Evolving Homeostatic Tissue Using Genetic Algorithms

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Extended Abstract

Homeostasis is a critical property of living beings that involves the ability to self-regulate in response to changes in the environment in order to maintain a certain dynamic balance affecting form and/or function. The importance of homeostasis is pronounced in multi-cellular organisms where function and structure needs to be regulated at ever increasing levels of organisation (Cunliffe, 1997).

In this talk we will address the evolution of homeostasis in a computational framework and investigate structural homeostasis in the simplest of cases, a tissue formed by a mono-layer of cells. To this end, we made use of a 3-d hybrid cellular automaton, an individual-based model in which the behaviour of each cell depends on its local environment (Gerlee and Anderson, 2009). This was implemented by using a response network, which for each cell takes extra-cellular cues as input, and whose output determines the phenotype or behaviour of the cell (cell division, movement, death).

Instead of dictating a given mapping from environment to phenotype, we made use of an evolutionary algorithm (EA) to evolve cell behaviour which gives rise to a homeostatic tissue (Streichert et al., 2003; Stanley and Miikkulainen, 2003; Andersen et al., 2009). The fitness of a genotype (response network) was evaluated by running the cellular automaton seeded with a single cell for given number of time steps. Cell types which can fill the domain with a mono-layer of cells are given the highest fitness, while those which either over-grow or fail to fill the domain are punished. We made use of two different fitness functions, one which uses a constant fitness evaluation where each cell type is tested for 200 time steps (constant), and another which increases the evaluation time for each successive generation (incremental). An example of run with a constant fitness evaluation scheme is shown in fig. 1.

Analysis of the solutions provided by the EA shows that the two evaluation methods gives rise to different types of solutions to the problem of homeostasis. The constant method leads to almost optimal solutions, which rely on a very high rate of cell turn-over, and this is achieved by fine-tuned balance between cell birth and death. The solutions from the incremental scheme on the other hand behave in a more conservative manner, only dividing when necessary, and generally have a lower fitness.

In order to test the robustness of the solution we subjected them to environmental stress, by wounding the tissue, and to genetic stress, by introducing mutations. The cell types with high turn-over were more robust with respect to wounding, healing faster and more accurately. The sensitivity to genetic perturbations depends on what type of mutations we consider. Copy mutations, which only occur when the cells divide, affect the tissues with a high turn-over, while cosmic ray mutations, which occur at a constant rate, are more detrimental to the conservative cell types.

The two evolved cell types analysed present contrasting mechanisms by which tissue homeostasis can be maintained. This compares well to different tissue types found in multi-cellular organisms. For example the epithelial cells lining the colon in humans are shed at a considerable rate (Podolsky and Babyatsky, 2003), while in other tissue types, which are not as exposed, the conservative type of homeostatic mechanism is normally found (Hooper, 1956).

These results will hopefully shed light on how multi-cellular organisms have evolved and what might occur when homeostasis fails, as for example in the case of cancer (Preston-Martin et al., 1990).

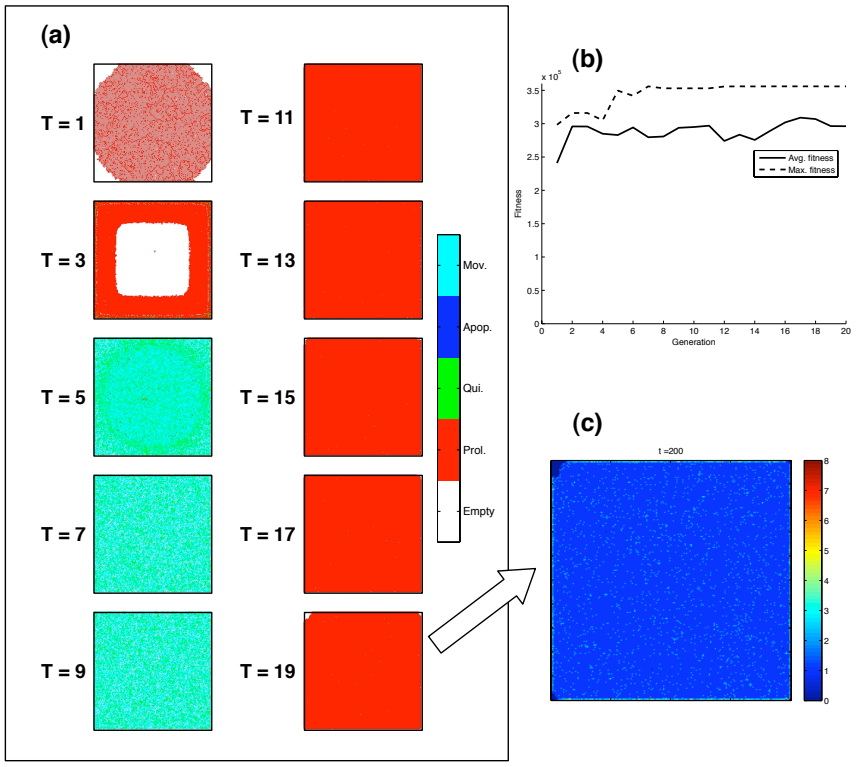

Figure 1: Time evolution of the EA. (a) shows the most fit genotypes at different generations in the run, where the process converges on a genotype which predominately proliferates. The time evolution of the average and maximum fitness is shown in (b), which, because of a weighted multi-objective fitness function, does not necessarily increase over time (Bentley and Wakefield, 1998). The cell density of the final genotype (T = 19) is shown in (c), and reveals that the solution arrived upon by the EA forms a mono-layer, and thus satisfies our criteria for a homeostatic genotype.

References

Andersen, T., Newman, R., and Otter, T. (2009). Shape homeostasis in virtual embryos. *Artificial Life*, 15(2):1–23.

Bentley, P. and Wakefield, J. (1998). *Soft Computing in Engineering Design and Manufacturing*, chapter Finding acceptable solutions in the pareto-optimal range using multiobjective genetic algorithms, pages 231–240. Springer Verlag.

Cunliffe, J. (1997). Morphostasis: an evolving perspective. *Med. Hypotheses*, 49(6):449–459.

Gerlee, P. and Anderson, A. R. A. (2009). Modelling evolutionary cell behaviour using neural networks: application to tumour growth. *Biosystems*, 95:166–174.

Hooper, C. E. S. (1956). Cell turnover in epithelial populations. *J Histochem Cytochem*, 4(6):531–540.

Podolsky, D. and Babyatsky, M. (2003). *Textbook of Gastroenterology*, chapter Growth and development of the gastrointestinal tract, pages 546–577. Lippincott, Philadelphia, PA.

Preston-Martin, S., Pike, M. C., Ross, R. K., Jones, P. A., and Henderson, B. E. (1990). Increased cell division as a cause of human cancer. *Cancer Res*, 50(23):7415–7421.

Stanley, K. and Miikkulainen, R. (2003). A taxonomy for artificial embryogeny. *Artificial Life*, 9(2):93–130.

Streichert, F., Spieth, C., Ulmer, H., and Zell, A. (2003). Evolving the ability of limited growth and self-repair for artificial embryos. In *Lect Notes Artif Int*, volume 2801, pages 289–298.