Predicting Embryonic Patterning using Mutual Entropy Fitness and in silico Evolution

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Short Abstract — **During embryogenesis the expression of Hox genes that define anterior-posterior identity follow general rules: temporal colinearity and posterior prevalence. We use in silico evolution controlled by a mutual information fitness to derive networks simulating patterning of embryos. Simple geometric models evolve in the computer along a "fitness funnel" by successive gene duplications. Evolved networks describe well major aspects of embryonic development and suggest experimental predictions on the evolutionary transitions from ancestral insects to those with more derived developmental programs such as fly.**

I. Introduction

EVOLUTION is the central theory of biology, still it is unclear if it can be used in a more predictive way, like a theory in physics. Some biologists like Gould have suggested that evolution is purely contingent, however the existence of convergent evolution shows that some aspects of evolution are reproducible and therefore amenable to theoretical predictions.

Recent biological studies have focused on the building of map of genetic interactions (or "gene networks"); from these, functional relationships and "design principles" have been derived. We have proposed a "reverse approach": using (computational) evolution to predict what biological networks could/should look like. Computational evolution functions like a genetic screen; it enumerates in an unbiased way all models that can be built from a predefined set of parts to achieve a certain function. It favors models that can be built by incremental improvements in fitness rather than via multiple neutral steps or transitions through less fit intermediates. Evolution is rapid when it can march along a fitness gradient.

In two previous papers we have evolved regulatory networks for segmentation and adaptation [1,2]. We present here the results of a computational evolution aiming at reproducing *Hox*-like embryonic patterning [3]. A mathematical measure for the quality or fitness of the embryonic pattern produced by a gene regulatory network is derived. Using this measure and *in-silico* evolution we derive gene-interaction networks (assumed to work cell autonomously) for anterior-posterior (AP) patterning under two developmental paradigms.

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II. Results

A. Fitness

We use a mutual information fitness to define "complexity" of embryonic patterning. This fitness rewards diversity of genetic expression and "uniqueness" of cell fate, in a "realizator" gene model.

B. Static gradient

Networks are first evolved under control of a static gradient, like the ancestral insect morphogen *Caudal*. Successive gene duplications lead to rapid evolution of hierarchical networks. Networks are intrinsically multistable; the morphogen level dictates final steady state of the cell. Posterior dominance - the fate of a cell is dictated the most posterior *Hox* gene expressed within it - spontaneously evolves, similar to what is observed in fly [4].

C. Dynamic Gradient

Second we evolve networks under control of translating morphogen. This mimics the developmental of vertebrates, which grow posteriorly, and pattern as they do so. A *timer* gene is then used, and the gene network downstream present similar structures as the networks evolved under static gradient. This explains the *Hox* temporal dynamics in vertebrates and suggests a possible evolutionary pathway at the network level from ancestral insects to insects with faster development such as fly and wasps [5].

III. Conclusion

Although the biochemistry of *Hox* is complex, the actual spatiotemporal expression phenotype is not, and major properties of this system could be recovered. *In-silico* evolution provides a quantitative demonstration that continuous positive selection can generate complex phenotypes from simple components by incremental evolution as Darwin proposed.

References

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