

# The 3D Structure of Epithelia Monolayers: Biology meets Math and Physics

Javier Buceta

Institute for Integrative Systems Biology (I2SysBio),  
CSIC-UV, C/ Catedrático Agustín Escardino Benlloch, 9 46980, Paterna (Valencia), Spain

Building and shaping tissues and organs relies on the ability of cells to efficiently pack together and regulate their interactions. Over the last years we have been working on the physical and mathematical aspect of this problem. Our contributions include the understanding of the role of cell size for regulating the signalling noise [1], the interplay of mechanical properties and patterning to achieve shape remodeling [4], the interaction between different cell populations [5], the development of tissue simulation codes for mechanobiology experiments [3], and the 3D organization of epithelial cells [2, 6]. As for the latter topic, we have shown that epithelial cells display a previously undescribed geometrical shape when tissues are subjected to bending (curvature): the scutoid (Fig. 1).



Fig. 1. Scutoids are novel shapes that allow epithelial cells to pack efficiently (from an energetic viewpoint) in tissues subjected to bending or folding.

The scutoidal shape allows cells to pack minimizing their energy and this discovery has opened the door to a deeper

understanding of morphogenesis. Yet, further consequences of this new paradigm in terms of the 3D cellular organization have remained elusive. Recently, we have addressed this problem using a combination of experiments, mathematical analyses, computer simulations, and biophysical approaches. In that context we have shown that the thickness and curvature of epithelial tissues are linked to the cellular connectivity via energetic cues. This principle explains how the topological and physical constraints inherent to living matter contribute to build functional complex shapes and lead to the self-organization of tissues.

- 
- [1] Javier Buceta. Finite cell-size effects on protein variability in Turing patterned tissues. *Journal of the Royal Society, Interface*, 14(133):20170316, 2017.
  - [2] Pedro Gómez-Gálvez, Pablo Vicente-Munuera, Antonio Tagua, Cristina Forja, Ana M Castro, Marta Letrán, Andrea Valencia-Expósito, Clara Grima, Marina Bermúdez-Gallardo, Óscar Serrano-Pérez-Higueras, Florencia Cavodeassi, Sol Sotillos, María D Martín-Bermudo, Alberto Márquez, Javier Buceta, and Luis M Escudero. Scutoids are a geometrical solution to three-dimensional packing of epithelia. *Nature communications*, 9(1):2960, 2018.
  - [3] Oriol Canela-Xandri, Samira Anbari, and Javier Buceta. TiFoSi: an efficient tool for mechanobiology simulations of epithelia. *Bioinformatics*, 36(16):4525, 2020.
  - [4] Samira Anbari and Javier Buceta. Self-sustained planar intercalations due to mechanosignaling feedbacks lead to robust axis extension during morphogenesis. *Scientific Reports*, 10(1):10973, 2020.
  - [5] Carla Prat-Rojo, Philippe-Alexandre Pouille, Javier Buceta, and Enrique Martín-Blanco. Mechanical coordination is sufficient to promote tissue replacement during metamorphosis in *Drosophila*. *The EMBO Journal*, 39(3), 2020.
  - [6] Pedro Gómez-Gálvez, Pablo Vicente-Munuera, Samira Anbari, Javier Buceta, and Luis M. Escudero. The Complex Three-Dimensional Organization of Epithelial Tissues. *Development*, 148(1):dev195669, 2021.