importance for the understanding of how regeneration evolved and could be useful for future regeneration therapies", claims Caterina La Porta, professor of General Pathology at the Department of Environmental Sciences and Policy of the University of Milan and coordinator of the research. In fact, inhibiting these genes might prove to be a useful approach to treat pathologies due to excessive fibrosis in humans.

Regeneration in distantly related species: common strategies and pathways
Maria Rita Fumagalli, Stefano Zapperi and Caterina A. M. La Porta
npj Systems Biology and Applications. 2017.
https://www.nature.com/articles/s41540-017-0042-z

Three questions to...
Maria Rita Fumagalli

Postdoctoral Research Fellow at Università degli Studi di Milano

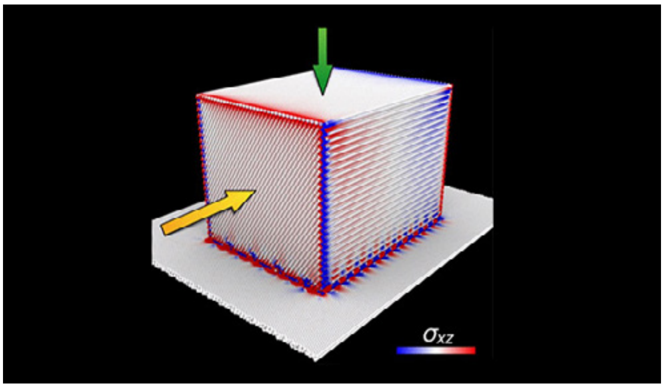
What's your field of research?
My research interests are mainly related to the study of common pattern of evolution in different biological systems. Since I have a quantitative background, I approach biological complex systems through both data analysis and modelling, but with a highly interdisciplinary attitude due to a constant collaboration with biologists. The increasing availability of -omics data allows to investigate various aspects of evolutionary conservation in a huge number of species.

What is the relationship between regeneration and the immune system?
The regenerative capabilities of an organism appear to be strictly linked to the immune system. Inflammatory response after injury is not only a defence mechanism against external microbes, but also plays a crucial role during tissue repair. Indeed, we observed a signature of the presence of a primordial immune response in very simple animals at early stages of regeneration. However, the acquisition of a more complex immune response is also often associated with scarring or fibrosis and has been suggested to contribute to impair tissue repair in vertebrates. This is a very intriguing aspect of evolution: increasing of complexity is not free of charge.

What are the main possible outcomes of your research and what impact could they have on evolutionary biology and medical research?

The aim of my work was to study whether different regeneration processes in unrelated species share a common genetic signature. Interestingly, a core of highly conserved and co-expressed genes have been shown to be involved in this process in very distant organisms, such as mouse and hydra. Thus, failure during regeneration process could be due to the involvement of multiple actors, such as the immune system related cells. Disentangling the complexity of regeneration process could help to find strategies to reduce excessive fibrosis in tissue after injury.

Frictional fronts: from atomic to tectonic scales



What happens when we make an object slide on a surface? Friction will prevent motion until the force we apply is strong enough. Friction is important in everyday life, allowing us to walk without slipping, and has far reaching technological implications for the functioning of mechanical devices and relevance for geological phenomena such as avalanches and earthquakes. The static friction force, as described by Amontons and Coulomb centuries ago, is proportional to the normal load and independent of the apparent contact area and can thus be described with a single parameter. Recent work showed, however, that the picture is more complicated. At the macroscopic level, frictional slip is ruled by the propagation of a shear crack breaking contact interface so that the process is similar to fracture.

Researchers from the Center for Complexity and Biosystems of the University of Milan decided to investigate friction at the atomic scale. To this end, they simulated the motion of an aluminium block pushed over a copper substrate. This is an idealized atomic scale system, with a perfect crystalline block moving over a perfectly ordered surface. As in macroscopic samples, if the lateral force applied to the block is not strong enough to overcome the friction due to the interaction between aluminium and copper atoms at the interface, then the block does not move. When the lateral force reaches a given threshold, the block instead slides over the substrate. Between the stable and moving phase, CC&B researchers identified a precursory activity, associated with the propagation and arrest of shear fronts on the contact interface, that is similar to the one observed in macroscopic objects in contact, or even at geological scales when tectonic plates are sliding against each other. In this nanoscale system, however, fronts display specific atomic-scale features due to the periodicity of the two crystals in contact and can not be described by macroscopic continuum mechanics.

The results of this study clearly shows that dynamic front propagation arises already at the atomic scales and shed light on the connections between nanoscale and macroscopic friction. The work is published in the recent issue of the Journal of Physical Chemistry Letters and is supported by ERC project SIZEFFECTS whose goal is to investigate how materials deforms at different length-scales.

Atomic-Scale Front Propagation at the Onset of Frictional Sliding
Silvia Bonfanti, Alessandro Taloni, Carlotta Negri,
Alessandro L. Sellerio, Nicola Manini and Stefano Zapperi
J. Phys. Chem. Lett., 2017, 8, pp 5438–5443
http://pubs.acs.org/doi/10.1021/acs.jpclett.7b02414

>>> RECENT RESEARCH FROM CC&B

BUbiNG: Massive Crawling for the Masses

by Paolo Boldi, Andrea Marino, Massimo Santini, Sebastiano Vigna

published in ACM Trans. Web (2018)

Excitation spectra in crystal plasticity

by Markus Ovaska, Arttu Lehtinen, Mikko J. Alava, Lasse Laurson, and Stefano Zapperi

published in Phys. Rev. Lett1 19, 265501 (2017)

Integrating experiment, theory and simulation to determine the structure and dynamics of mammalian chromosomes

by G. Tiana and L. Giorgetti

published in Curr. Opin. Struct. Biol. 49 , 11 (2018)

Three questions to...
Silvia Bonfanti
Postdoctoral Fellow at Università degli Studi di Milano

What's your field of research?
My field of research is physics of complex systems; specifically my interests encompass a wide variety of subjects ranging from biophysics to condensed matter physics.
It is always surprising for me to discover how the complex behaviour of many diverse systems is largely based on the same principles.
For example, some of the concepts that I am applying to the study of protein folding, such as the rugged energy landscape, have been developed in the study of glasses. Computer simulations are the main tools that I use to tackle such different systems, capturing their universal behaviours and gaining new insights.

Why it is important to study friction dynamics at both the atomic and the macroscopic level?
Friction is ubiquitous in nature: from the sliding of the chalk on the blackboard up to the complex evolution of an earthquake, it involves many different time and length scales. Although this phenomenon has been studied since long time for many industrial and technological applications, the microscopic origin of friction is still unsolved, representing an active research field. As it can be naively deemed, macroscopic friction should emerge from atomic scale complex interactions and processes at the contact interface. However, bridging the gap between micro and macro-scales is an extremely challenging problem that we are studying in our group. Furthermore, investigating friction at the nanoscale level is essential to keep up with recent advances of nanotechnology and nanobiology.

What are the main possible outcomes of your research?
In our recent paper, we studied the onset of frictional slip on the atomic scale by simulating the motion of an aluminum block pushed by a slider on a copper substrate. We identified the formation of dynamic slip front propagation and precursory activity of the frictional slip, which are hallmarks of dynamical aspects of friction observed in macroscopic experiments. The analysis of stress patterns during slip, however, revealed subtle effects due to the lattice structures that originate from the nature of atomic scale, which hinders a direct application of linear elastic fracture mechanics. Our results illustrate that the origin of dynamic front propagation arises from the atomic scales and shed light on the similarity/difference between atomic-scale and macroscopic friction, paving the way for understanding the connections between these separated length scales.

CC&B is a Coordinated Research Center at the University of Milan
Research within CC&B is supported by the European Research Council
CC&B cooperates with the ISI Foundation www.isi.it

>>> UPCOMING EVENTS

Paolo Biscari
Dipartimento di Fisica, Politecnico di Milano

Using Poincaré half-plane to understand Crystal Elasto-Plasticity

April 20th 2018
12.30 — Caldirola Room,
Physics Department
Via Celoria 16, Milano

Massimo Locati
University of Milan

TBA

May 18th 2018
12.30 — Caldirola Room,
Physics Department
Via Celoria 16, Milano

Carlo Piccardi
Dipartimento di Elettronica, Informazione e Bioingegneria, Politecnico di Milano
(joint work with Lucia Tajoli, Dipartimento di Ingegneria Gestionale, Politecnico di Milano)

Complexity, Centralization, and Fragility in Economic Networks

May 24st 2018
12.30 — Caldirola Room,
Physics Department
Via Celoria 16, Milano

Giampaolo Cristadoro
University of Milano-Bicocca

The common origin of symmetry and structure in genetic sequences

June 7th 2018
12.30 — Caldirola Room,
Physics Department
Via Celoria 16, Milano

David Barone
Cell Proliferation Unit, Department of Biology, University of Padua, Italy

cAMP and Salicylate Control Yeast Cell Quiescence (a pilot phenotypic study)

June 11th 2018
12.30 — BS Room,
Via Celoria 26, Milano