ACTIVE MATTER MEETS BIOENGINEERING: HOW MODELS OF ACTIVE TISSUE MECHANICS CAN IMPROVE BIOFABRICATION

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Background

Tissues are living materials that adapt their mechanical and rheological properties to the physical environment, which in turn alter the biological fate of its constituent cells. This needs to be taken into account in the development of new biofabrication processes, where engineers require quantitative material models that predict the rheological behavior of living cellular products and relate the physical micro-environment to cell fate.

The last years have seen great improvements in active matter models of cell and tissue biophysics. Continuum approaches include active hydrodynamic models, which consider a tissue at long timescales as a contractile, active fluid with nematic and turbulent properties [1]. Prevailing cell-based mechanical models of tissues are the vertex model and its derivatives, which have been particularly successful in examining tissue rigidity transitions [2] and tissue rheology [3]. A recent development of vertex model is the active foam model [4], which considers tissues as foam-like structures, with individual cells behaving as active 'bubbles' or droplets, a paradigm that is also reflected in the active shell model for single cell mechanics [5]. However, despite their success in biological applications such as cancer and development, these models have not yet been widely adopted in the context of biofabrication.

Recent Advances

This perspective presents our latest developments in computational modelling of active tissues. We first revisit a theoretical hydrodynamic description of tissues as polar active fluids to explain the observation of collective contact guidance of epithelial cells following topological substrate cues, and demonstrate the close analogy between hydrodynamic theory and simulations of polar, self-propelled particles. Next, we introduce a novel active foam model of 3D tissues based on an active shell description of cells [6]. We demonstrate that the introduction of bond lifetime in this model through cell-cell friction qualitatively effects the jamming phase diagram. As such, this parameter represents a novel physical mechanism for tissue jamming with direct biological analogues in processes such as the epithelial-to-mesenchymal transition and tumor progression. Applied to the phenomenon of tissue spheroid fusion [7], this model predicts that a wide variety of micro-mechanical and material properties can be obtained by varying cell activity and cell-cell interfacial tension (contractility), including complete and arrested fusion and arrested versus fluidized tissue rheology, Fig. 1. Finally, we demonstrate how these structures can be harnessed in bioprinting different geometries of artificial tissue constructs.

Bart Smeets is currently assistant professor at the Biosystems department of KU Leuven, where is head of the particulate dynamics lab. His research focuses on the mechanical and rheological characterization of self-organized tissues. His previous research includes research stays at the lab of Prof. X. Trepat at IBEC, Barcelona and the lab of P. Silberzan at Institut Curie, and a postdoctoral fellowship at MeBioS, KU Leuven. He is the author of 34 publications in peer-reviewed journals and more than 70 contributions to international and national conferences.

Future directions

In the context of biofabrication, the active foam behavior of self-assembled tissues interacts with the encapsulating material, such as the bio-ink, to establish the biomechanical properties of engineered tissue constructs. Going forward, integrated multi-scale and multi-physics models that take into account this integration will be needed in order to become an integrative part of the engineering pipeline for biofabrication.

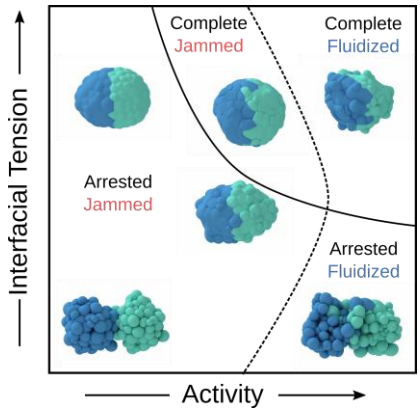

***Figure 1**. Phase diagram of spheroid fusion based on active foams*

References

1. Alert et al., Ann. Rev. Cond. Matt. Phys. 13.10.1146, 2022.
2. Petridou et al., Cell 184.7: 1914-1928, 2021.
3. Alt et al., Philos. Trans. R. Soc. 372.1720: 20150520, 2017.
4. Kim et al. Nat. phys., 17.7: 859-866, 2021.
5. da Rocha et al., J Mech. Phys. Solids: 104876, 2022.
6. Cuvelier et al., Soft Matt. 17.27: 6603-6615, 2021.
7. Ongenae et al., Front. in Phys.: 321, 2021.

Acknowledgements

This work was performed by the Particulate Dynamics lab of MeBioS KU Leuven in collaboration with the lab of P. Silberzan at Institut Curie, Paris. We acknowledge support from KU Leuven internal funding C14/18/055.