Theory and Practice of Optimal Mutation Rate Control in Hamming Spaces of DNA Sequences

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Evolution as an Information Dynamic System

- EPSRC Sandpit '*Math of Life*' (July, 2009):

- Three year project (2010–12)

  Middlesex University : Roman Belavkin
  University of Warwick : John Aston
  University of Keele : Alastair Channon & Elizabeth Aston
  University of Manchester : Chris Knight & Rok Krasovec

Introduction: Optimal Mutation Rates

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- May depend on changes in the environment (Bjedov et al., 2003).

Preliminaries

Individuals and Fitness

Let Ω — all individual organisms, $f : \Omega \to \mathbb{R}$ fitness function, $x = f(\omega)$.

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- $T := \Big(P(x_{s+1} \mid x_s)\Big)$ — Markov operator, $p_s := P(x_s)$

$$p_{s+1} = Tp_s = \sum_{x_s} P(x_{s+1} \mid x_s)\, P(x_s) \quad \Rightarrow \quad p_{s+t} = T^t p_s$$

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- $\mu(x)$ — control function, $T_{\mu(x)}$, $\mathbb{E}_{\mu(x)}\{x_{s+t}\}$.

Optimal Fitness Value Functions

Instantaneous

- Maximum adaptation in no more than λ generations

$$\overline{x}(\lambda) := \sup_{\mu(x)} \{\mathbb{E}_{\mu(x)}\{x_{s+t}\} : t \leq \lambda\}$$

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Information Dynamics (Belavkin, 2010, 2011)

- Maximum adaptation in no more than λ bits between p_s and p_{s+t}:

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Relatively Monotonic Landscapes

Representation : alphabet $\{1, \ldots, \alpha\}$, genotypes $\omega \iff (\alpha_1, \ldots, \alpha_l)$.

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Question

Rugged landscape?

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f is locally monotonic (isomorphic) relative to a metric d, if there exist $B(\top, l) := \{\omega : d(\top, \omega) \leq l\}$, $\top = \sup \Omega$, such that $\forall\, a, b \in B(\top, l)$:

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Example (Needle in a haystack)

$f(\omega) = 1$ if $d(\top, \omega) = 0$; $f(\omega) = 0$ otherwise.

Mutation and Adaptation in a Hamming Space

$\bullet a$

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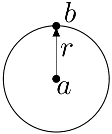

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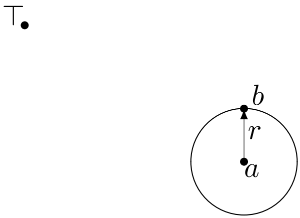

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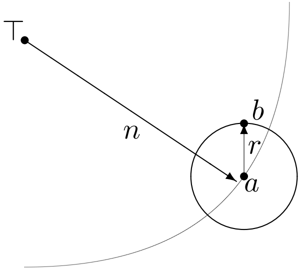

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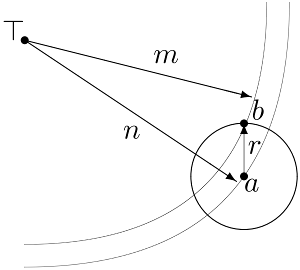

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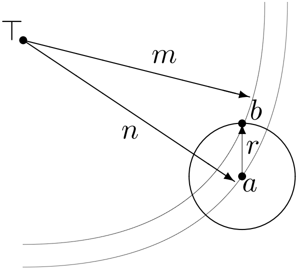

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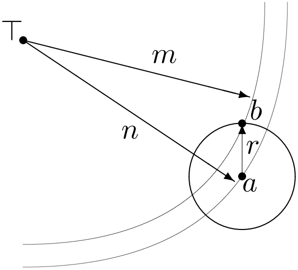

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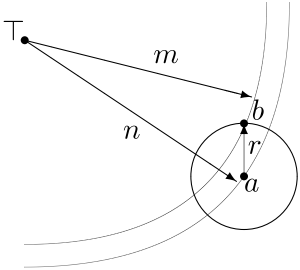

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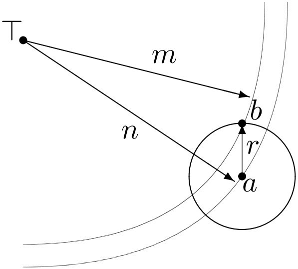

- Expand for all $r \in [0, l]$:

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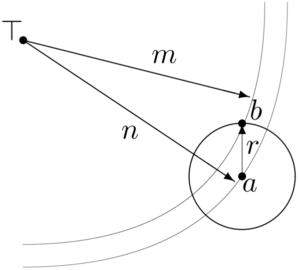

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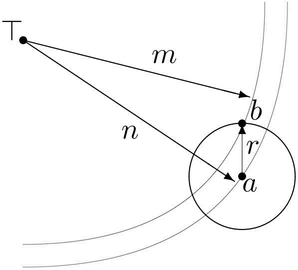

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Adaptation in One Generation

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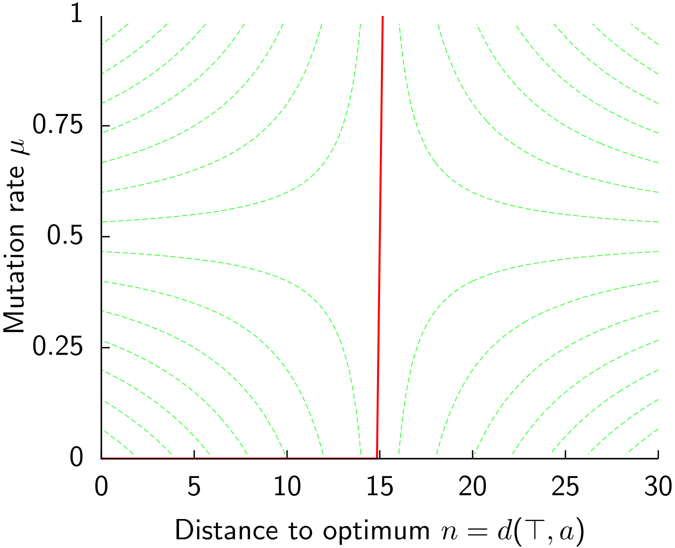
- Minimize $\mathbb{E}\{n_{s+t}\}$ subject to $t \leq 1$.
- In this case the optimal function is

$$\mu(n) := \begin{cases} 0 & \text{if } n < l(1 - 1/\alpha) \\ \frac{1}{2} & \text{if } n = l(1 - 1/\alpha) \\ 1 & \text{otherwise} \end{cases}$$

Step function



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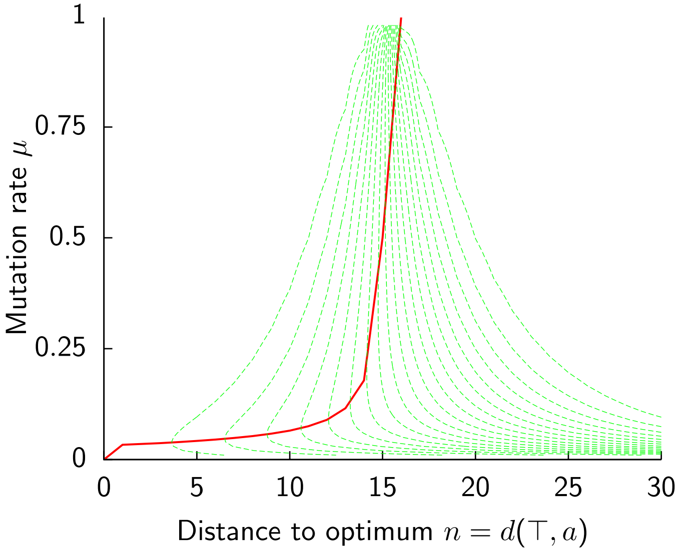
- This corresponds to maximization of $\mathbb{E}\{u(m,n)\}$, where

$$u(m,n) := \begin{cases} 1 & \text{if } m < n \\ 0 & \text{otherwise} \end{cases}$$

$\max P_{\mu}(m < n \mid n)\}$



Mutation to Optimum

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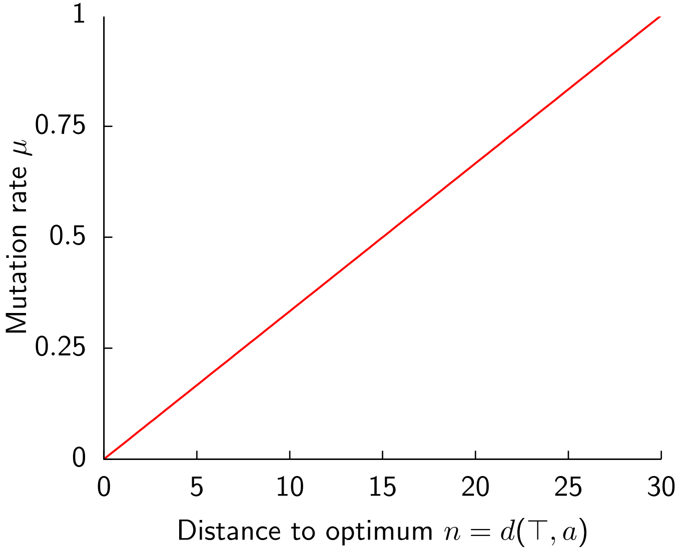
- *Optimal for Boolean landscapes (Needle in a haystack).*

Linear function



Information Heuristics $t \leq \lambda \iff I_{KL}(p_{s+t}, p_s) \leq \lambda$

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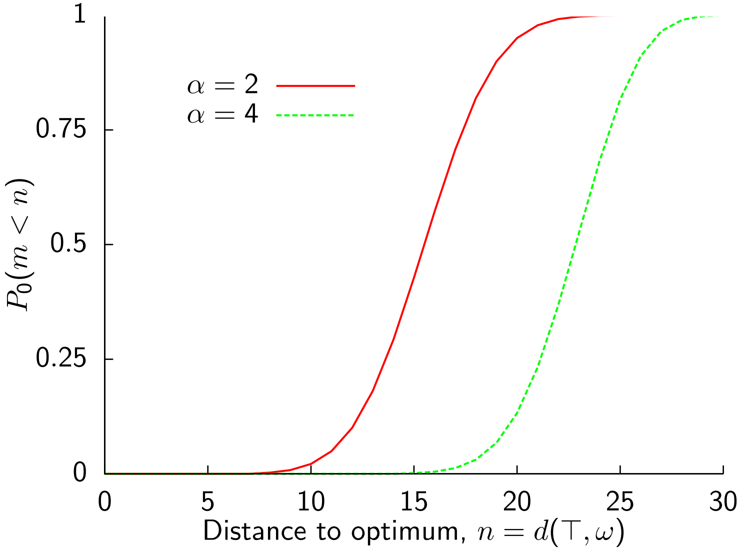
Informed Mutation Rate

In a (weakly) monotonic landscape we can use CDF of empirical frequency P_e of observed fitness values:

$$P_0(m) \iff P_e(x) \quad \text{and} \quad P_0(m < n) \iff P_e(x_r > x)$$

'Informed' Mutation function



Practice: Evolving Optimal Mutation Rates

Inner GA

Genotypes : sequences in $\mathcal{H}_\alpha^l$.

Populations : 100 individuals.

Generations : $t = 500$.

Evolution : mutation only.

Objective : maximize $x = f(\omega)$.

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Meta GA

Genotypes : functions $\mu(x)$, $\mu \in [0, 1]$.

Populations : 100 individuals.

Generations : $t = 5 \cdot 10^5$.

Evolution : tournament selection, recombination, mutation.

Objective : maximize $\mathbb{E}\{x\}$ in Inner GA at the last generation.

Experimental Results

1. $\mathcal{H}_2^{30}$ (i.e. $\alpha = 2$, $l = 30$) and fitness $f(\omega) = -d(\top, \omega)$, where d is Hamming metric.

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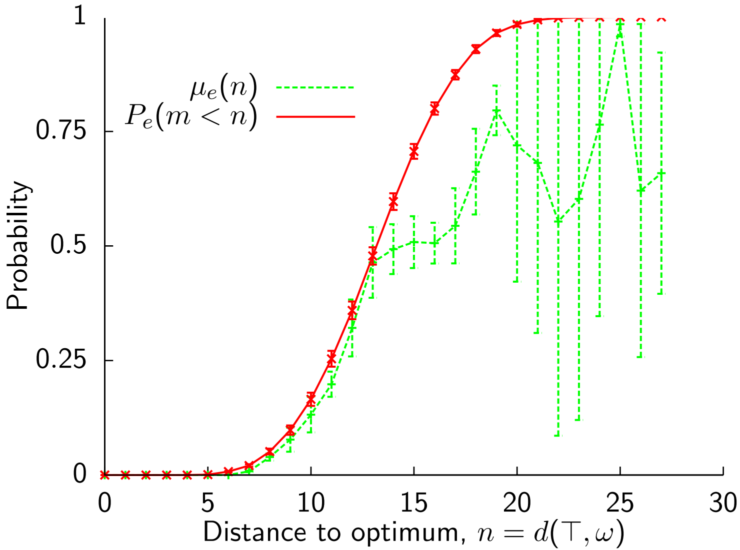
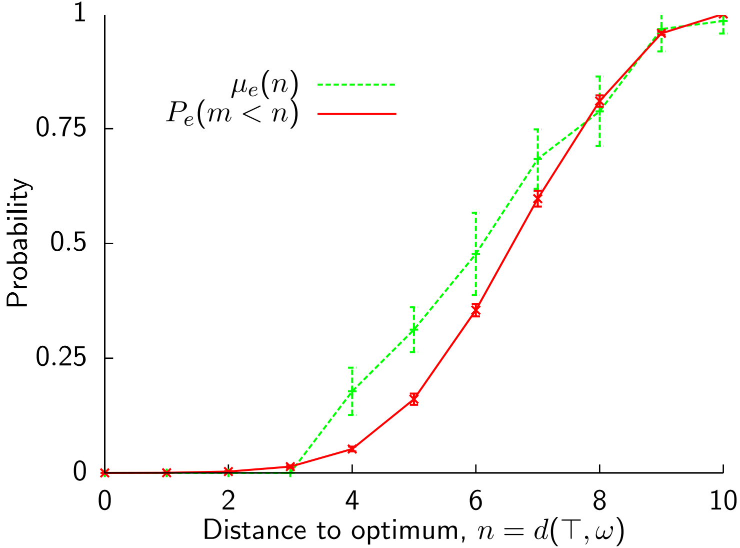
Output

- $\mu_e(x)$ — evolved mutation rate functions.
- $P_e(x_r > x)$ — CDFs of empirical distributions $P_e(x)$ of fitness.

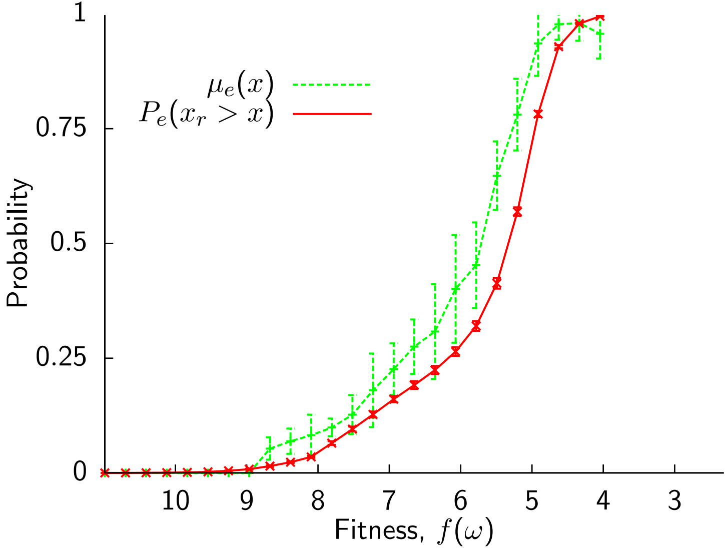
$\mathcal{H}_2^{30}$, fitness $f(\omega) = -d(\top, \omega)$



$\mathcal{H}_4^{10}$, fitness $f(\omega) = -d(\top, \omega)$



$\mathcal{H}_4^{10}$, fitness the aptamer landscape (Rowe et al., 2010)



Conclusions and Questions

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Ackley, D. H. (1987). An empirical study of bit vector function optimization. In L. Davis (Ed.), *Genetic algorithms and simulated annealing* (pp. 170–204). Pitman.

Bäck, T. (1993). Optimal mutation rates in genetic search. In S. Forrest (Ed.), *Proceedings of the 5th International Conference on Genetic Algorithms* (pp. 2–8). Morgan Kaufmann.

Belavkin, R. V. (2010). Information trajectory of optimal learning. In M. J. Hirsch, P. M. Pardalos, & R. Murphey (Eds.), *Dynamics of information systems: Theory and applications* (Vol. 40). Springer.

Belavkin, R. V. (2011). On evolution of an information dynamic system and its generating operator. *Optimization Letters*, 1–14. (10.1007/s11590-011-0325-z)

Bjedov, I., Tenaillon, O., Gerard, B., Souza, V., Denamur, E., Radman, M., et al. (2003). Stress-induced mutagenesis in bacteria. *Science*, *300*(5624), 1404-9.

Cox, M. M., Keck, J. L., & Battista, J. R. (2010). Rising from the ashes: DNA repair in Deinococcus radiodurans. *PLoS Genet*, *6*(1), e1000815.

Eigen, M., McCaskill, J., & Schuster, P. (1988). Molecular quasispecies. *Journal of Physical Chemistry*, *92*, 6881-6891.

Fisher, R. A. (1930). *The genetical theory of natural selection*. Oxford: Oxford University Press.

Fogarty, T. C. (1989). Varying the probability of mutation in the genetic algorithm. In J. D. Schaffer (Ed.), *Proceedings of the 3rd International Conference on Genetic Algorithms* (pp. 104–109). Morgan Kaufmann.

Hakem, R. (2008). DNA-damage repair; the good, the bad, and the ugly. *Embo J*, *27*(4), 589-605.

Mühlenbein, H. (1992, September). How genetic algorithms really work: Mutation and hillclimbing. In einhard Männer & B. Manderick (Eds.), *Parallel problem solving from nature 2* (pp. 15–26). Brussels, Belgium: Elsevier.

Ochoa, G., Harvey, I., & Buxton, H. (1999). Error thresholds and their relation to optimal mutation rates. In *Proceedings of the Fifth European Conference on Artificial Life (ECAL'99)* (Vol. 1674, pp. 54–63). Berlin: Springer-Verlag.

Orr, H. A. (2005). The genetic theory of adaptation: a brief history. *Nat Rev Genet*, *6*(2), 119-27.

Rowe, W., Platt, M., Wedge, D. C., Day, P. J., & Kell, D. B. (2010). Analysis of a complete DNA-protein affinity landscape. *Journal of Royal Society Interface*, *7*(44), 397–408.

Vafaee, F., Turán, G., & Nelson, P. C. (2010). Optimizing genetic operator rates using a Markov chain model of genetic algorithms. In M. Pelikan & J. Branke (Eds.), (pp. 721–728). ACM.

Yanagiya, M. (1993). A simple mutation-dependent genetic algorithm. In S. Forrest (Ed.), *Proceedings of the 5th International Conference on Genetic Algorithms* (p. 659). Morgan Kaufmann.