

Dieu My Nguyen

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Reading 3: Cellular Computing, Automata, Global-to-local Theory

Paper 1: Principles of Development, Chapter 1 and Chapter 13 (embryogenesis and regeneration), Lewis Wolpert

Regeneration is a superpower. Amphibians and hydras are no short of being superheroes.

I am fascinated by chapter 13. On some level, humans can also regenerate. Our papercuts and small wound eventually heal themselves by forming scar tissues. But if my leg is cut off, I can expect, with very high certainty, that I will not grow a new one as a cockroach would.

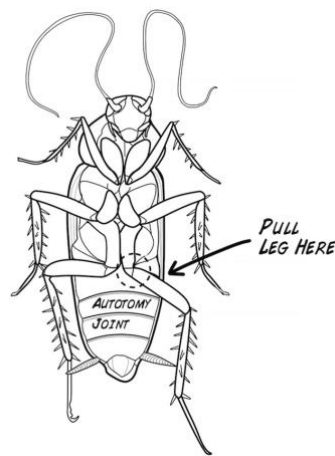
Amphibians are the icons of epimorphosis. The chapter did not focus on salamanders, but they excel at the art of limb regeneration. Cut off a salamander's leg and we won't see scar tissue forming. Instead, we'd see a wound epidermis. With chemical instructions from this epidermis, the nerves at the cut site regrow and mature cells dedifferentiate back to their immature state and divide. They form the mass called a blastema, which gives rise to the regenerated limb. It is amazing that the once mature cells can "remember" what they used to be to revert back to, and that, in the course of the growth of a new limb, these stem-like cells may differentiate once again, to be the type they were at the mature state or as a new cell type (transdifferentiation).

I wonder what the role of the immune system is in regeneration (or tissue repair in general). I've seen papers discussing how macrophages (a type of immune cell that scavenge for worn-out cells, debris, or foreign bodies) are a necessary component of epimorphic regeneration in the ear injury and regeneration of African spiny mice¹. And macrophages also play a role in tissue scarring and healing overall. I wonder if there's any research on how macrophages might affect amphibian regeneration. If we reduce or remove all the macrophages in, say, a salamander, can we expect its lost leg to regrow (statistically) much slower or not at all?

Also, I've had the chance to remove a cockroach's leg in the name of neuroscience experiments. I tugged on the femur to pull off one of the legs. The neuroscientist folks I

¹ Simkin J et al. (2017) Macrophages are necessary for epimorphic regeneration in African spiny mice. eLife. DOI: 10.7554/eLife.24623

worked with used to cut the leg, but found that pulling it makes the roach regenerate faster (back to full size within 125 days)².



Furthermore, I also used to go catching grasshoppers for more neuroscience experiments. Strangely, most of the hoppers I caught lost a hindleg. The frequency was uncanny. I thought it must've been the way I caught them with my hands that made a leg fall off. But as it turns out, grasshoppers can shed one or both hindlimbs to escape a predator or if the limb is damaged. It's a process called autotomy. Interestingly, a 1991 paper found that the grasshoppers actually don't regenerate this lost limb³. Now I wonder if there are more info on this process and more findings supporting the lack of regeneration.

Paper 2: Automated Global-to-Local Programming in 1-D Spatial Multi-Agent Systems, Daniel Yamins, Radhika Nagpal, Intl. Conf on Autonomous Agents and Multi-Agent Systems (AAMAS), 2008.

² Marzullo TC (2016) Leg Regrowth in *Blaberus discoidalis* (Discoid Cockroach) following Limb Autotomy versus Limb Severance and Relevance to Neurophysiology Experiments. PLoS ONE 11(1): e0146778. <https://doi.org/10.1371/journal.pone.0146778>

³ Arbas EA, Weidner MH (1991) Transneuronal induction of muscle atrophy in grasshoppers. J Neurobiol. 1991 Jul;22(5):536-46.

Paragraph or two on any/some of the following points:

What do you feel the main contribution of this paper is? What's the essential principle that the paper exploits? What did you find most interesting about this work?

This paper presents an analysis of global-to-local programming for pattern formation problems in 1-D multi-agent systems. Like the biological and computational systems we have read about so far, the multi-agent system this paper focuses on is decentralized and is made up of identically programmed individual agents whose computational constraints are local. Each has limited memory and processing power. Communications among the agents only occur with neighbors. However, the goals and tasks of the system that these individual agents belong to are defined globally.

In this paper, the authors aimed the design a “global-to-local” compiler for 1-D pattern formation. The compiler is composed of a combination of four subproblems/ techniques: the existence, construction, resource, and description problems. The compiler takes as input a pattern and resource parameters, and outputs a local rule creating the pattern. I see their approach as inverse engineering the parts that make up a sum. Overall, I have long been fascinated with the diverse and complex emergent properties that arise from a group of individuals with limited capabilities (like ants and honeybees), and this paper helps me look at this phenomenon through a computational perspective, which is new and useful.

Short answers to the questions below

One major strength of the paper

The paper is fairly readable even for those not experienced with this topic or algorithms. I enjoy the authors’ bio inspiration, the fruit fly and gene expression that produces a pattern of colored stripes. I also like the clarification that there are many studies seeking to understand local-to-global connections (given a local rule of the agent, what patterns will emerge), but what this paper focuses on is the inverse: given an emerged pattern, what are the rules that produce it?

One weakness of this paper

The authors clearly stated that this paper focuses on 1-D systems, but that “many questions in spatial multi-agent systems turn out to be essentially 1-D in nature.” One example is the biological inspiration: the *Drosophila* embryo is, in actuality, a 3-D ellipsoid, but the radial symmetry it forms is a 1-D pattern. I wonder though, whether it is true we can simplify

other multi-D systems into 1-D as the authors state. This is not a weakness of the paper per se, because I don't have the background in these topics to assess and don't have the intuition to turn 3-D objects into 1-D, but I'd be interested in a more substantial explanation.

Short discussion of

One question or future work direction you think should be followed. Or some insight/connection you think is interesting to pursue.

Can the concepts of this global-to-local compiler be applied to multi-D models? The authors mention that they can reduce the dimensionality of multi-D objects in order to use this compiler. But can the compiler be generalized such that it can address multi-D pattern formations?

I am thinking (biologically) about possible mutations in individual agents. These would be seen as perturbations to the global goals the collective is trying to complete. I'm interested in the rate or error/mutation in the individuals, and what this may mean for the collective. In some cases in biology, a single nucleotide error could be fatal.