

Computational continuum modeling of cell aggregation phenomenon

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Biological aggregates, such as organoids, bacterial colonies, cell spheroids, and tumors, are formed by a myriad of individual interacting cells. The dynamics of the formation of such aggregates is driven by inter-cellular forces which are intrinsically out of equilibrium. This out-of-equilibrium state leads the aggregate to behave differently compared to a normal viscous droplet and can be modeled as an active material rendering a time dependent behavior. Simulation of such phenomena can be applied to model bacterial colonies formation, tissue spreading, wound healing, tumor growth, etc. A prototypical example of active multicellular aggregates are the bacterial microcolonies of *Neisseria gonorrhoeae* which is a commonly transmitted disease. Each *N. gonorrhoeae* bacterium is surrounded by thin flexible filaments called pili. Pili are retractable appendages which enable the bacteria to move on a substrate or to interact with other bacteria and form aggregates. Retraction of an attached pili pair between two bacteria generates the pulling force which causes the bacteria to attract each other. At the micro-scale, there exist three major forces that act on each individual bacterium: the attraction pili-pili mediated force from the bacterium with which the pili connections have been made; the steric repulsion force from an already attached bacterium; and the friction between the bacterium and the substrate. These three forces govern the overall dynamics of the problem. Kuan et al. [1] adopted the coarse grained continuum approach to develop the equations governing the medium. Motivated by the work of Kuan et al. [1], we present a non-linear continuum mechanic theory to formulate such phenomena in a Lagrangian framework. A mixed finite element formulation is presented to solve the couple-field time-dependent formulation. Taylor–Hood elements are adopted to overcome the stability issues associated with LBB condition while satisfying the continuity equation. The developed framework could be broadly exploited in the context of dense cellular aggregates etc.

REFERENCES

[1] Hui-Shun Kuan, Wolfram Pönisch, Frank Jülicher, and Vasily Zaburdaev. “Continuum theory of active phase separation in cellular aggregates”. *Physical Review Letters* (2021) **126**:018102.