Abstraction for dealing with the Multiple Realizability of Evolution

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data crunching

Use computer...
... control experiments
... visualize data

simulate experiments

general algorithms

computer programs

build artificial biologies

bioinformatics
data crunching

Use computer…
… control experiments
… visualize data

simulate experiments

computer programs

genetic algorithms

build artificial biologies

bioinformatics

**Practical skills** from CS
applied to the
outputs of field X
Use computer...
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Practical skills from CS applied to the outputs of field X

simulate experiments

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bioinformatics

abstraction and multiple realizability

algorithms

Theorems, lemmas, and proofs

genetic algorithms

conceptual analysis

Mathematical techniques from CS applied to the conceptual grounding of field X
Use computer…
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Practical skills from CS
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bioinformatics

Computational-X

abstraction and multiple realizability

algorithms

genetic algorithms

Theorems, lemmas, and proofs

Algorithmic-X

conceptual analysis

conceptual analysis

build artificial biologies

Computational-X

multiple realizability

Simulate experiments

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Practical skills from CS
applied to the outputs of field X

Mathematical techniques from CS
applied to the conceptual grounding of field X

bioinformatics

Theorems, lemmas, and proofs

Algorithmic-X
Idealization
How do we reason about arbitrary triangles?

Theoretical Abstraction

Idealization

Abstraction

Kaznatcheev, A. (2019)
Computational complexity as an ultimate constraint on evolution
Genetics, 302000.2019
Fitness Landscapes and Constraints

Some mapping from genotypes (or phenotypes) to fitness. + an idea of which genotypes (or phenotypes) are near each other and which are not.

“In a rugged field of this character selection will easily carry the species to the nearest peak”
- Wright (1932)
Fitness Landscapes and Constraints

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+ an idea of which genotypes (or phenotypes) are near each other and which are not.

A genotype is a **local fitness peak** if all nearby genotypes are of the same or lower fitness.

A **constraint** is anything that prevents evolution from finding a local fitness peak.

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Algorithms and Problems

Different population structures, developmental structures, trait co-variants, standing variation, etc… can produce different evolutionary dynamics and correspond to **different algorithms**.

Families of different fitness landscapes correspond to **different problems**.
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Fitness Landscapes and Constraint of Computation

Local fitness peaks vs. Constraint of Computation

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Local fitness peaks vs. Constraint of Computation

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Now, for any probability of failure $0 < \delta < 1$, let $m_\delta = \frac{\log \frac{1}{\delta}}{2 - \log 3}$ (where log is base 2).

**Theorem 24.** There exist semismooth fitness landscapes on $2nm_\delta$ loci that with probability $1 - \delta$, take $2^n$ or more fittest mutant steps to reach their fitness peak from a starting genotype sampled uniformly at random.

**Theorem 27.** Finding a local optimum in the NK fitness landscape with $K \geq 2$ is PLS-complete.

**Theorem 35.** If $\mathbf{PLS} \neq \mathbf{P}$ and $\log(f_{\text{max}}/f_\delta) \in O(n^k)$ then (for NK-model with $K \geq 2$) a local $s$-approximate peak cannot be found in time polynomial in $n$ and $\log \frac{1}{s}$. 
<table>
<thead>
<tr>
<th>Landscape type</th>
<th>Max allowed epistasis type</th>
<th>Hardness of reaching local optima</th>
</tr>
</thead>
<tbody>
<tr>
<td>smooth</td>
<td>[\text{AB, Ab, aB, ab}]</td>
<td><strong>Easy</strong> for all strong-selection weak-mutation (SSWM) dynamics</td>
</tr>
<tr>
<td>semismooth</td>
<td>[\text{AB, Ab, aB, ab}]</td>
<td><strong>Hard</strong> for SSWM with random fitter mutant or fittest mutant dynamics</td>
</tr>
</tbody>
</table>
| rugged         | \[\text{AB, Ab, aB, ab}\]  | **Hard** for all SSWM dynamics: initial genotypes with all adaptive paths of exponential lengths  

**Hard** for all evolutionary dynamics (if \(FP \neq PLS\))  
**Easy** for finding approximate local peaks with moderate optimality gap: selection coefficient can drop-off as power law  
**Hard** for approximate local peaks with small optimality gap: selection coefficient cannot drop-off exponentially |
What if we only care about the area of triangles?

Empirical Abstraction

- Idealization
- Abstraction

Kaznatcheev, A. (2017)
Two conceptions of evolutionary games: reductive vs effective.
BioRxiv: 231993.

Fibroblasts and Alectinib switch the evolutionary games played by non-small cell lung cancer
Reductive vs effective games (in cancer)

\[ G_{\text{eff}} = \begin{pmatrix} 2.6 & 3.5 \\ 3.1 & 3.0 \end{pmatrix} \]

\[ G_{\text{red}} = \begin{pmatrix} 2.6 & 3.5 \\ 3.1 & 3.0 \end{pmatrix} \]

\[ G_{\text{red}} = \begin{pmatrix} 2.6 & 3.7 \\ 2.9 & 3.0 \end{pmatrix} \]

\[ G_{\text{red}} = \begin{pmatrix} \cdot & \cdot \end{pmatrix} \]
Reductive vs effective games (in cancer)

(a) Replicator dynamics for parental-resistant NSCLC.
(b) Two dimensional game space.

\[
\begin{align*}
P & \left( \begin{array}{cc} A & B \\ C & D \end{array} \right) \Rightarrow \begin{cases} 
\frac{d}{dt} N_P = N_P \left( \frac{A N_P + B N_R}{N_T} \right) \\
\frac{d}{dt} N_R = N_R \left( \frac{C N_P + D N_R}{N_T} \right)
\end{cases}
\end{align*}
\]

\(S_p\): parental growth rate
\(S_R\): resistant growth rate

\(dP/dt = p(1-p)((B-D)(1-p) - (C-A)p)\)

where \(N_T = N_P + N_R\) and \(p = N_P/N_T\).

Fibroblasts and Alectinib switch the evolutionary games played by non-small cell lung cancer
Thank You!

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