Adaptation on rugged fitness landscapes

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K. Jain & S. Seetharaman, Genetics **189**, 1029 (2011)

K. Jain, EPL **96**, 58006 (2011)

Outline

A model of adaptation

- has few parameters, offers a good testing ground

- some theoretical predictions (Orr, 2002) have been experimentally verified (Rokyta et al., 2005)

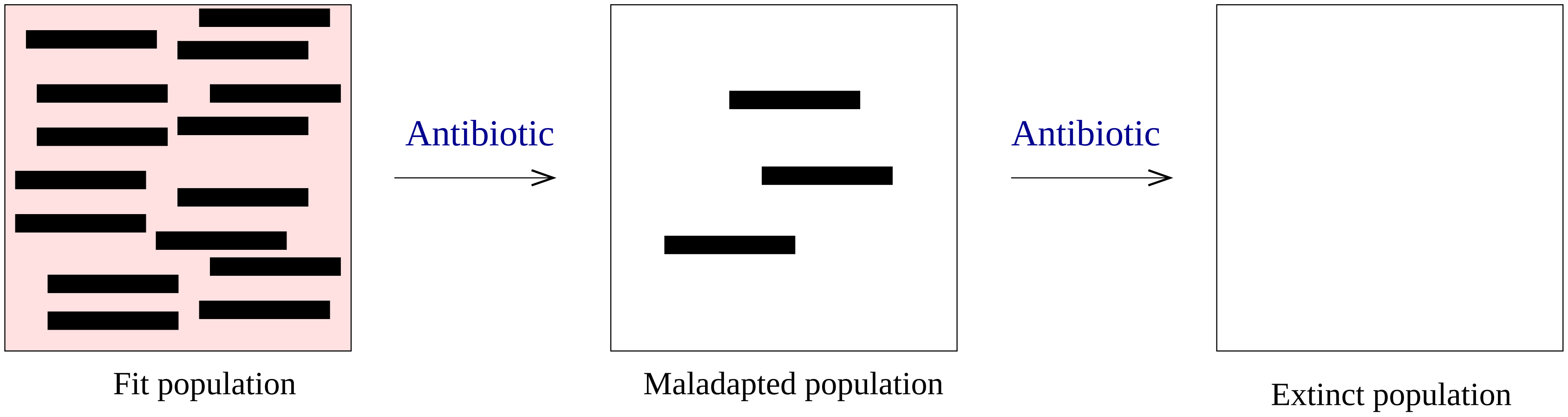
Our results

- analytically calculate quantities of interest

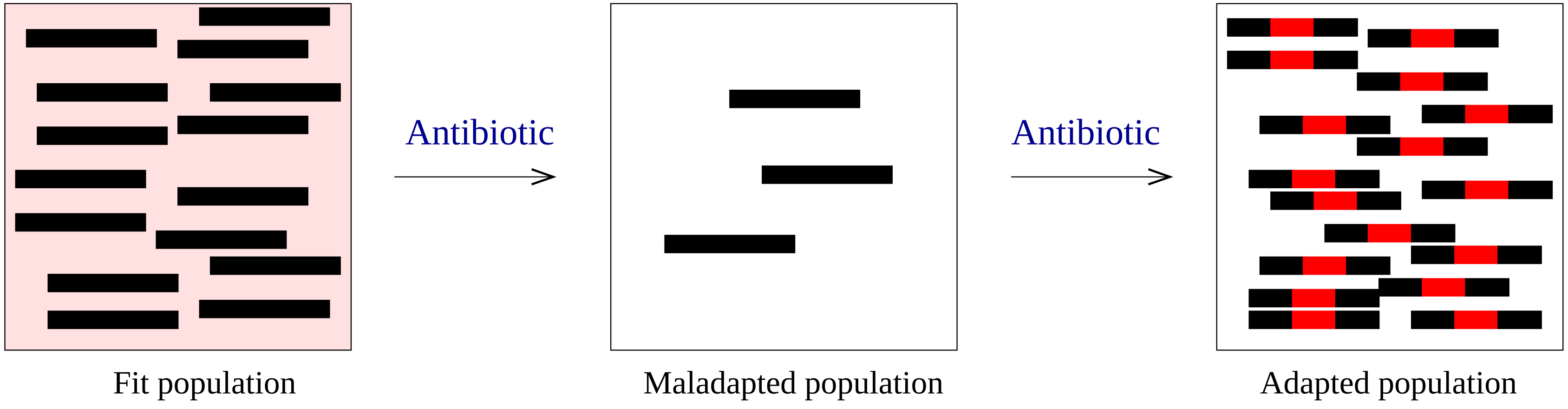
- make experimentally testable predictions

Adapt or Perish ... (H. G. Wells)

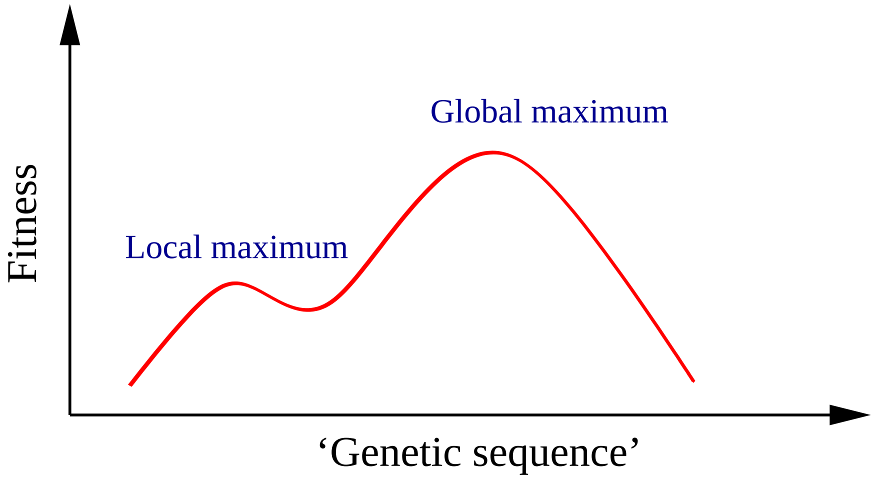
A maladapted population will either die

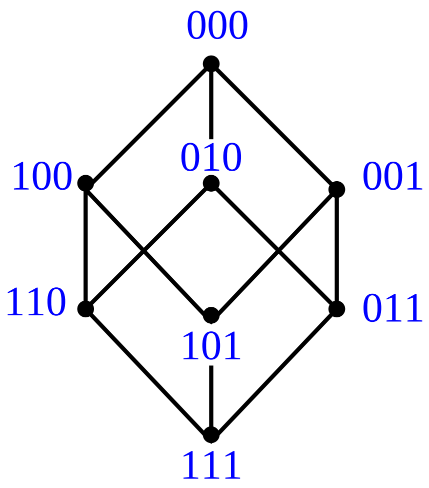


or acquire beneficial mutation(s)

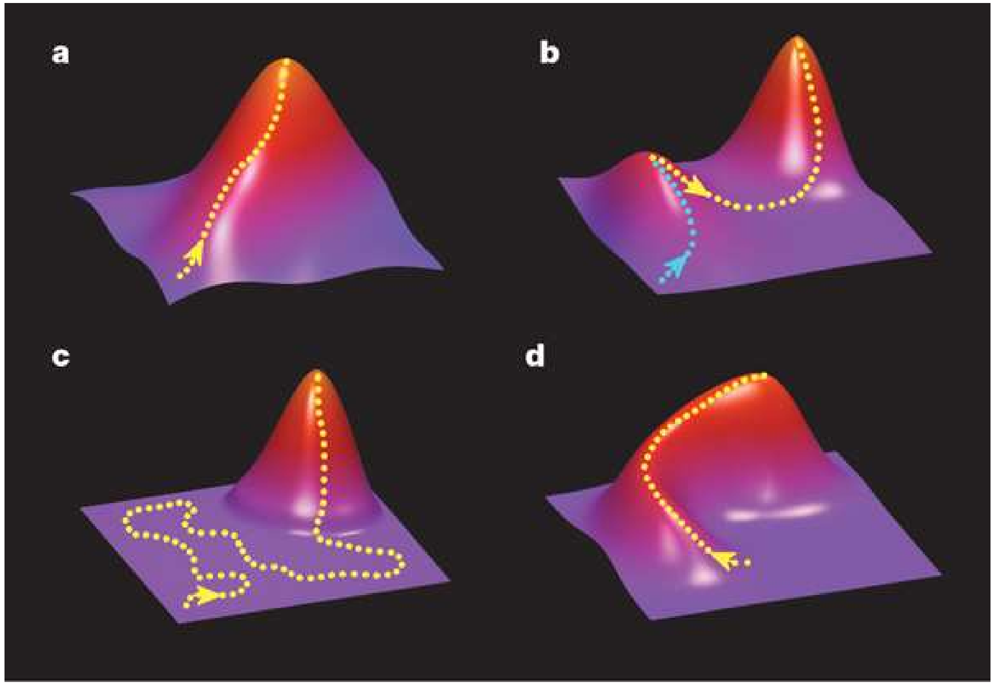


Fitness landscapes

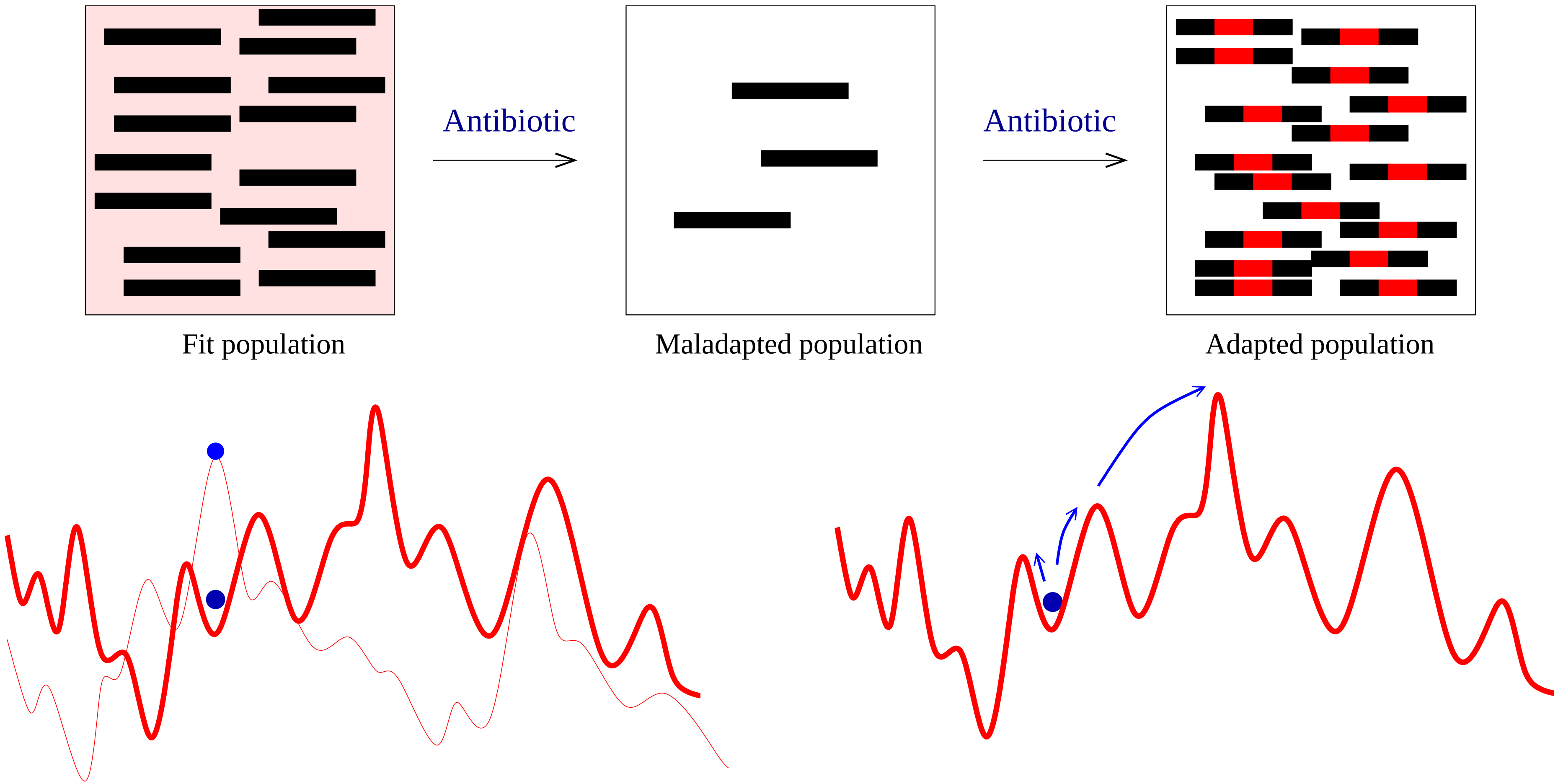




Hamming space for binary sequence of length $L = 3$



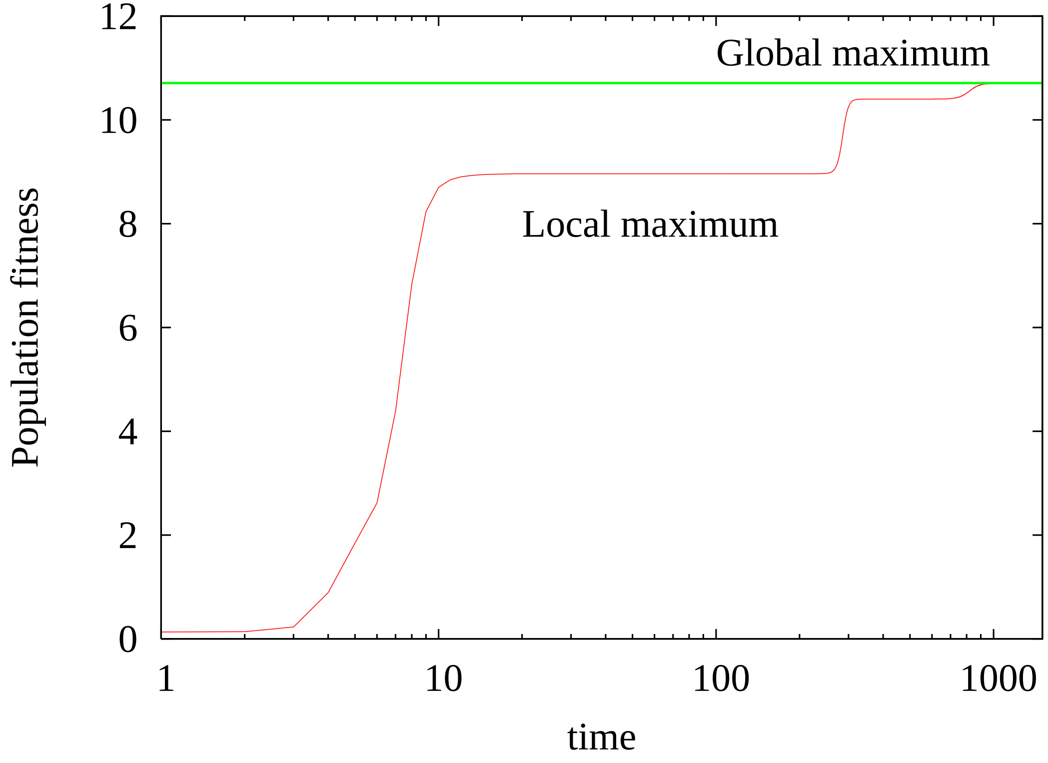
Climbing the fitness landscape (Wright, 1932)



Regimes in adaptation dynamics (Jain & Krug, Genetics 2007)

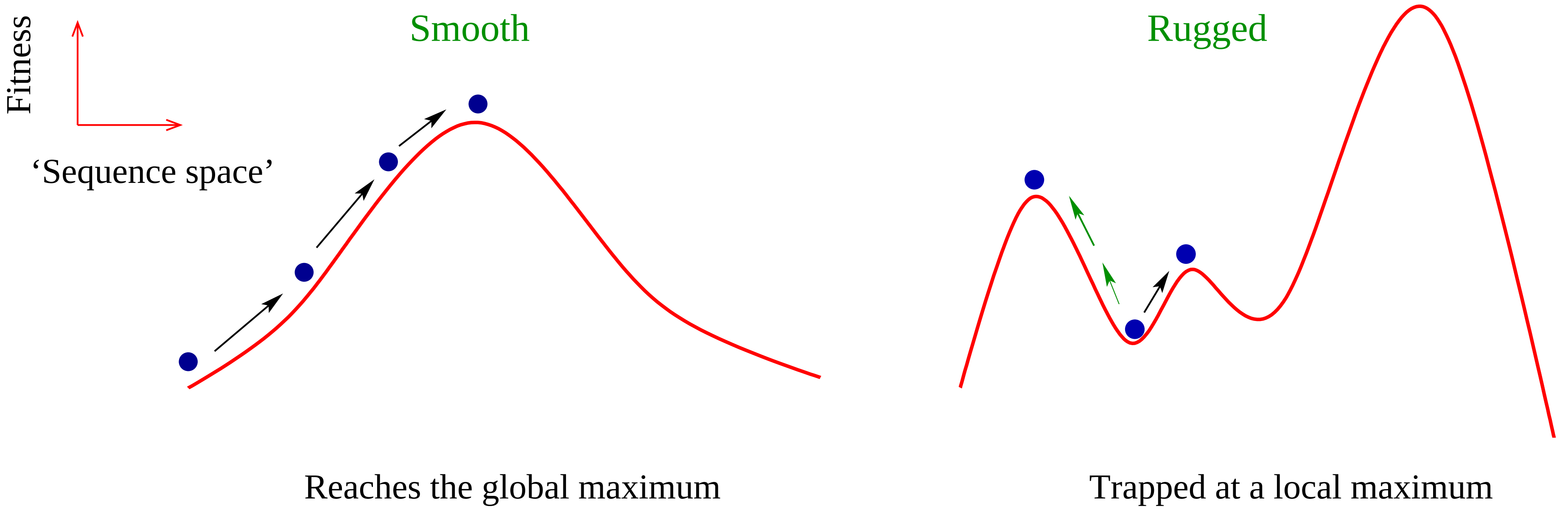
Important parameter n: number of mutants produced per generation

If $n \gg 1$: polymorphic population, scan the whole fitness landscape quickly



Regimes in adaptation dynamics (Jain & Krug, Genetics 2007)

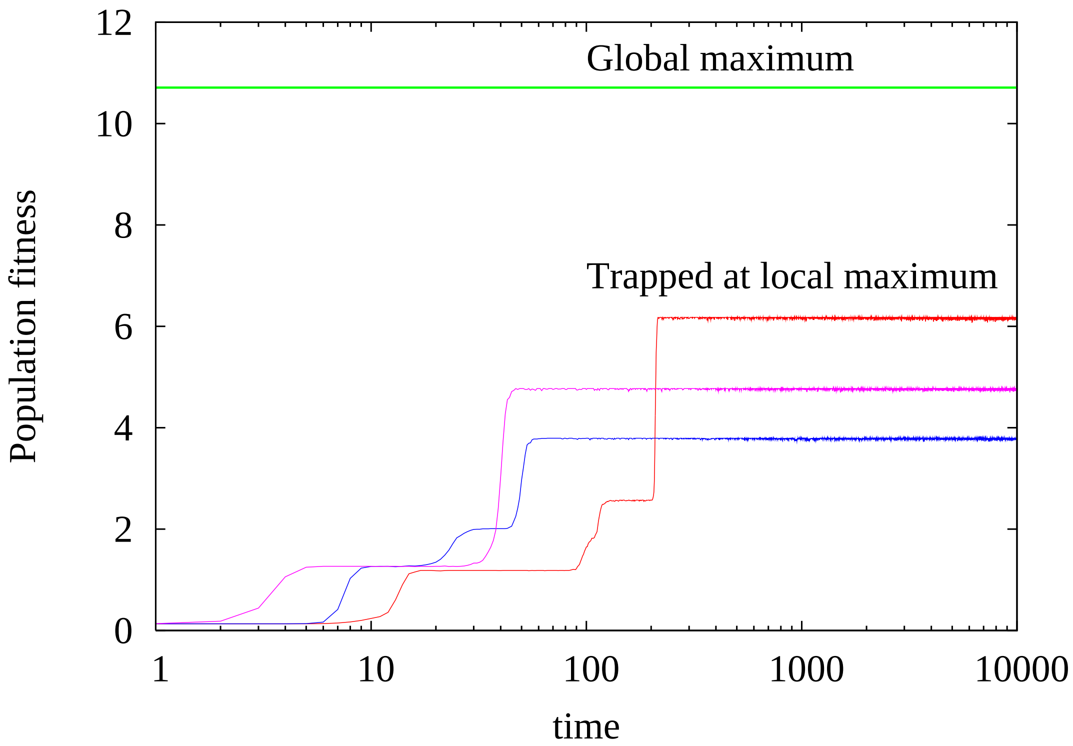
If $n \ll 1$: population is ‘myopic’, can scan at most one-mutant neighbors



In this talk: Uphill walk on maximally rugged fitness landscapes

Adaptive walk on rugged fitness landscapes

Population walks uphill until it hits a local fitness maximum

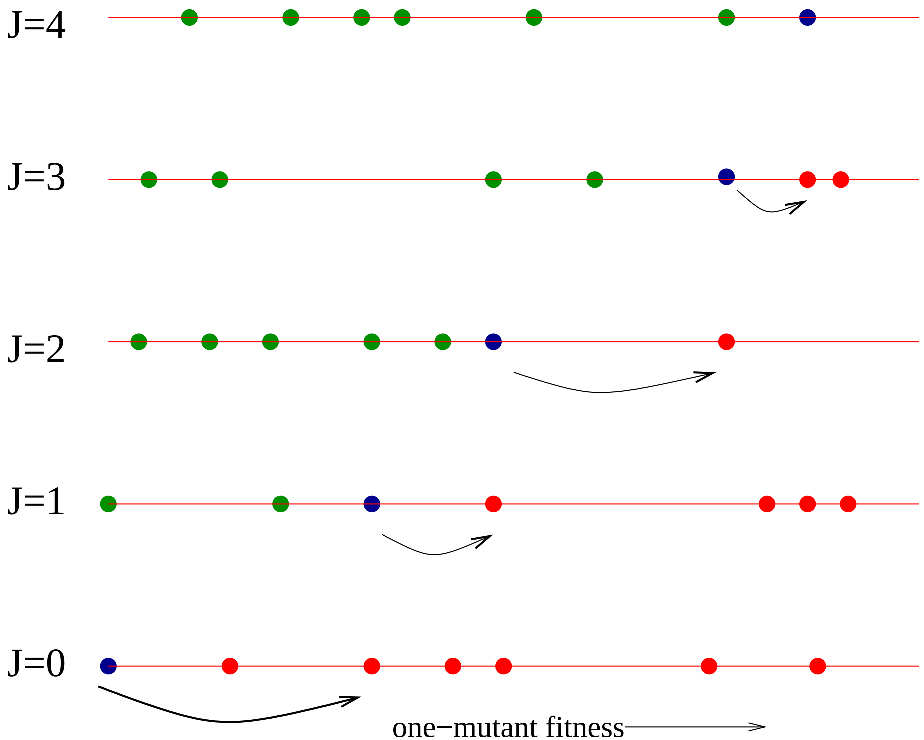


First step in the walk is well studied (Orr 2002; Orr 2006; Joyce et al. 2008)

Statistical properties of the entire walk?

Adaptive walk (Gillespie, 1984)

- Need to consider only L one-mutant neighbors
- Always walk uphill until no better fitness is available



- Transition probability $\propto$ Mutant fitness-Current fitness

Length of the adaptive walk

In this talk: fitnesses are independent and identically distributed

Choice of fitness distribution motivated by extreme value theory:

$$p(f) = \begin{cases} (1+\kappa f)^{-\frac{1+\kappa}{\kappa}} \ , \ \kappa < 0, f < -1/\kappa \\ e^{-f} \ , \ \kappa \to 0 \\ (1+\kappa f)^{-\frac{1+\kappa}{\kappa}} \ , \ \kappa > 0 \end{cases}$$

Note that mean of $p(f)$ is finite when $\kappa < 1$

Average number of steps to a local peak?

For $\kappa < 1$: Average walk length diverges with L

For $\kappa > 1$: Average walk length is a constant

Length of the adaptive walk: an argument

Transition probability $T(f \leftarrow h) = \underbrace{Lp(f)}_{\text{sequences with fitness f}} \times \frac{f-h}{\sum_{g>h} g-h}$

For $\kappa < 1$: Replace $\sum_{g>h} g-h$ by an integral for large L

$$T(f \leftarrow h) = \frac{(f-h)p(f)}{\int_h dg(g-h)p(g)}$$: finite for f-h $\sim \mathcal{O}(1)$

Walk goes on indefinitely for infinite L

For $\kappa > 1$: Replace $\sum_{g>h} g-h$ by largest term $\sim L^\kappa$ & $Lp(f) \sim \mathcal{O}(1)$

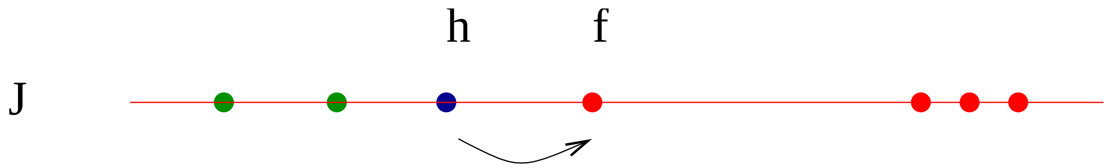
$$T(f \leftarrow h) \sim \frac{f-h}{L^\kappa}$$: finite for f-h $\sim \mathcal{O}(L^\kappa)$

Since local optimum also has fitness L^κ, walk terminates

Adaptive walk for $\kappa < 1$

$\mathcal{P}_J(f) =$ Prob(fitness is f at the Jth step in the walk)

Recursion equation for $\mathcal{P}_J(f)$:



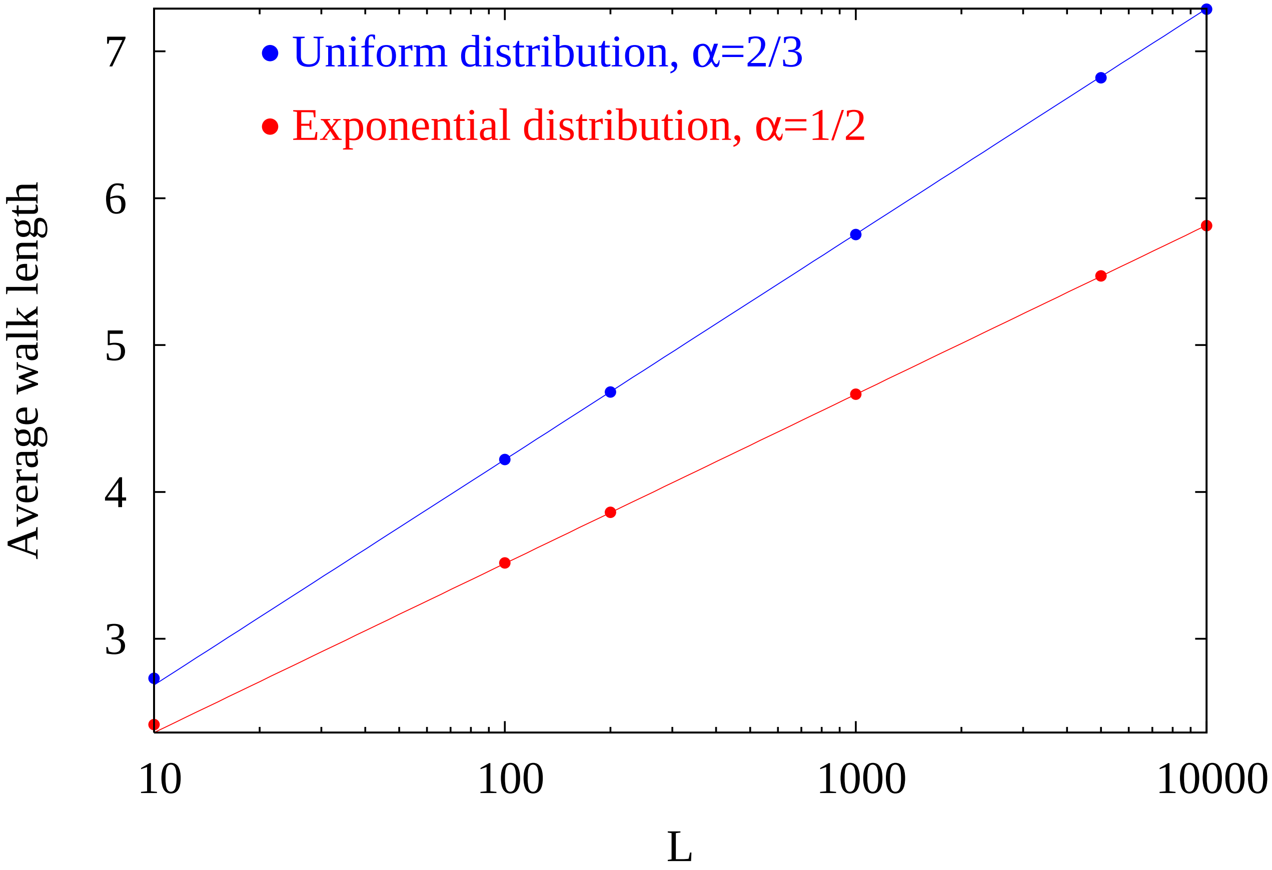
$$\mathcal{P}_{J+1}(f) = \int_0^f dh \quad \underbrace{\frac{(f-h)p(f)}{\int_h^u dg(g-h)p(g)}}_{\text{Transition prob} \propto \text{fitness gap}} \quad \underbrace{(1 - q^L(h))}_{\text{Prob(fitness>h available)}} \quad \mathcal{P}_J(h)$$

where

$$q^L(h) = \text{Prob(none are better than } h\text{)} = \left(\int_0^h dg p(g) \right)^L$$

Adaptive walks are short

$$\text{Average walk length} \approx \left(\frac{1-\kappa}{2-\kappa}\right) \ln L \;, \;\; \kappa < 1$$

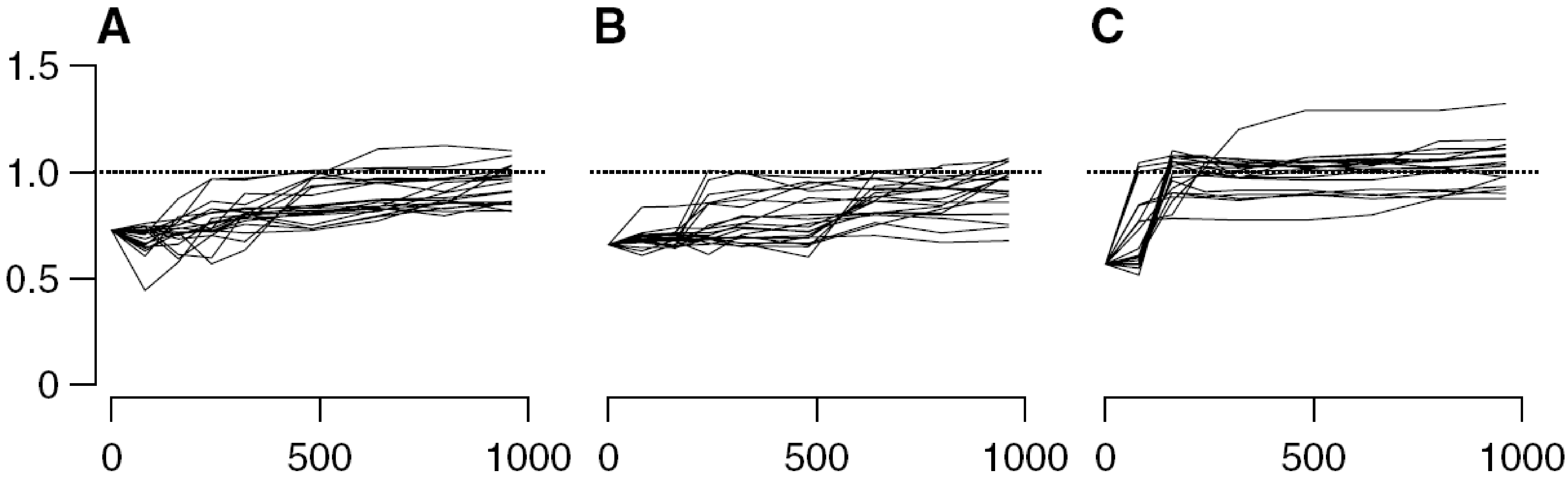


Entire adaptive walk: experiments (Gifford et al., 2011)

20 replicate populations of *A. nidulans* evolved for 800 generations

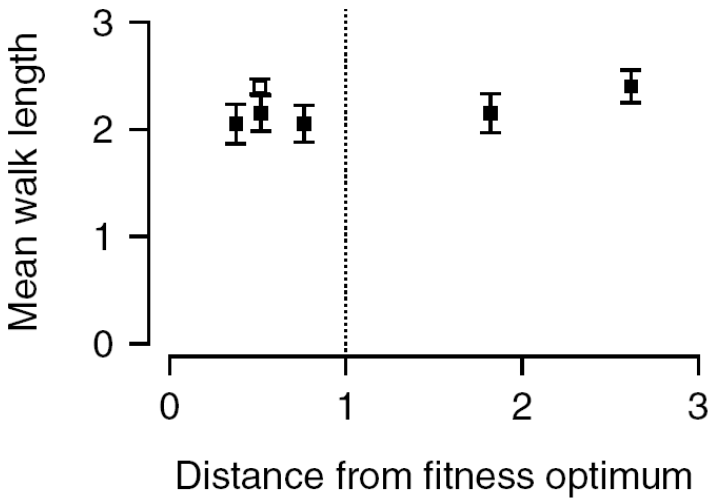
Fitness (growth rate) of the colony measured

For different initial conditions, counted substitutions until fitness saturated



Average walk length: experiments (Gifford et al., 2011)

(i) about 2 steps long (ii) independent of initial conditions



Suggests $\kappa > 1$ in *A. nidulans*. This needs experimental verification

Summary

- Described a model of adaptation; requires L and κ
- Theoretical result on the number of steps to a local fitness peak

Other results

- Assumption of independently distributed fitnesses can be relaxed
- Certain distributions can be computed