Abstraction for dealing with the Multiple Realizability of Evolution

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data crunching

Use computer…
… control experiments
… visualize data

simulate experiments

genetic algorithms

computer programs

build artificial biologies

bioinformatics

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Practical skills from CS
applied to the
outputs of field X

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Practical skills from CS
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abstraction
and
multiple realizability

Theorems,
lemmas, and
proofs

algorithms

conceptual analysis

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

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Computational-X ⟷ **Algorithmic-X**

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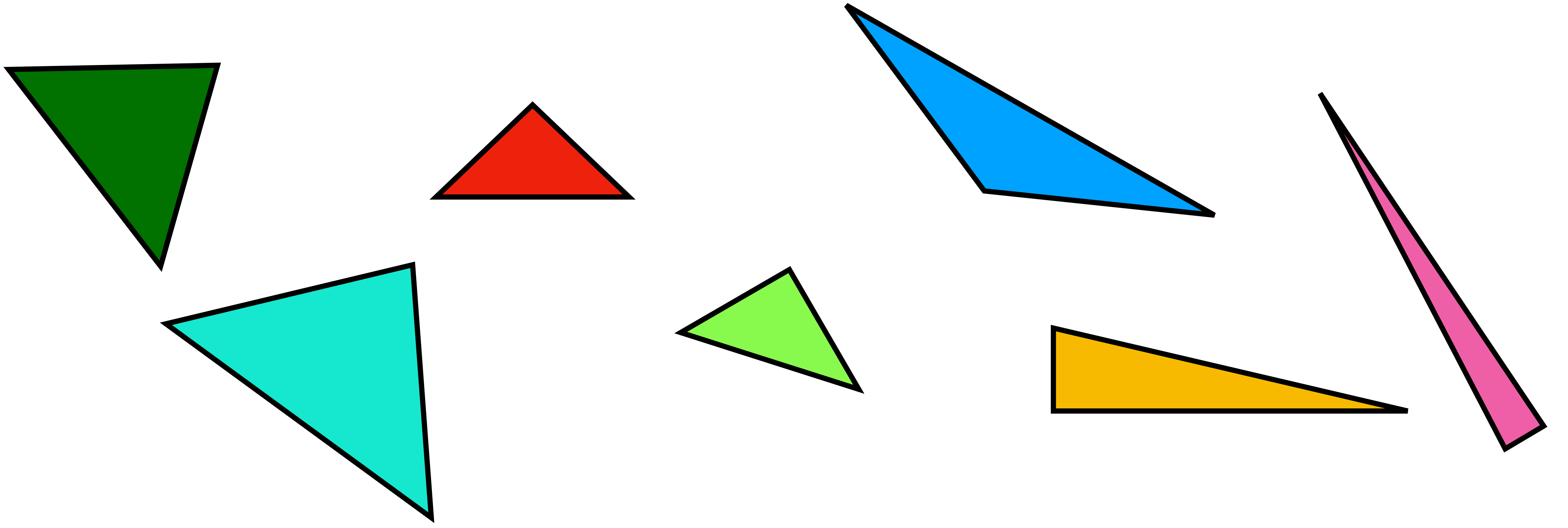
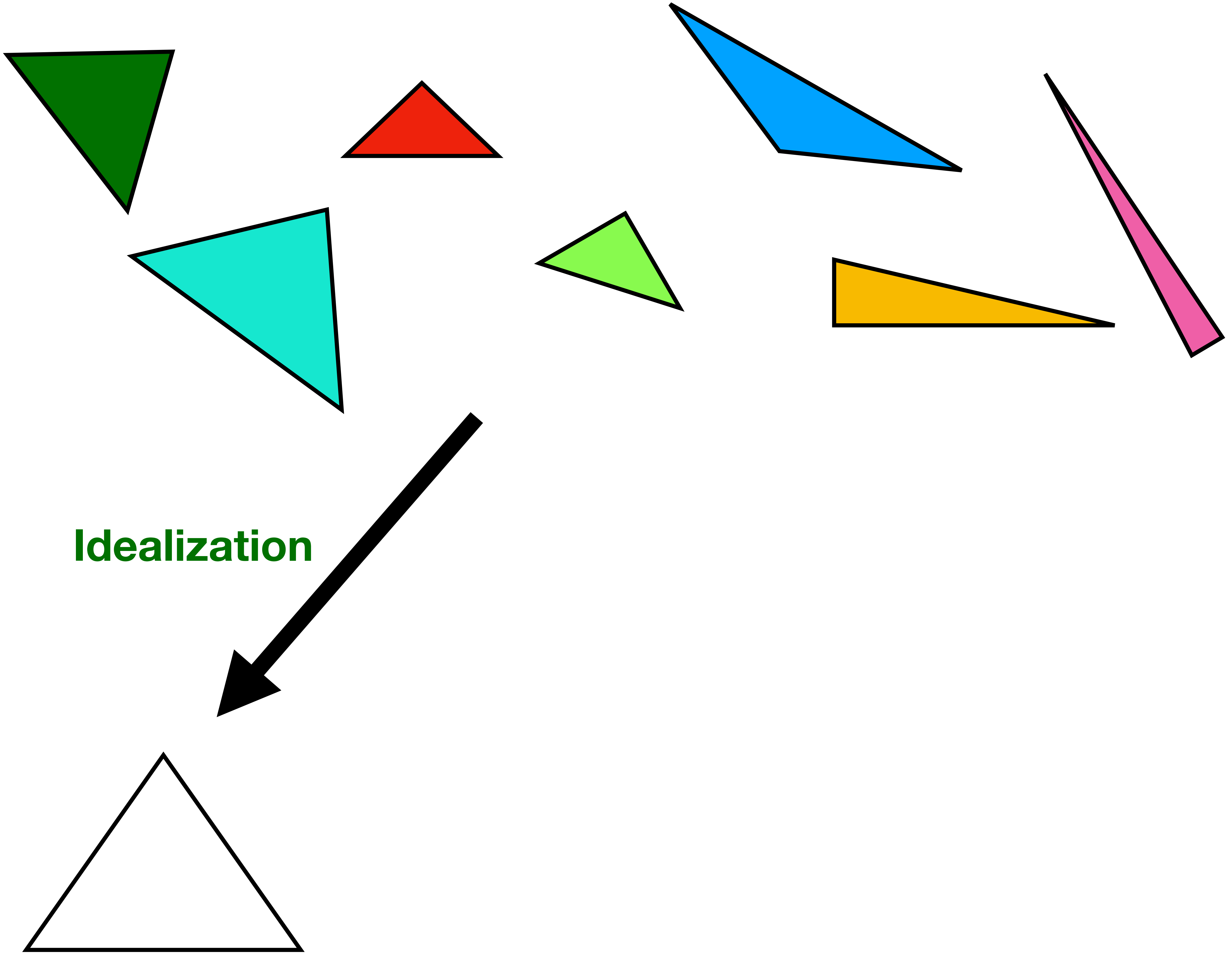
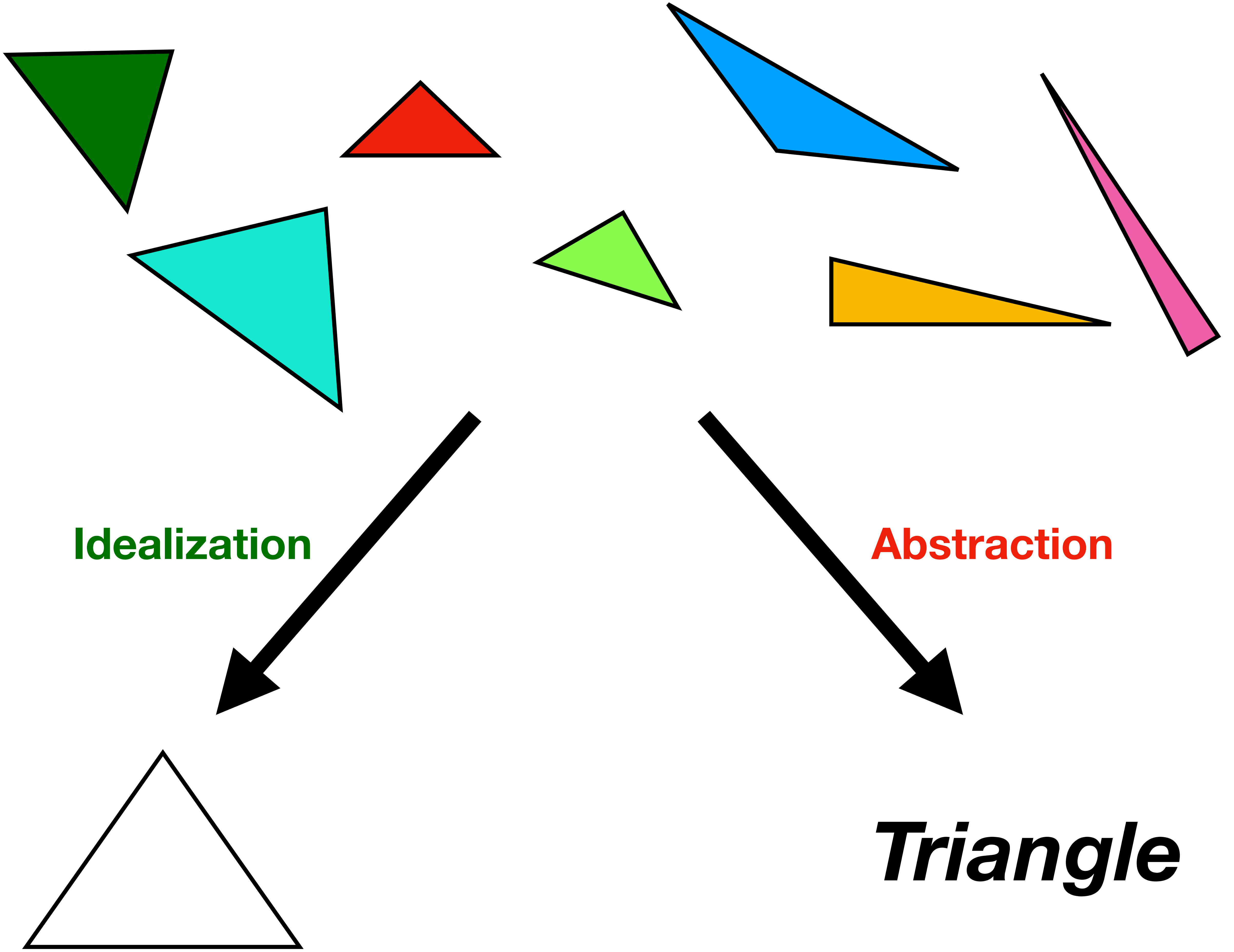


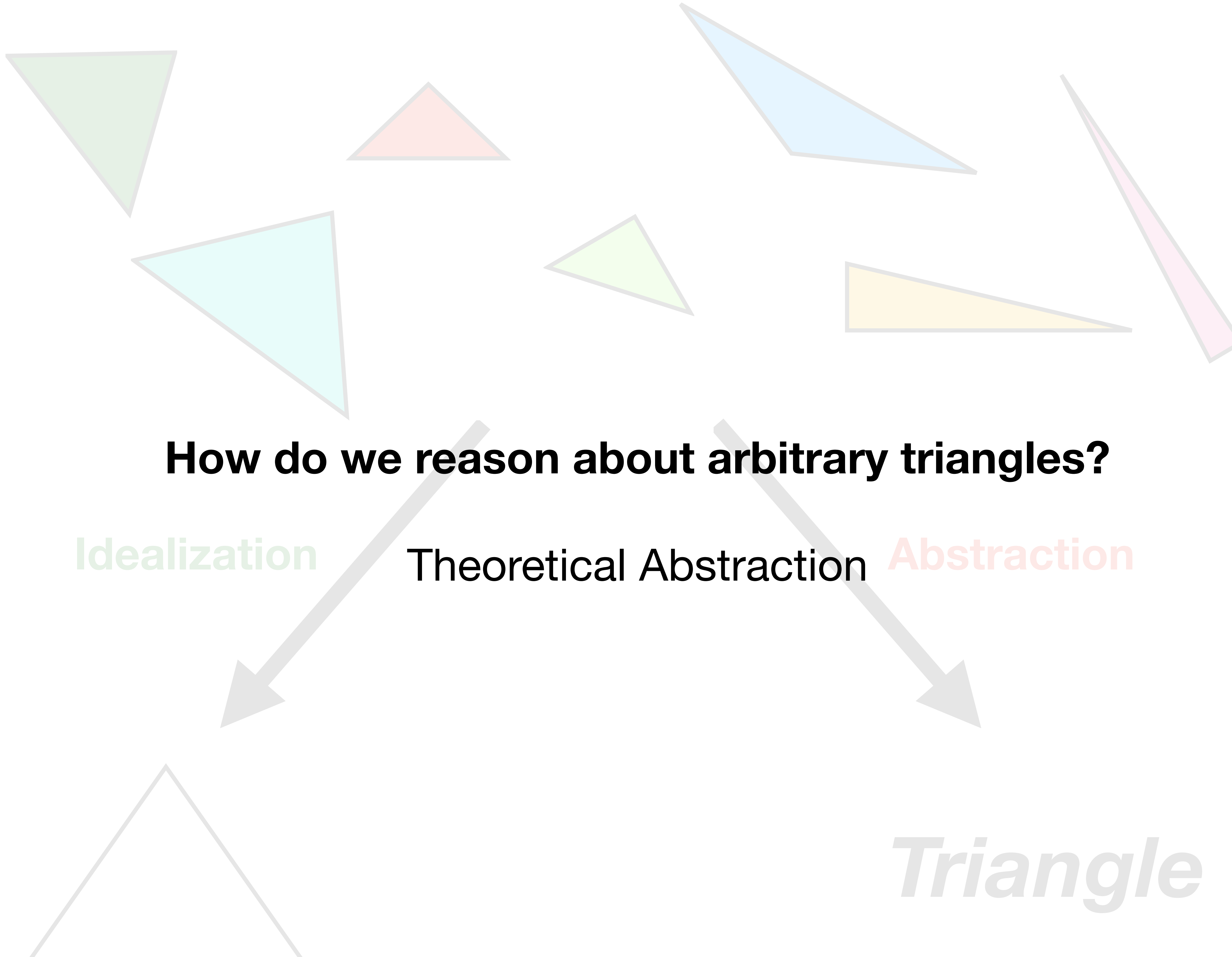

Idealization



Idealization
Abstraction
Triangle

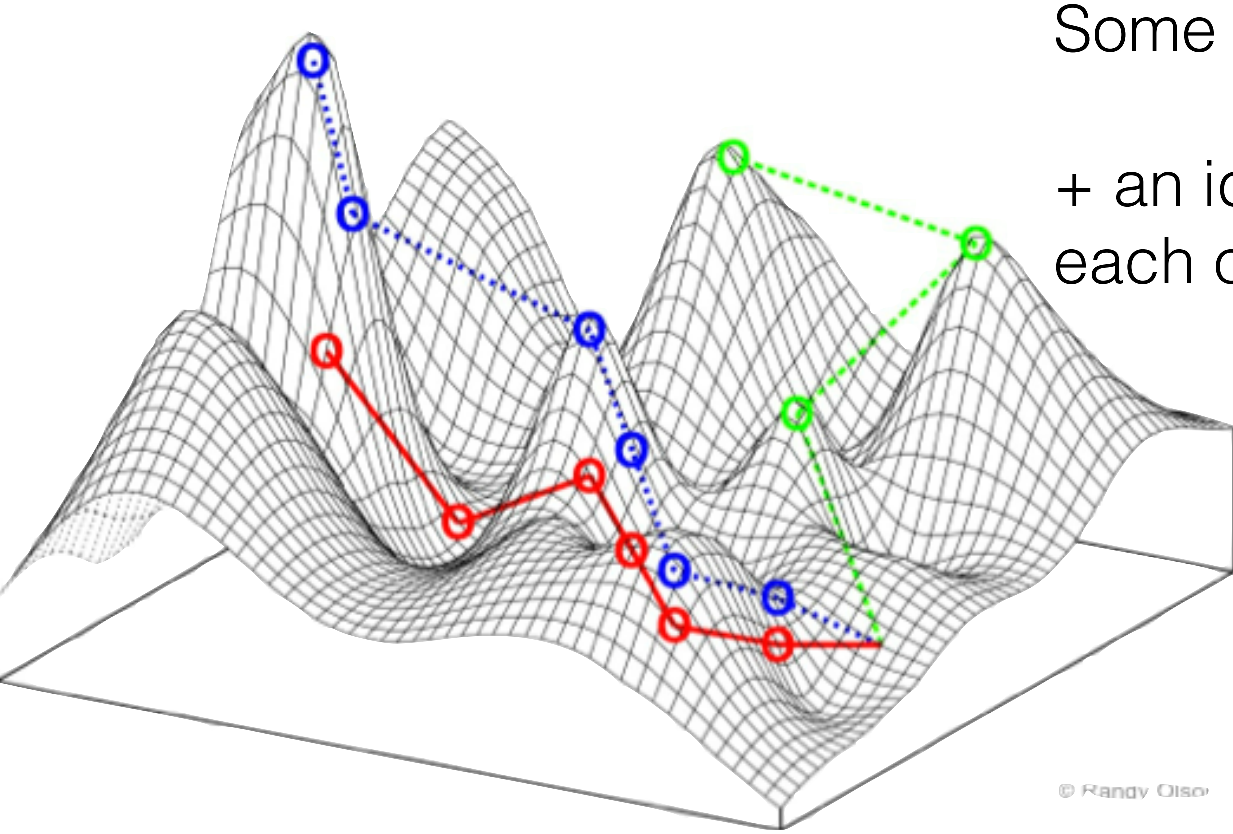
How do we reason about arbitrary triangles?

Theoretical Abstraction



Kaznatcheev, A. (**2019**)
Computational complexity as an ultimate constraint on evolution
Genetics, 302000.2019

Fitness Landscapes and Constraints



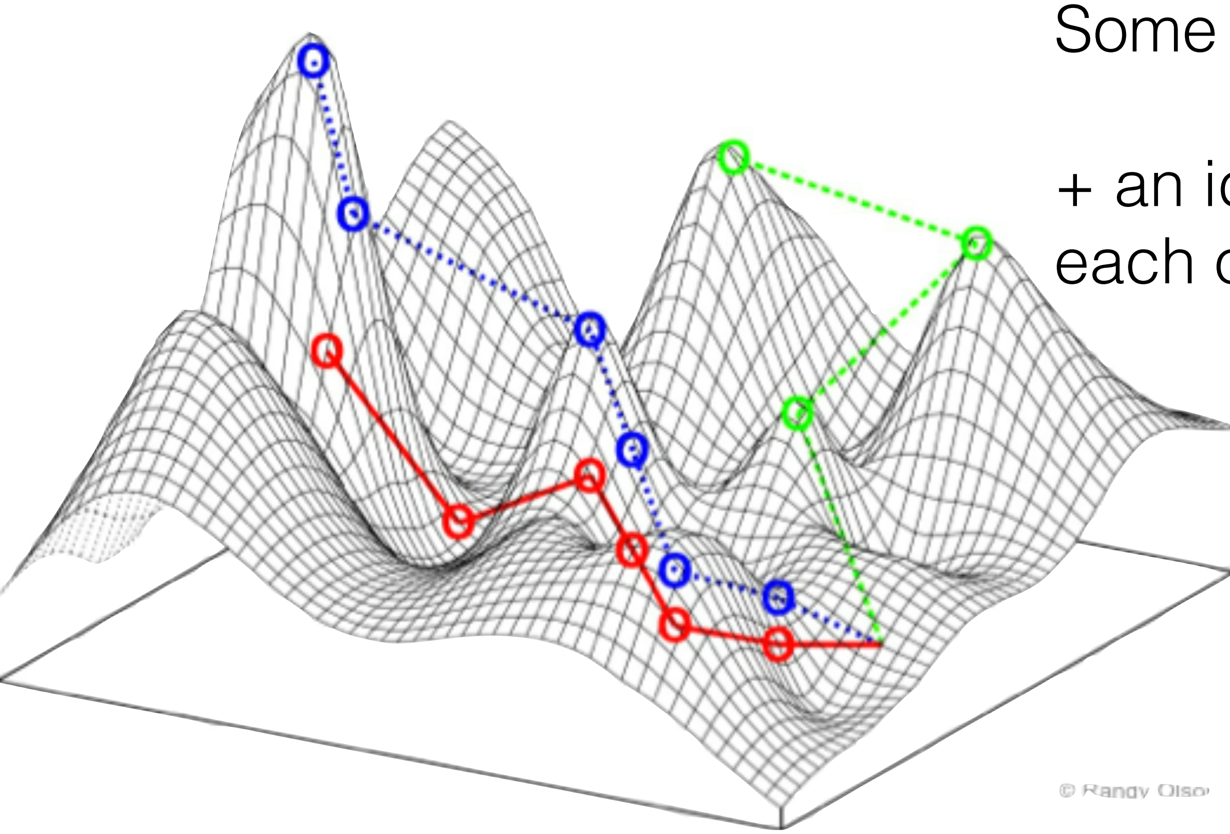
Some mapping from genotypes (or phenotypes) to fitness.

+ 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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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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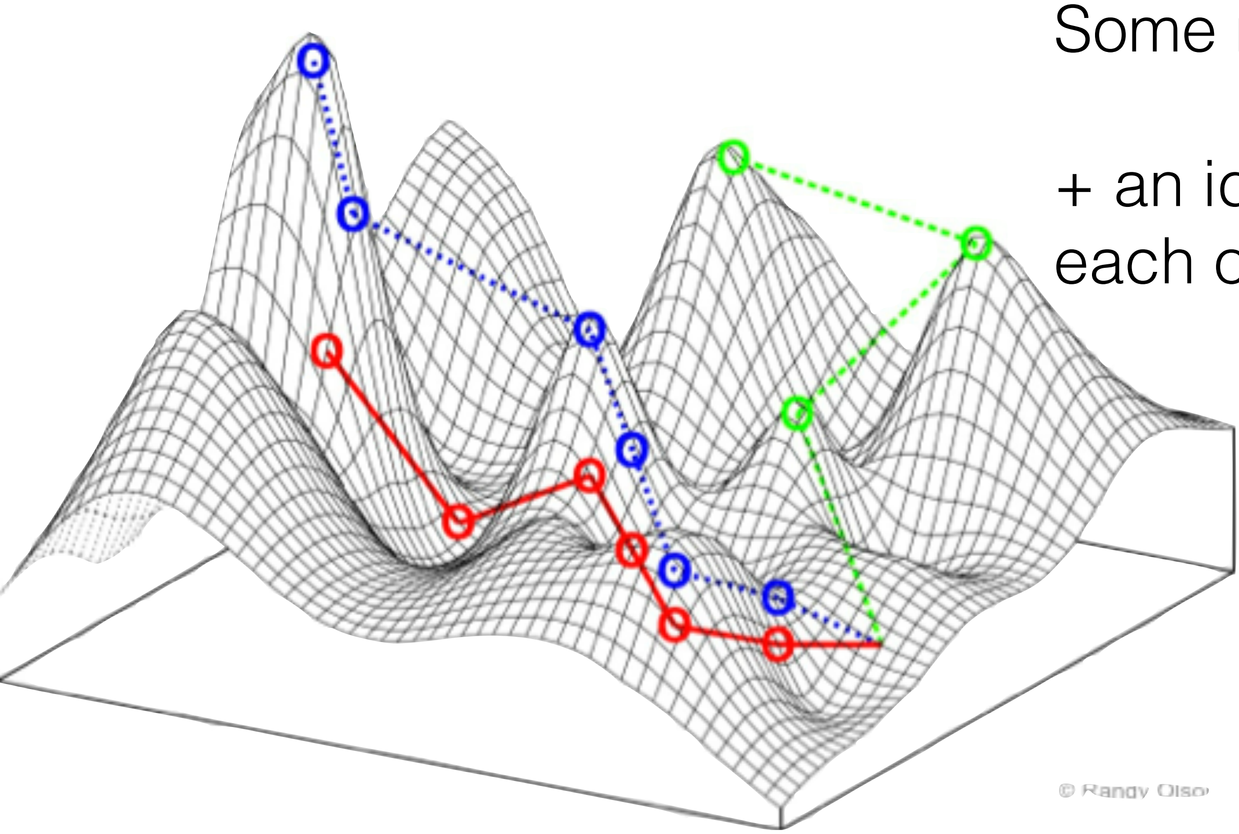

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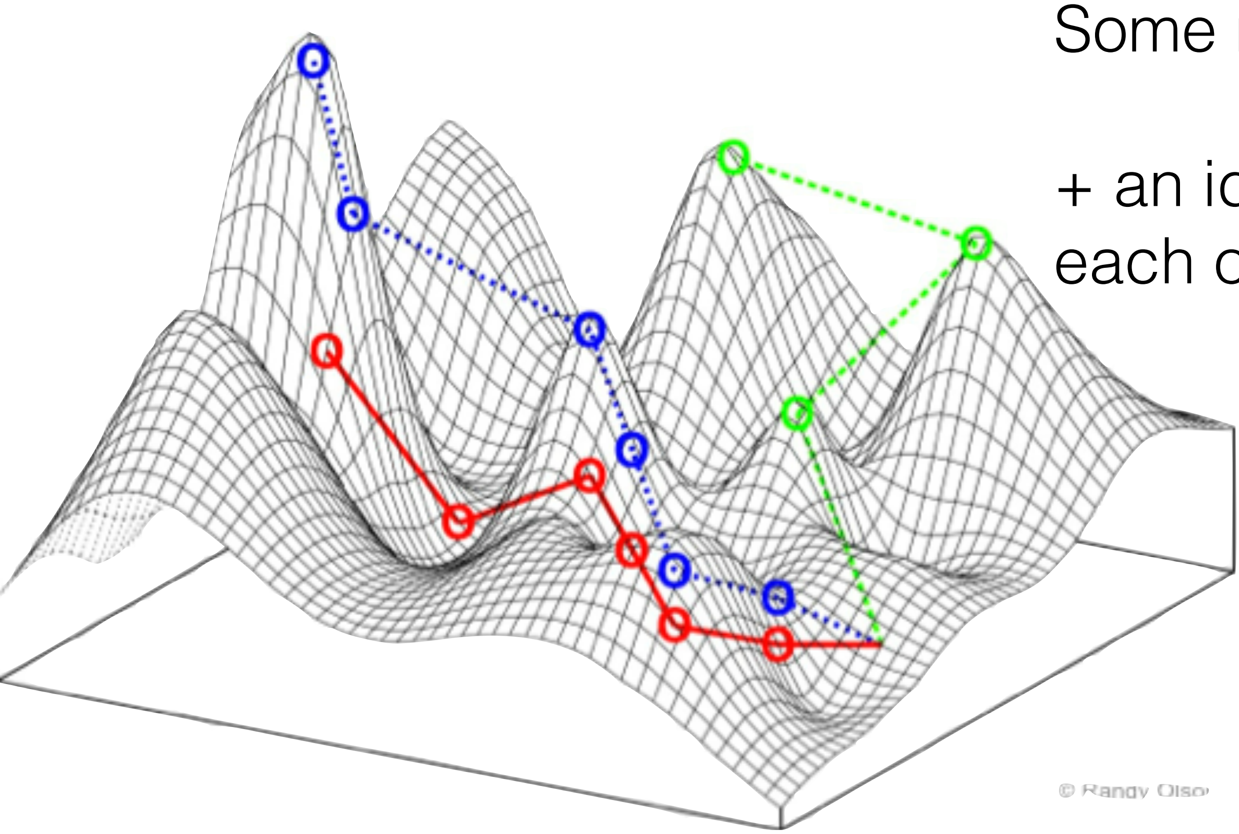
Algorithms and Problems

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**

Fitness Landscapes and Constraints



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Algorithms and Problems

Different population structures, developmental structures, trait co-variants, standing variation, etc…
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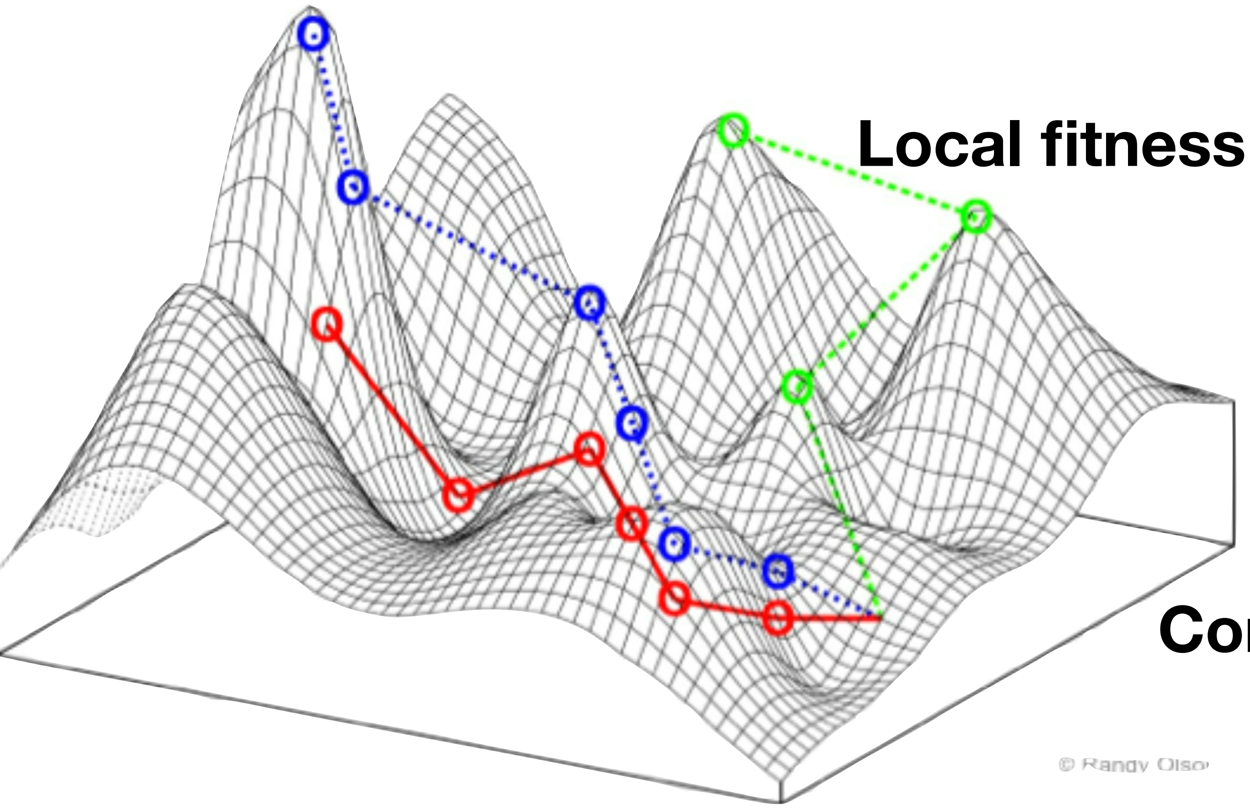
proximal constraints

Families of different fitness landscapes
correspond to **different problems**

ultimate constraints

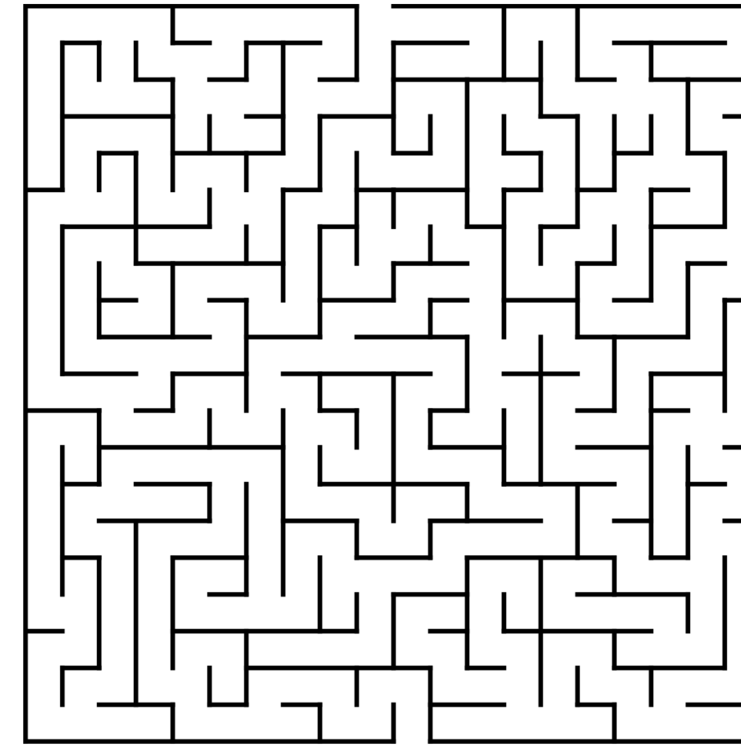
Fitness Landscapes and Constraint of Computation



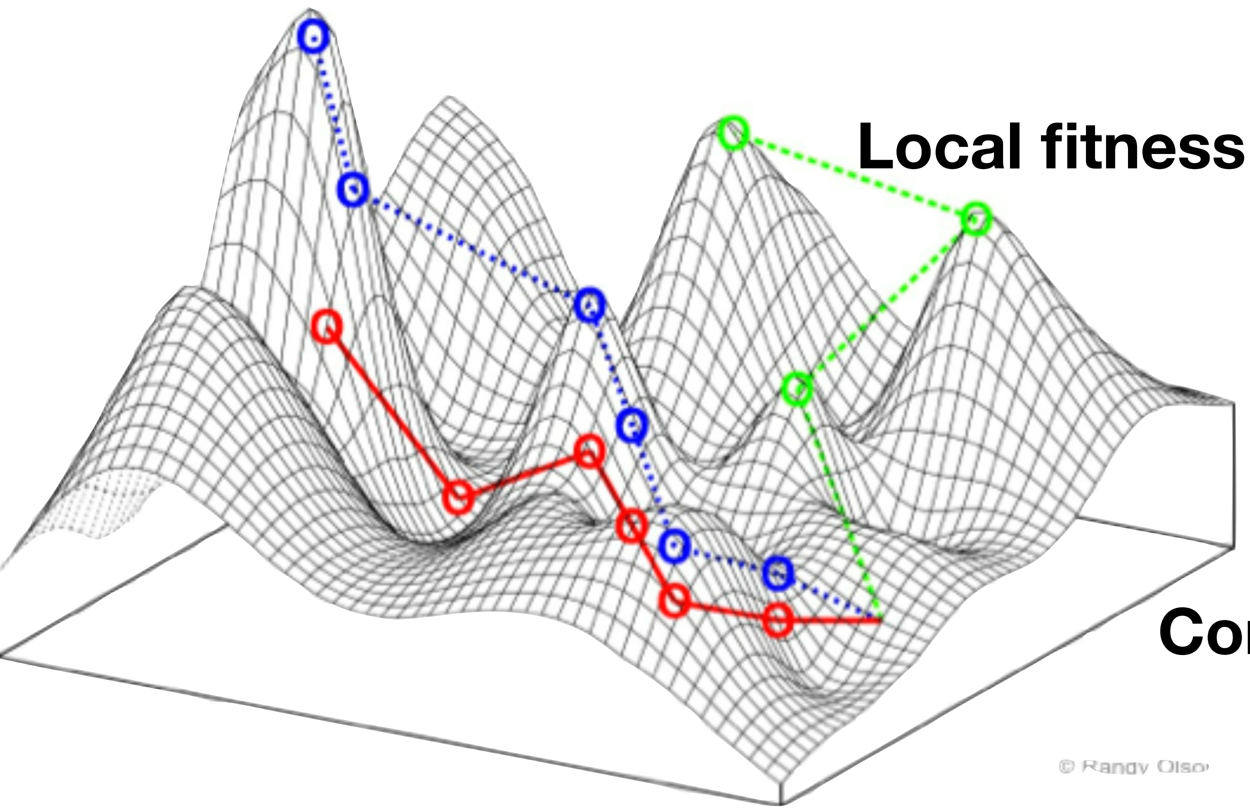
Local fitness peaks

vs.

Constraint of Computation



Fitness Landscapes and Constraint of Computation



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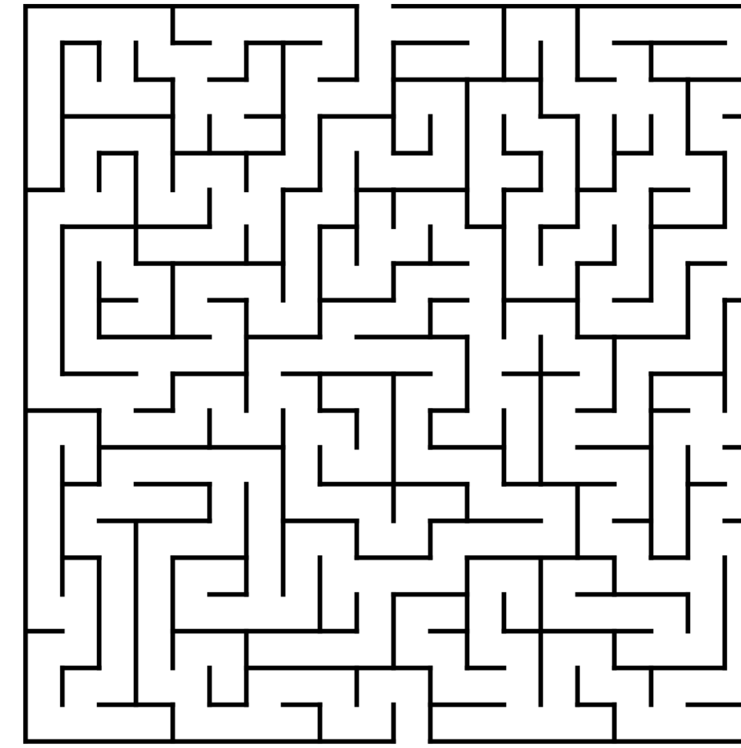

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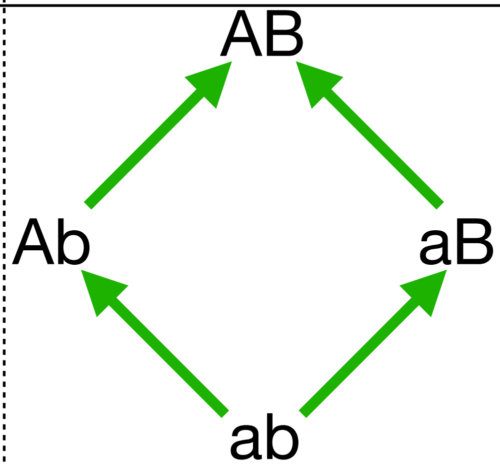
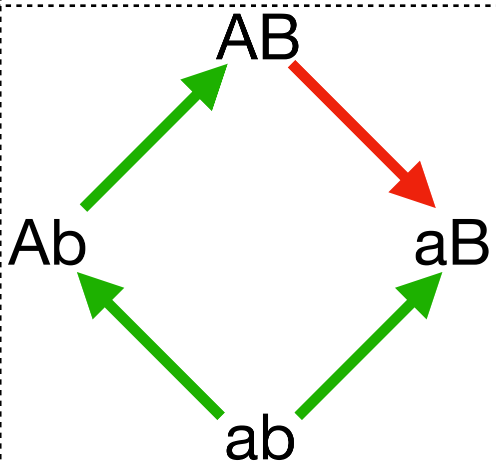
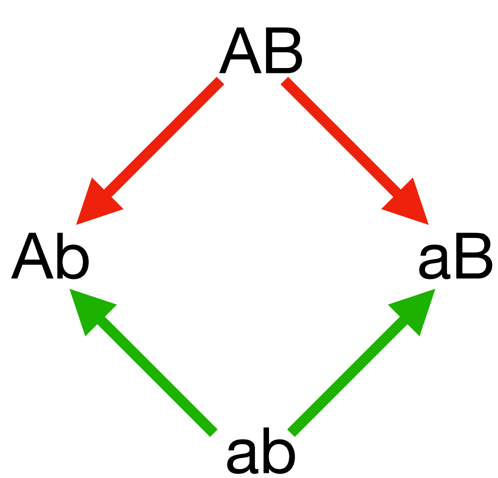
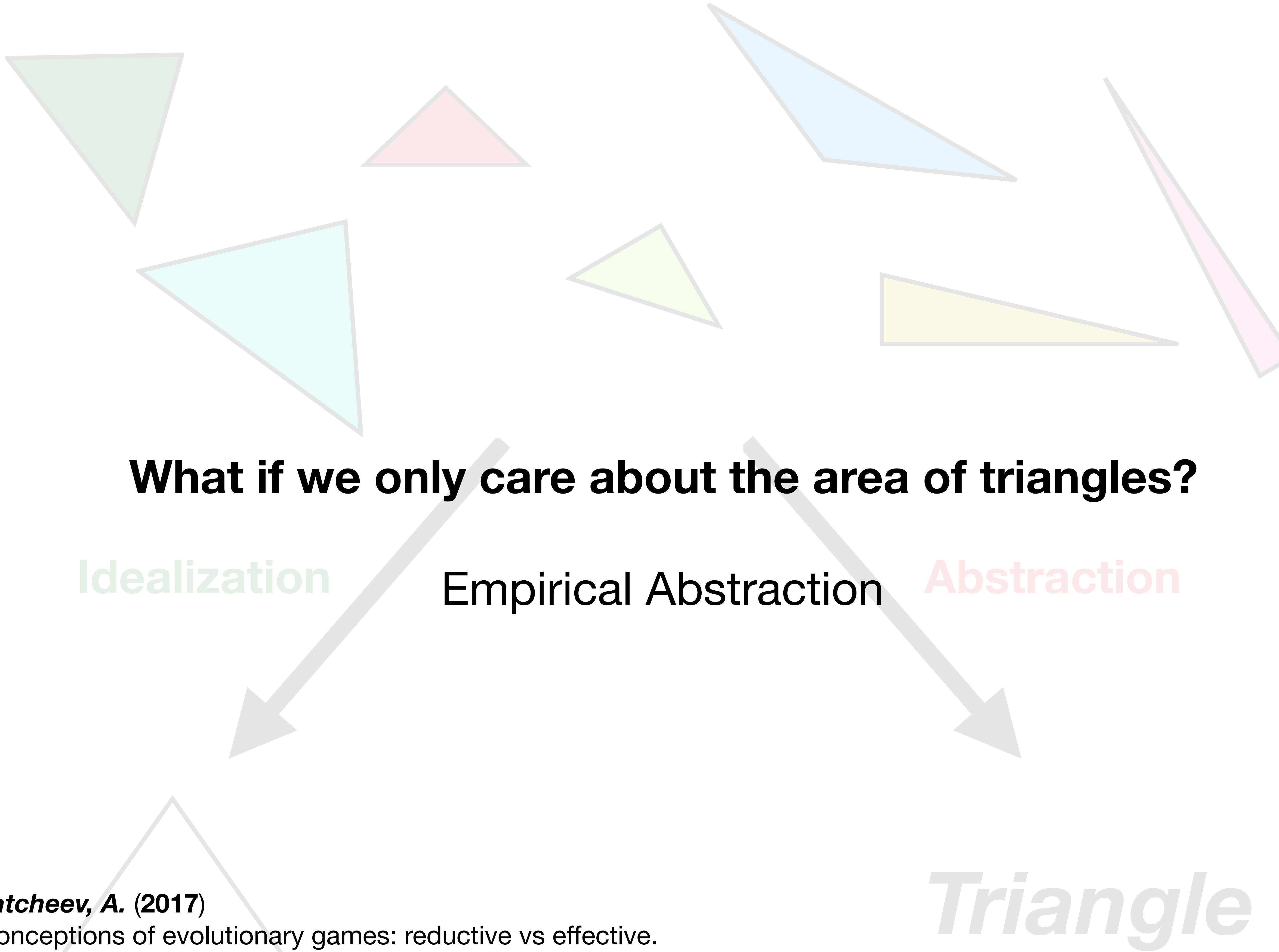
Now, for any probability of failure $0 < \delta < 1$, let $m_\delta = \frac{\log \frac{1}{\delta}}{2 - \log 3}$ (where log is base 2).

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 $PLS \neq P$ and $\log(f_{max}/f_\delta) \in O(n^k)$ then (for NK-model with $K \geq 2$) a local s-approximate peak cannot be found in time polynomial in n and $\log \frac{1}{s}$.*

Landscape type	**Max allowed epistasis type**	**Hardness of reaching local optima**
smooth	 magnitude	**Easy** for all strong-selection weak-mutation (SSWM) dynamics
semismooth	 sign	**Hard** for SSWM with random fitter mutant or fittest mutant dynamics
rugged	 reciprocal sign	**Hard** for all SSWM dynamics: initial genotypes with all adaptive paths of exponential lengths **Hard** for all evolutionary dynamics (if FP != 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**



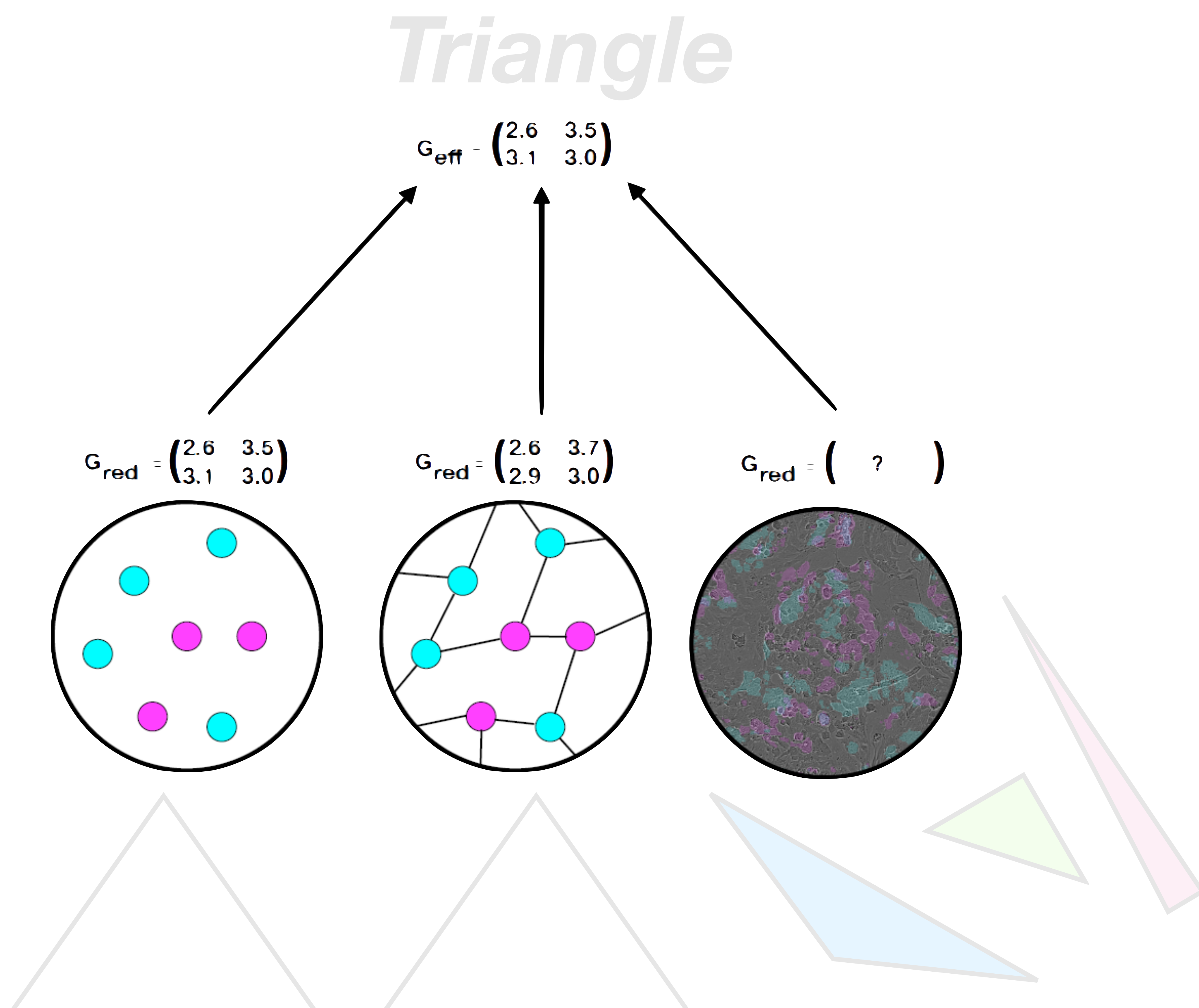
What if we only care about the area of triangles?

Empirical Abstraction

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

Kaznatcheev, A., Peacock, J., Basanta, D., Marusyk, A. & Scott, J.G. (**2019**)
Fibroblasts and Alectinib switch the evolutionary games played by non-small cell lung cancer
Nature Ecology & Evolution 12(108): 20150154.

Reductive vs effective games (in cancer)



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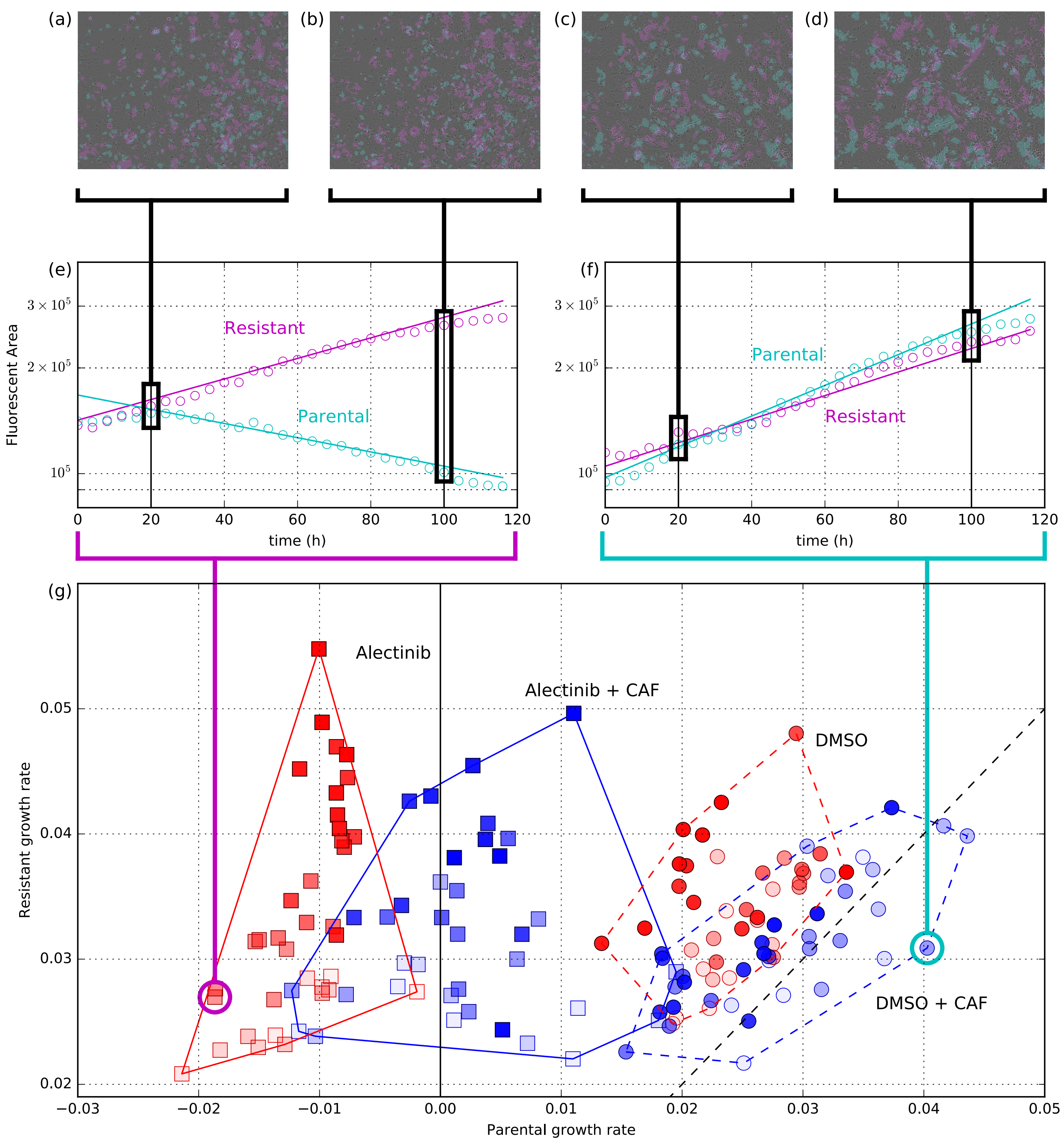
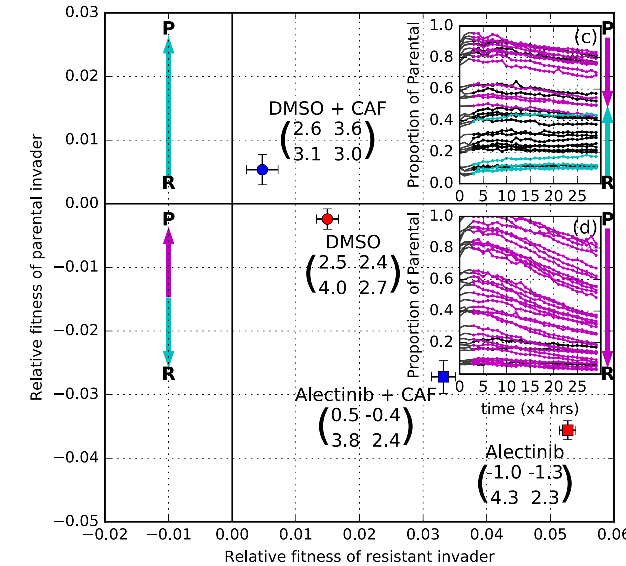


$$\begin{array}{c|cc} & P & R \\ \hline P & A & B \\ R & C & D \end{array} \Rightarrow \begin{cases} \frac{d}{dt}N_P = N_P \overbrace{\left(A\frac{N_P}{N_T} + B\frac{N_R}{N_T}\right)}^{\hat{w}_P:\text{ parental growth rate}} \\ \frac{d}{dt}N_R = N_R \underbrace{\left(C\frac{N_P}{N_T} + D\frac{N_R}{N_T}\right)}_{\hat{w}_R:\text{ resistant growth rate}} \end{cases}$$

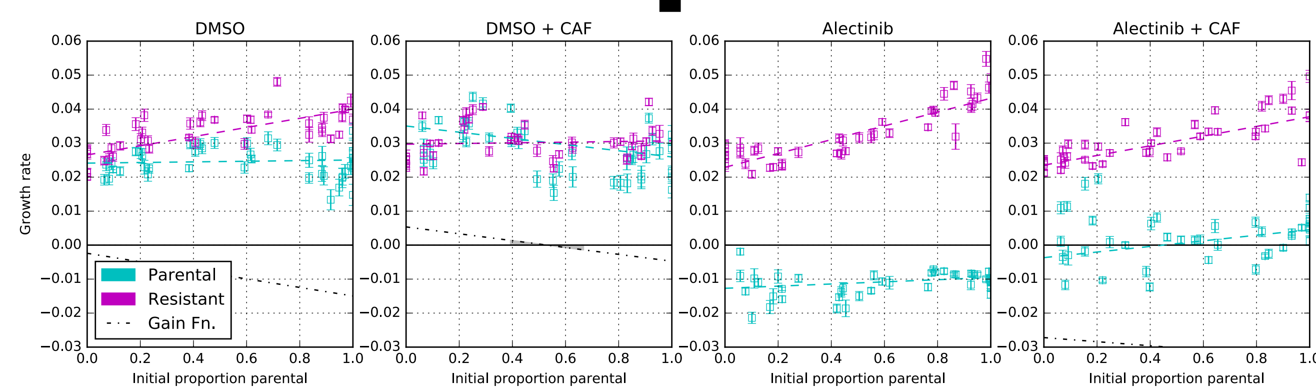
$$\Rightarrow \frac{dp}{dt} = p(1-p)\overbrace{\Big(\underbrace{(B-D)}_{\text{relative fitness of parental invader}}(1-p) - \underbrace{(C-A)}_{\text{relative fitness of resistant invader}}p\Big)}^{\text{gain function for } p}$$

where $N_T = N_P + N_R$ and $p = \frac{N_P}{N_T}$.

(a) Replicator dynamics for parental-resistant NSCLC.



(b) Two dimensional game space.



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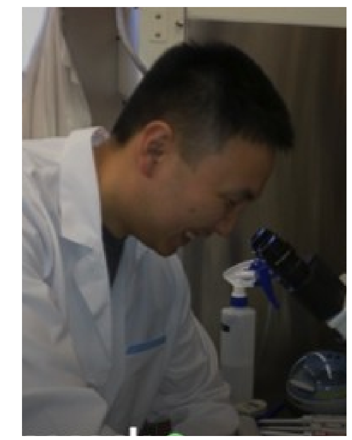
MOFFITT CANCER CENTER

David Basanta

Jeffrey Peacock



Andriy Marusyk

Cleveland Clinic

Jacob G Scott

Thank You!

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