COMPUTATIONAL MODELING OF WOUND CLOSURE

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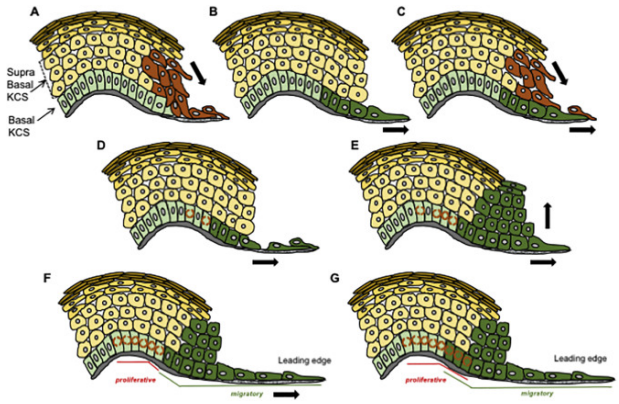

Effective summary

Wound healing is a complex process [2] in which the skin heals itself after injury, and many of the underlying mechanisms are still poorly understood. One of the important processes is wound closure (or so-called re-epithelialization). Without an appropriate wound closure, patients will develop a chronic wound and even a skin cancer in the long term [2].

It has been observed that the same (optical) diagnosis of the wound sometimes results in a completely different healing process, which indicates that wound healing is patient-oriented (e.g. age and stiffness of the skin). With mathematical models, one can convert these patient characteristics to input parameters and predict the specific healing process from the model.

In this project, we focus on the epidermis layer of the skin, which consists of several layers and phenotypes of cells. However, how theses layers and cells coordinate the wound closure is still not yet fully clear. We wish to investigate various hypotheses for re-epithelialization proposed in [3] with an existing agent-based framework [1], i.e. cellular automata model, where the cells are represented as discrete agents migrating and proliferating by local rules. The model includes proliferation, migration due to overcrowding, pushing, pulling and upward a chemical gradient. Such a model facilitates investigation into the closure characteristics and the dynamics of the skin layers based on the nature of cell proliferation and migration.

Background

In this project, we consider the side-view (cf. the top figure) of the wound, and model the subsequent wound closure process by an agent-based model in two spatial dimensions with several layers of the cells of possibly different phenotypes.

The project starts with one layer/line of cells: when there are only limited spaces and forces are applied on the both end side of the line, how would the in-between cells respond? Intuitively, with receiving the forces from both sides, these cell can either "escape" or die. However, it is not clear yet how the cell makes such a decision. Next is the question of multiple layers of cells and their interaction and the scenario becomes more complicated.

In the long run, we expect to develop a patient-oriented model including the patients' characteristics, facilitating prediction of the healing process and its interference.

There are several foreseen challenges in the project. First, proper biological assumptions are needed, particularly regarding the cellular activities under mechanical pressure. Second, converting these biological assumptions to the model is not always straightforward, in addition to unknown parameter values. Last but not least, it is always a challenge to validate a model particularly in a quantitative manner.

References

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[3] P. Rousselle, F. Braye, and G. Dayan. "Re-epithelialization of adult skin wounds: Cellular mechanisms and therapeutic strategies". In: *Advanced Drug Delivery Reviews* 146 (June 2019), pp. 344–365. DOI: 10.1016/j.addr.2018.06.019. URL: https://doi.org/10.1016/j.addr.2018.06.019.

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