



RELATIVELY DISPARATE CONSEQUENCES OF RESOURCE ABUNDANCE ON THE EVOLUTION OF MULTICELLULAR DIGITAL ORGANISMS.

Towards a general definition of developmental complexity

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Abstract

Development in metazoan organisms consists of a series of steps that give rise to inter-cellular heterogeneities and signaling capabilities required for growth and sustenance of the organism in its environmental niche. The way such developmental mechanisms evolve also depends on the ability of the organismal genomes to store information. We have used Avida – an artificial life software platform to study how development associated processes change during evolution. Avida uses an agent-based model wherein auto replicating evolvable computer programs compete for resources through innovation and deployment of a variety of mathematical tasks. In order to simulate multicellular clusters, we introduce spatially discrete and isogenic multicellular sub-populations in the world - called demes. Such a framework allows us to track the evolutionary dynamics of a series of quantifiable metrics, such as the number and diversity of distinct unicellular phenotypes, the developmental time as well as the degree to which organisms in the deme communicate and sense their surroundings. Our experiments indicate - perhaps unsurprisingly - a nonlinear disparate relationship between the evolution of the genome and what can be encapsulated by considering all the above phenotypic metrics as, developmental complexity. These experiments also lend credence to the importance of the externality provided by the multicellular structure of developing organisms over single-cell genomes.

Questions

1. Are organisms evolving under different external environments constrained to develop through fundamentally distinct mechanisms?

2. What is the contribution of intrinsic genomic features and extrinsic structural features to fitness in these organisms as they evolve under different conditions?

3. How does the mode of evolution of these intrinsic and extrinsic features change when compared between multicellular and unicellular replicators?

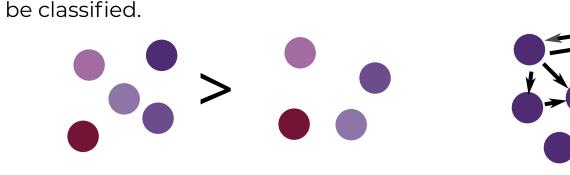
4. Can we construct a rigorous information theoretic measure to define developmental complexity in this minimal system?

Previous Work

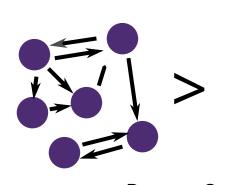
Goldsby et al. (2012) showed that addition of a task-switching cost during evolution of multicellular groups predisposes them to high instances of division of labor.

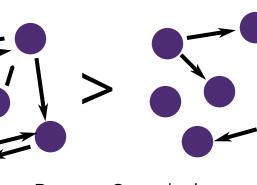
Adami et al. (2000) formulated an information theoretic measure of genomic complexity and showed that major transitions in fitness during evolution are associated with an increase in this complexity.

McShea (1996) described a repertoire of modalities under which metazoan complexity can



Object Complexity





Process Complexity + Hierarchial complexities

Duclos et al. (2019) argued for the inclusion of epigenetic features (sensu Waddington) into a definition of biological complexity. (including developmental mechanisms).

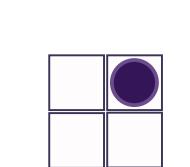
Bar-Yam (2004) discussed the role of complexities at multiple scales and a tradeoff due to differential organisation.

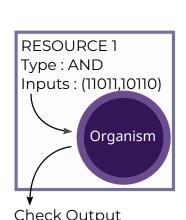
McShea (2002) puts forward, and tests using examples, the hypothesis that an increase in complexity at a higher level is accompanied by a decrease in complexity of the lower level components.

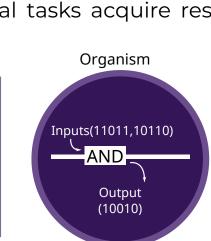
Avida

• Agent based simulation framework with genotype-phenotype discretization (A artificial, -vida - life) (Ofria et. al, 2004)

• Genome is made of instructions from an instruction set. (Turing complete) • Organisms that perform certain mathematical tasks acquire resources and reproduce faster.

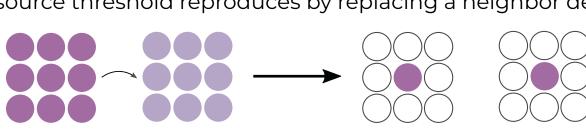






To model multi-cellular organism dynamics, the Avida world may be divided into subpopulations - or demes.

- •.Organisms in a deme reproduce independently of organisms in other demes and place offspring only within the same deme. There is no mutation during this process.
- Organisms can donate their accumulated resources to the deme. A deme that reaches a particular resource threshold reproduces by replacing a neighbor deme.



• We assay deme properties by isolating them in a test environment. The world geometry is periodic.

Method

Deme Runs

World size in X:5

World size in Y: 1000

Deme size: 25 (5x5) - total max 200 demes

1. A single organism with an ancestral genotype is injected into an empty deme.

2. The organisms can incorporate instructions that allow them to communicate with neighbors, sense their position in the deme, and even exit or join the germline of their

3. Phenotypic heterogeneity can arise due to formation of information processing pipelines inside the deme.

Unicellular runs

World size in X: World size in Y:200

Number of organisms: max 200 organisms

These organisms reproduce as soon as they genome is completely executed.

Measurements

A single long evolutionary run is conducted for 1.5 million updates. The demes/organisms from each update are taken and analysed in a separate isolated environment where different properties are measured.

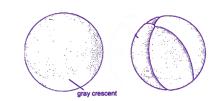
Fitness of an organism: Metabolic rate divided by doubling time of the organism

Fitness of a deme: Average rate of resource acquistion divided by doubling time.

Terminology

Development

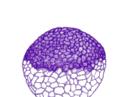
Development of organisms is the well regulated process wherein cells divide, differentiate and proliferate in tissues, set up a body axis, and form organs.

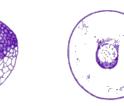
















https://embryology.med.unsw.edu.au/embryology/index.php/Frog_Development

Multicellular fitness (MCF) Fitness of the multicellular demes calculated as the amount of resources acquired during

the gestation period divided by the deme doubling time. Single-cellular Fitness (SCF)

Fitness of a single cell in the deme calculated as the metabolic rate divided by single cell

Messaging

doubling time.

Ability of organisms to send inputs/outputs to neighbors. Quantified as number of messaging-related instructions in the genome.

Sensing Ability of organisms to sense their spatial position in the world. Quantified as number of

sensing-related instructions in the genome.

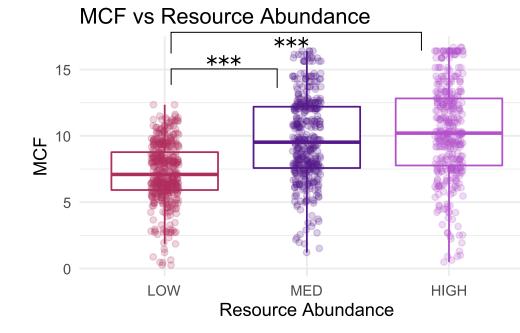
Regulation

Ability of organisms to regulate certain parts of genome based on conditional testing. Quantified as number of regulatory instructions in the genome.

Effect of resource abundance

Fitness under same environment

Organisms evolving under restrictive environments might be more efficient in utilisation of resources. Under this assumption, organisms evolved at lower resource abundances must perform better when compared against organisms that have evolved with large amounts of resources present in the environment



However, we see that the multi-cellular fitness of the organisms evolved at low resource conditions is much lower.

We attribute this to the lack of sufficient time for variability to arise in the population given that the organisms grow slower in the intermediate and high resource cases.

The single-cell fitness is also affected even

though the selection happens at a multi-

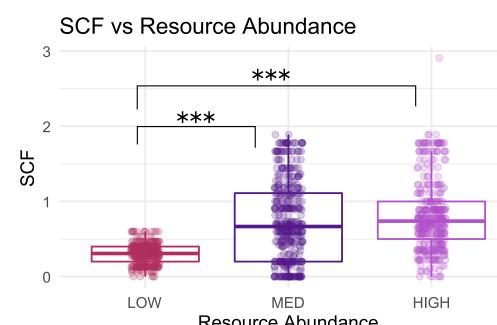
Result: Single cells of organisms evolving under lower resource conditions are less

fit when compared to other organisms

that have evolved for the same

evolutionary time but with ample

Result: Organisms evolving under lower resource conditions are less fit when compared to other organisms that have evolved for the same evolutionary time but with ample resources in their environment.



resources in their environment. Resource Abundance

This trend is captured only in one out of four replicates. Cells in these organisms reproduce extremely fast but the organisms themselves divide slowly.

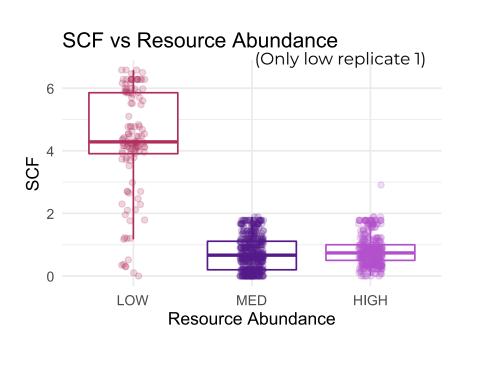
Replicate one evolves high levels of single cell fitness even under low resource

conditions.

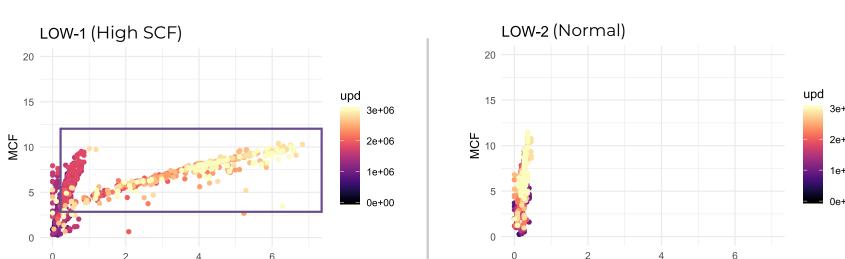
This phenomena is very similar to that in **cancer phenotypes**. We hypothesise that these cells will be outcompeted sooner or later by organisms in which this increase scf is outsourced to the whole organism.

Exception : Replicate 1

cellular level.



This might even be an intermediate stage in evolution of high fitness multi-cell organisms. The effect can be seen much more clearly in a MCF-SCF plot showing an increased inclination towards the SCF side at low resource abundance.



Effect on multiscale evolution

 $scf = b_{1s} * T + b_{2s} + \eta(log(\sigma) = b_{3s} * T)$

Fitness in these multicellular clusters can be enhanced genomically (where every single cell increases its resource uptake rate) or epi-genomically, where the developmental features become necessary and only the multicellular ensemble increases its fitness. We use two linear models with scaling variance at the two scales to calculate the degree to which evolution happens at the epi-genomic or genomic scale.

mcf = b_{1m} * T + b_{2m} + $\eta(\log(\sigma)=b_{3m}$ *T), where T is the evolutionary time

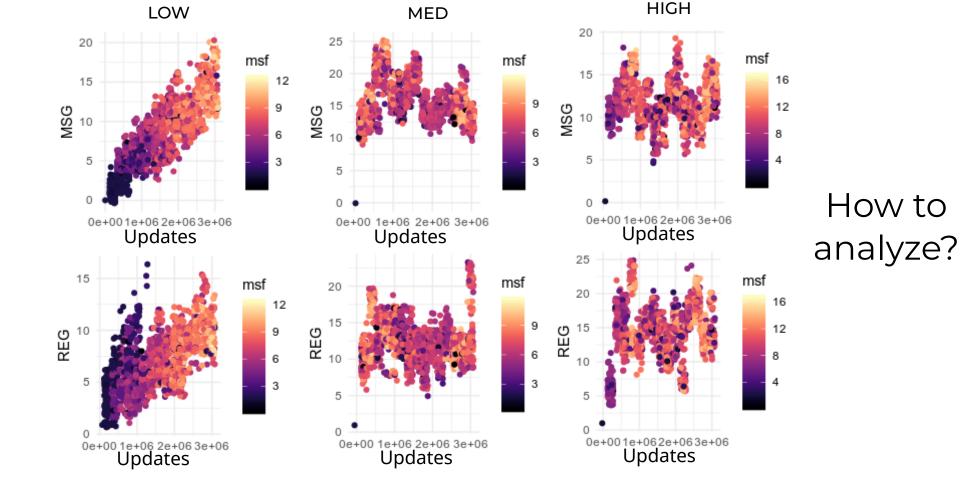
The ratio b_{1m}/b_{1s} gives the degree of epi-genomic fitness contribution relative to the genomic contribution. (With Low-1) MED MED

scf = single-cell fitness, mcf = multi-cell fitness, T = time, η = variability with given standard deviation

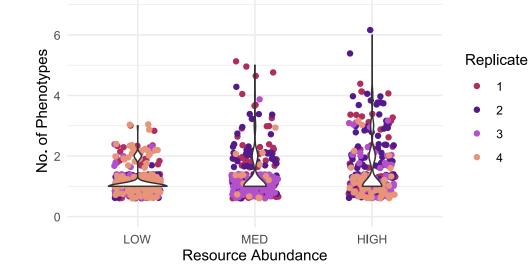
Result: Organisms evolving under lower resource conditions tend to increase their

Effect on epi-genomic pathways (preliminary data)

multicellular fitness without a corresponding increase in single cell fitness.



Effect on phenotypic diversity Phenotype number vs Resource Abundance



The number of phenotypes in the demes is calculated by measuring the set of tasks each cell performs during its lifetime.

While most demes seem to have cells with only a single phenotype, a small number show more than one phenotypes. This number increases for higher resource conditions.

Result: Organisms evolving at high resource conditions show a greater number of phenotypes in their constituent cells.

Effect of evolutionary context

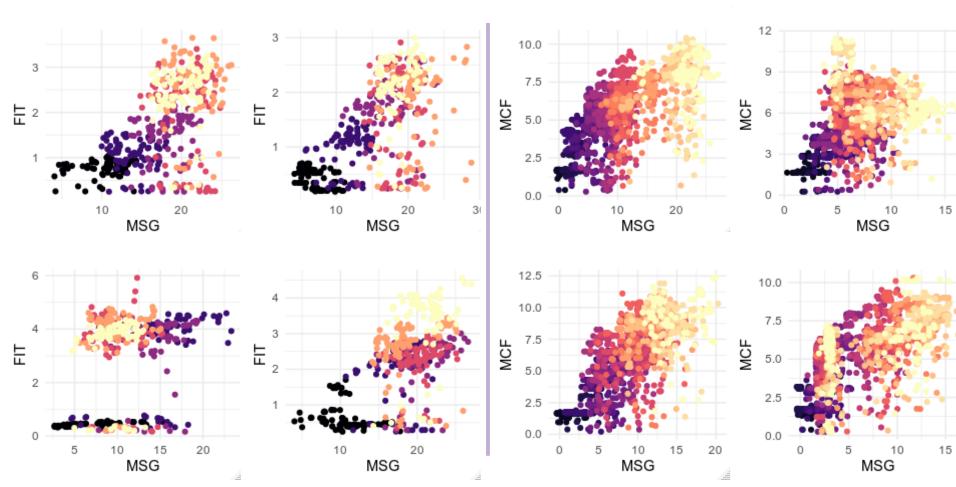
The evolutionary context under which an organism evolves is defined by the type of interactions it has with others and the level at which selection operates in the system.

In a unicellular context, organisms are allowed to communicate amongst each other but are selected as single cells.

In a multicellular context, both inter deme and intra deme communication is allowed but organisms are selected as an entire deme.

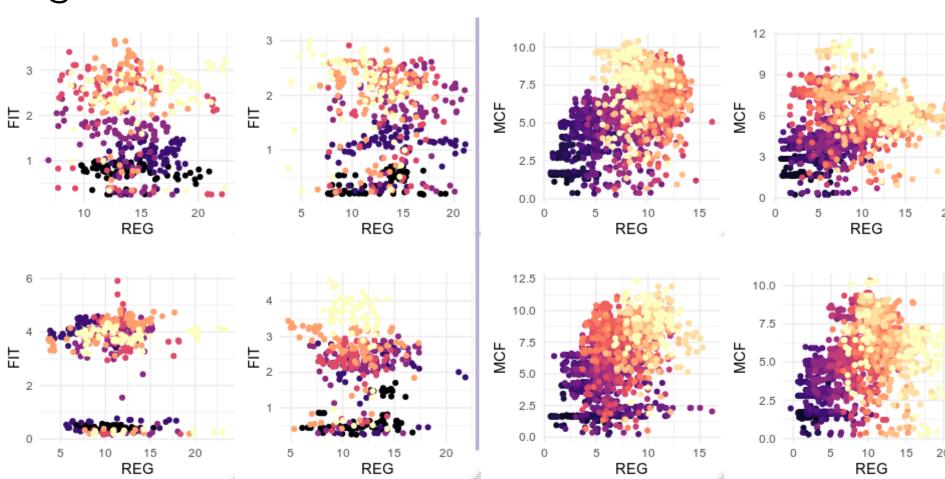
(All the following experiments are done at a LOW resource abundance) MULTICELLULAR UNICELLULAR

Messaging



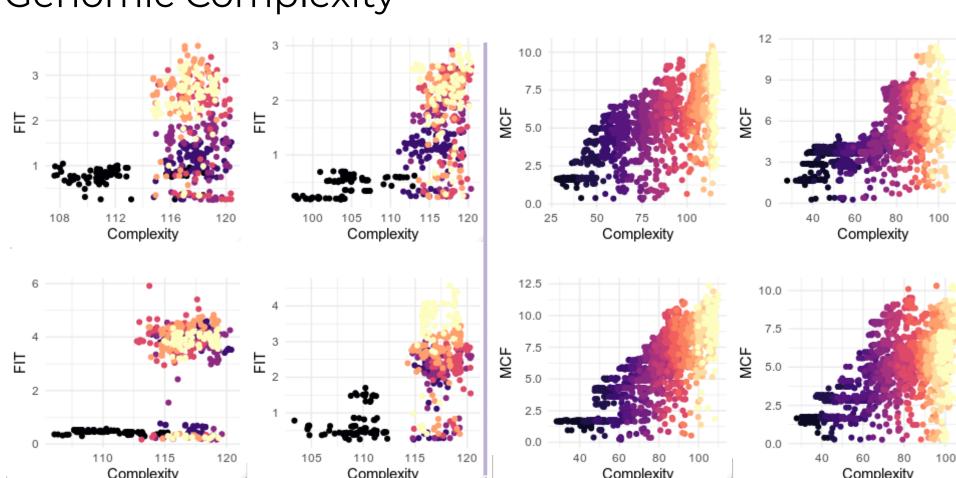
Organisms use messaging to improve fitness under both unicellular and multicellular contexts

Regulation



Organisms under multicellular contexts evolve a large degree of regulatory pathways, where they correlate well with fitness of the organisms. However, organisms in a unicellular context are not significantly aided by an increase in regulation.

Genomic Complexity



Both multicellular and unicellular contexts lead to high complexity genomes over evolutionary time (as expected). The kinetics of this increase in complexity however differs under the two scenarios.

Conclusion

In this work, we present a new framework to answer questions involving the evolution of developmental pathways in multi-cellular organisms and present results indicating the relative importance of genomic complexity and extra-genomic pathways in unicellular and

multicellular organisms. Our results indicate that low resource conditions facilitate extra-genomic pathways to be incorporated as a functional processes.

They also hint towards the relatively important but disparate roles of genomic complexity and other developmental functions in unicellular and multicellular evolving organisms.

Future work

Design statistical methods to quantify the actual role played by messaging/sensing in

fitness acquisition. **Repeat** the experiments for more runs.

Normalise for global births across multiple resource conditions

Use the McShea and Adami complexities to define a unified metric of biological complexity and model how it evolves over evolutionary time

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