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Towards a whole-tissue model of the intestine.

The intestinal epithelium is a paradigmatic system to study regenerative tissues. In this tissue the stem cells are confined to a well-defined niche at the bottom of invaginations called crypts. The progeny of these stem cells specify into different functional lineages and regenerate the entire tissue within a few days.
A multitude of genetically altered mouse stems show not only changes in this turnover but also clear morphological changes of the entire intestine. In order to explain these phenotypes a whole-tissue approach is required.
Recently, we introduced an off-lattice model of single crypt dynamics [1]. This model explains crypt dynamics in steady state and after perturbations in agreement with experimental data. We here present a modelling framework that allows extending this model to multi-crypt systems representing a first step towards a whole-tissue model.
We implemented a Cellular Potts Model on a curved surface representing multiple crypts and applied the regulatory mechanisms and organisation concepts of our off-lattice model. This enables us to cover the self-organisation of cell production and loss in the tissue, which is assumed as fixed in the former model. We provide first simulation results applying this model to circadian rhythms of intestinal turnover and compare the results to experimental data [2].

References

[1] P. Buske et.al., *A comprehensive model of the spatio-temporal stem cell and tissue organisation in the intestinal crypt.* PLoS Comput Biol 2011 **7** e1001045.
[2] J.M. Qiu, et.al.,*Cell migration in the small and large bowel shows a strong circadian rhythm.* Epithelial Cell Biol 1994 **3(4)** 137–148.