Biophysical approaches to explain the 3D cellular packing of epithelia.

Pedro Gómez-Gálvez[1,2,†], Pablo Vicente-Munuera[1,2,†], Samira Anbari[3,4,†], Antonio Tagua[1,2,†], Carmen Gordillo-Vázquez[1,2], Ana M. Palacios[1,2], Antonio Velasco[1], Carlos Capitán-Agudo[1], Clara Grima[5], Valentina Annese[1,2], Rafael Robles[5], Alberto Márquez[5], Javier Buceta[6,*], Luis M. Escudero[1,2,*]

[1]Instituto de Biomedicina de Sevilla (IBiS), Hospital Universitario Virgen del Rocío/CSIC/Universidad de Sevilla and Departamento de Biología Celular, Universidad de Sevilla. 41013 Seville, Spain

[2]Biomedical Network Research Centre on Neurodegenerative Diseases (CIBERNED), Madrid, Spain

[3]Chemical and Biomolecular Engineering Department, Lehigh University. Bethlehem, PA 18018, USA

[4]Current address: Biomedical Engineering Department, Johns Hopkins University. Baltimore, MD 21205, USA

[5]Departamento de Matemática Aplicada I, Universidad de Sevilla. Seville 41012, Spain

[6]Institute for Integrative Systems Biology (I^2SysBio), CSIC-UV, Paterna (Valencia) 46980, Spain

[†]These authors contributed equally to this work.

[*]Corresponding authors

Epithelial cell organization and the mechanical stability of tissues are closely related. In this context, it has been recently shown that packing optimization in bended/folded epithelia is achieved by a surface tension energy minimization mechanism that leads to a novel cellular shape: the *scutoid* [1]. However, further cellular and tissue level implications of this new developmental paradigm remain unknown. I will present new data on the relation of this complex cellular shape and the connectivity between cells. We address this problem using a combination of computational, experimental, and biophysical approaches in tubular epithelia. We dissect the contribution of the energetic drivers inducing the complex three-dimensional packing of these tissues. We conclude that tubular epithelia satisfy a novel principle, the “Flintstones’ law”, that links tissue geometry and energetic profiles with the average cellular connectivity in epithelia. Our study unveils a quantitative morphogenetic law with key physiological consequences.

[1] Gómez-Gálvez, P., Vicente-Munuera, et al. Nature Communications, 9, 2960 (2018).