

## DIPARTIMENTO DI FISICA E CHIMICA - DiFC

Direttore: prof. Gioacchino Massimo Palma



## Phase transitions in cancer metastasis

13th November 2025, aula AP1, DIFC, Edificio 18, Viale delle Scienze

## Caterina A. M. La Porta and Stefano Zapperi

Center for Complexity and Biosystems, University of Milan

The spread of cancer metastasis depends on a sequence of molecular factors involving adhesion molecules. but also on mechanical and geometrical effects affecting cancer cell migration [1]. In this talk, we discuss our recent work showing how concepts related to the physics of complex systems, such as non-equilibrium phase transitions, the jamming transition, and turbulent active nematic flow, can be used to quantitatively describe the behavior of metastatic spread in vitro [2] and in vivo [3]. By controlling adhesion and confining pressure in vitro, it is possible to construct a phase diagram for migrating cancer cells that involves transitions between jammed and unjammed states, and from laminar to turbulent active nematic flow [2]. Collective invasion of metastatic cancer cells injected into the deep dermis of the mouse quantified using intravital multiphoton microscopy and three-dimensional image analysis reveals a multicellular but low-cohesive migration mode characterized by rotational patterns which self-organize into persistent tracks with orientational nematic order, confirming that the active turbulent scenario is relevant for collective cancer cell migration in vivo [3]. We also discuss the role of molecular factors in metastasis by introducing a Boolean network model for epithelial mesenchymal transition (EMT), a process by which polarized epithelial (E) cells acquire mesenchymal (M) characteristics [5]. Using the model, we construct a topographic map of the cell phenotypes revealing a multitude of metastable hybrid phenotypic states, separating stable epithelial and mesenchymal states, and is reminiscent of the free energy measured in glassy materials and disordered solids. We discuss the implications of E/M hybrid states for metastatic spread.

- [1] Font-Clos F, Zapperi S, La Porta CA. Blood flow contributions to cancer metastasis. iScience. (2020) 22;23(5).
- [2] La Porta, C.A.M. and Zapperi, S., Phase transitions in cell migration. Nature Reviews Phys., 2 (2020) 516. [3] Ilina, O. et al. Cell cell adhesion and 3D matrix confinement determine jamming transitions in breast cancer invasion, Nature cell biology 22, (2022) 1103.
- [4] Chepizhko, O., Armengol-Collado, J.M., Alexander, S., Wagena, E., Weigelin, B., Giomi, L., Friedl, P., Zapperi, S. and La Porta, C.A. M., 2025. Confined cell migration along extracellular matrix space in vivo, Proceedings of the National Academy of Sciences, 122 (2025) e2414009121.
- [5] Font-Clos F, Zapperi S, La Porta CA. Topography of epithelial mesenchymal plasticity. Proceedings of the National Academy of Sciences. (2018) 115(23):5902-7.



