

# Genome evolution: coding structures and evolvability

# Last time

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- How ecosystem dynamics can facilitate evolutionary adaptation
- individual based and ecosystem based "solutions"
- evolution of multiple coding to cope with the prevailing mutation rates

## **Genome and gene regulatory network evolution**

using different basic simplified setups.

### 1. Bag of genes and TF binding sites to code for GRN

- neutral evolution with DUPLICATIONS/DELETIONS (not only point mutation)
- == stochastic dynamic system -j attractor
- generates GRN structure similar to Yeast (powerlaw connectivitt FFL)

**random mutations =/= randomisation**

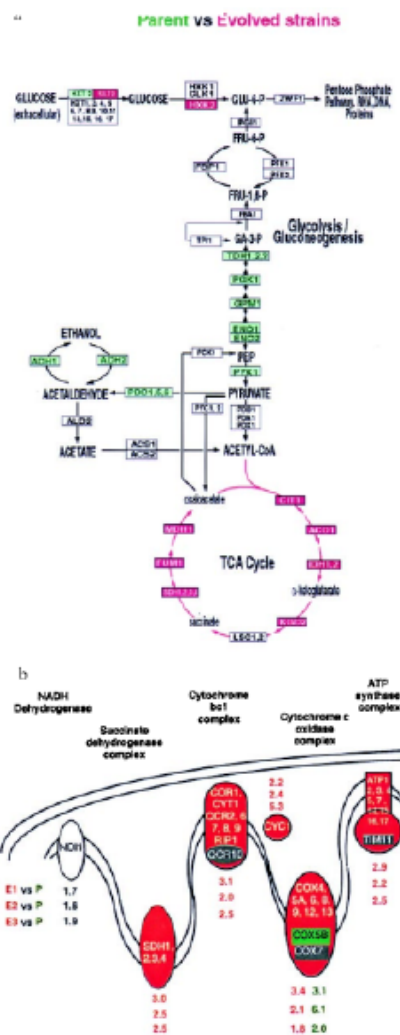
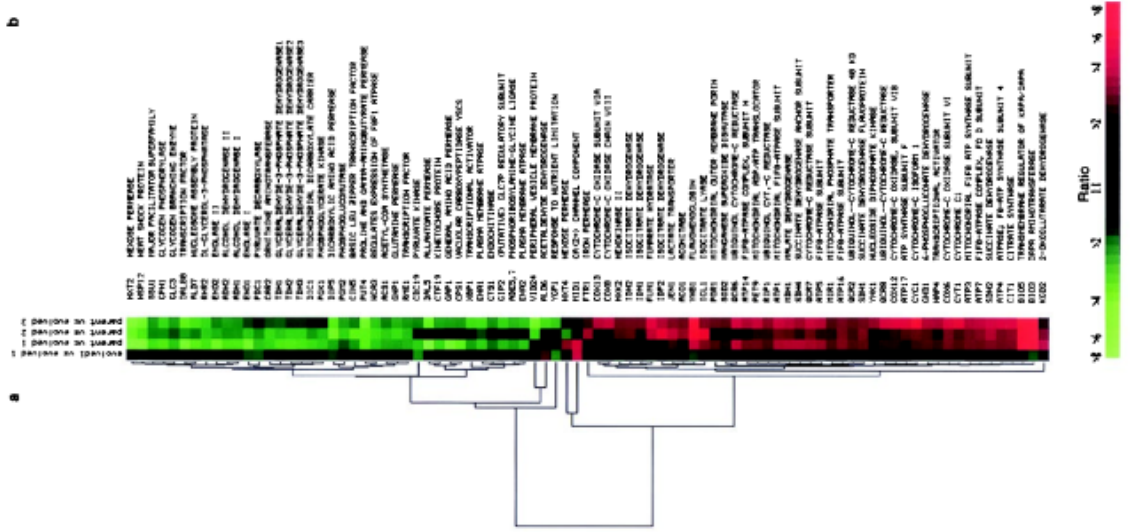
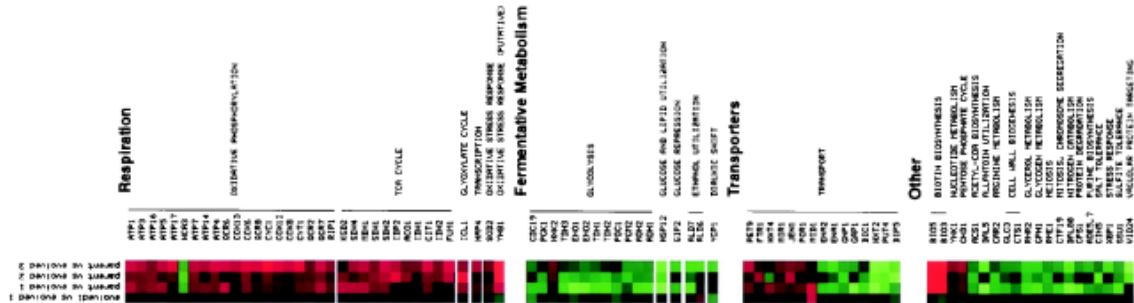
**Yeast regulatory network evolution**  
**Some “surprising” observations from short term**  
**evolution experiments**  
**( Ferea et al 1999, Dunham et al 2002)**

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- very efficient adaptation in short period
- major changes in gene expression in short evolutionary time: ca 600 genes differentially expressed in period that no more than 7 mutations expected
- changes in gene expression make “sense” with respect to adaptation
- resemble regulatory adaptation
- many gross chromosomal rearrangement (GCR)
- similar GCR in duplicate evol experiment

**evolved evolvability?**

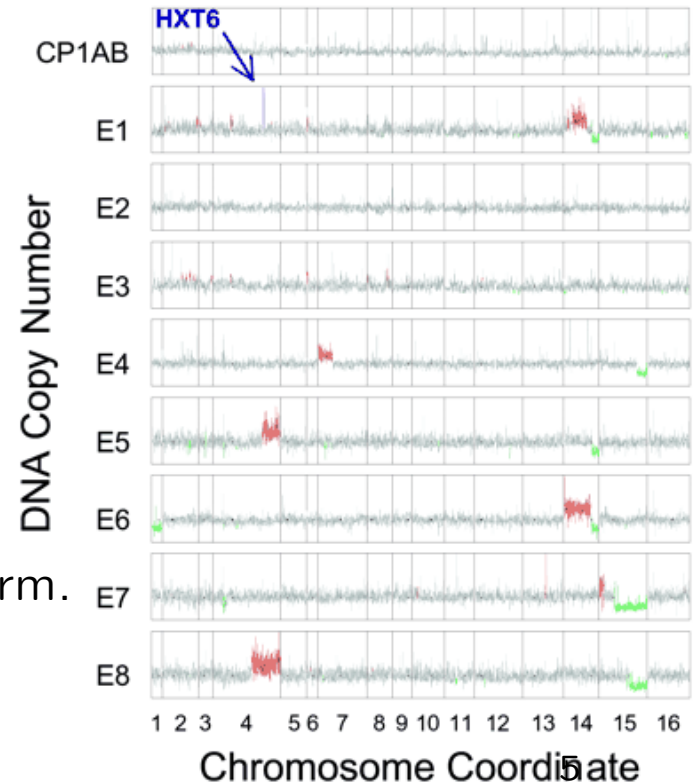
# regulatory and/vs evolutionary 'adaptation' gene expression changes in strain evolved on low glucose med



# “Mutational priming” seen in yeast evolution

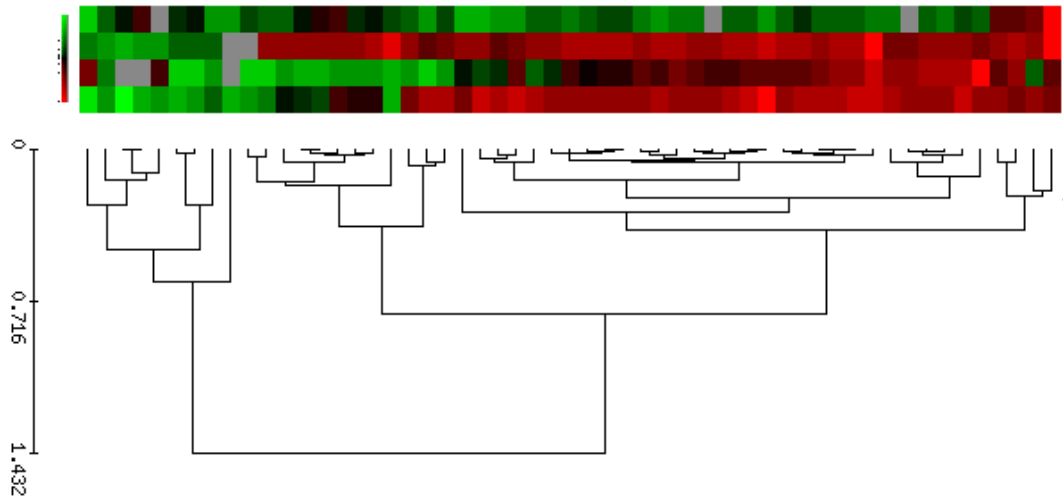
“Characteristic genome rearrangements in experimental evolution of *Saccharomyces cerevisiae*”  
(Dunham et al PNAS 2002)

repeated duplication and loss  
at the same breakpoints  
3\* in C14 near CIT1 (citrate synthetase)  
3\* in C4 amplific. high-affinity hexose perm.  
transposon-related sequences at  
the breakpoints.

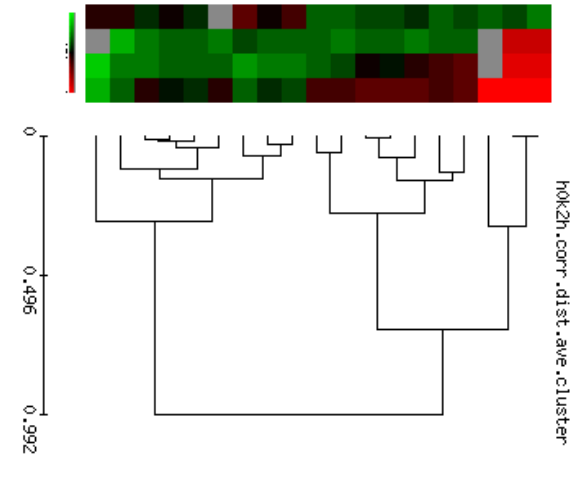


# overexpression of deleted genes, underexpression of duplicated genes

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duplicated genes



deleted genes

**Are these properties of short term evolution a generic property of mutation/selection in evolving systems with explicit genome-network mapping?**

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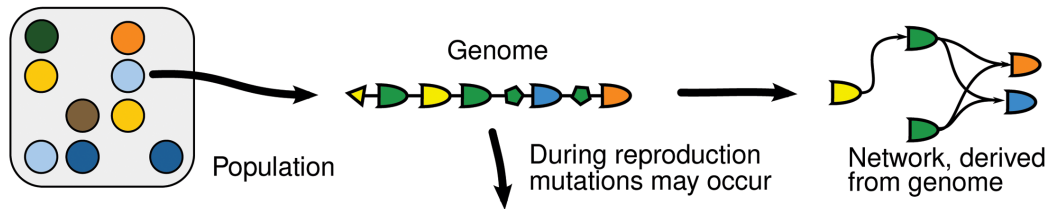
By evolution of genome structure?

By evolution of transcriptome structure?

# basic course grained representation of a genome chain of genes, TF binding sites, transposon, ....

*“Pearls on a string model”*

## A Overview of the model

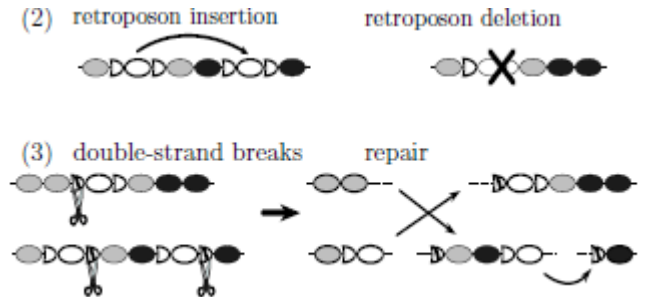
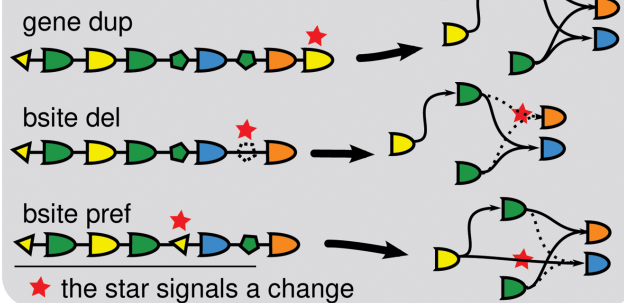


## C Evolutionary targets

	A	genes on	genes off
B	genes on		
genes off			



## B Effect of mutations



Genetic operators: beyond point mutations:

(DupDel: single genes, TBS; LCR: random, targeted)



# selforganization of genomes by transposon mutational dynamics evolution of evolvability

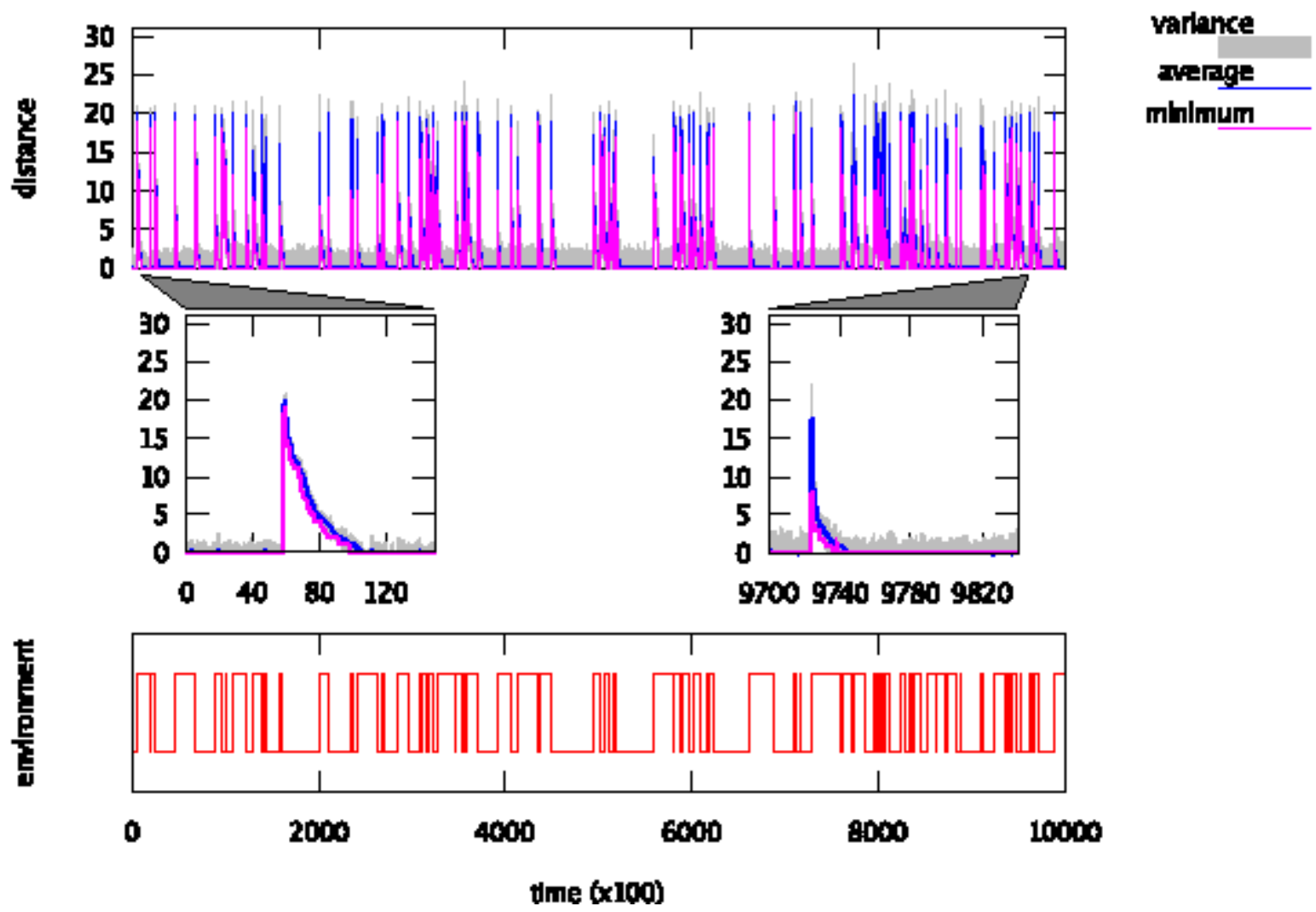
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## mutational dynamics

- gene duplication; gene deletion.
- transposon duplication;
- transposon deletion; leaves breakpoints
- double stranded breaks and repair  
→ gross chromosomal rearrangement

## selection

- fluctuating environment
- need 2 copies of part of the genes in one environment



## self organization of the genomes clustering of genes which need to be duplicated

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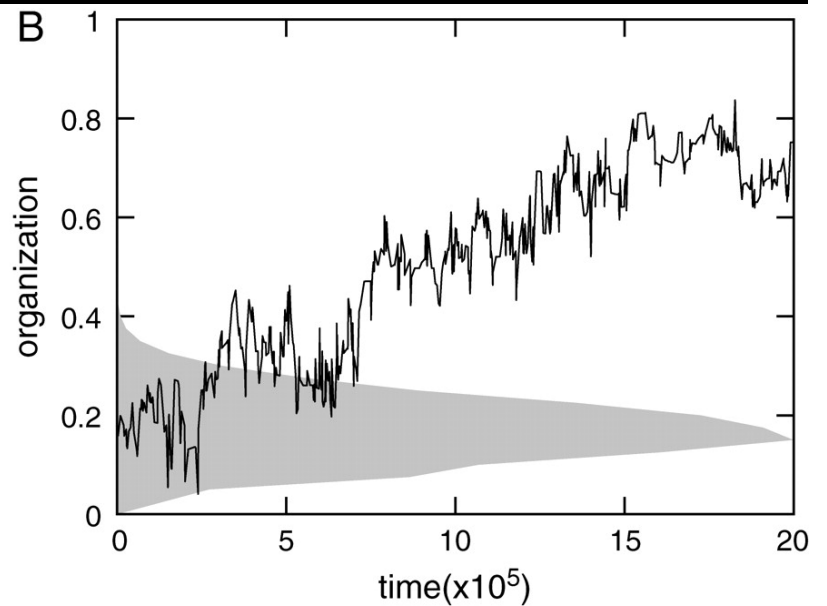
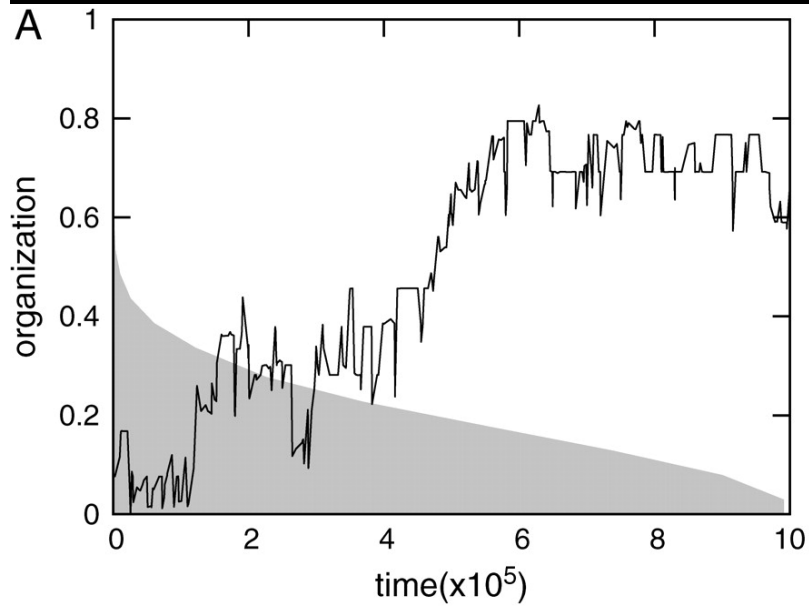
- Randomly generated genome (at start simulation):



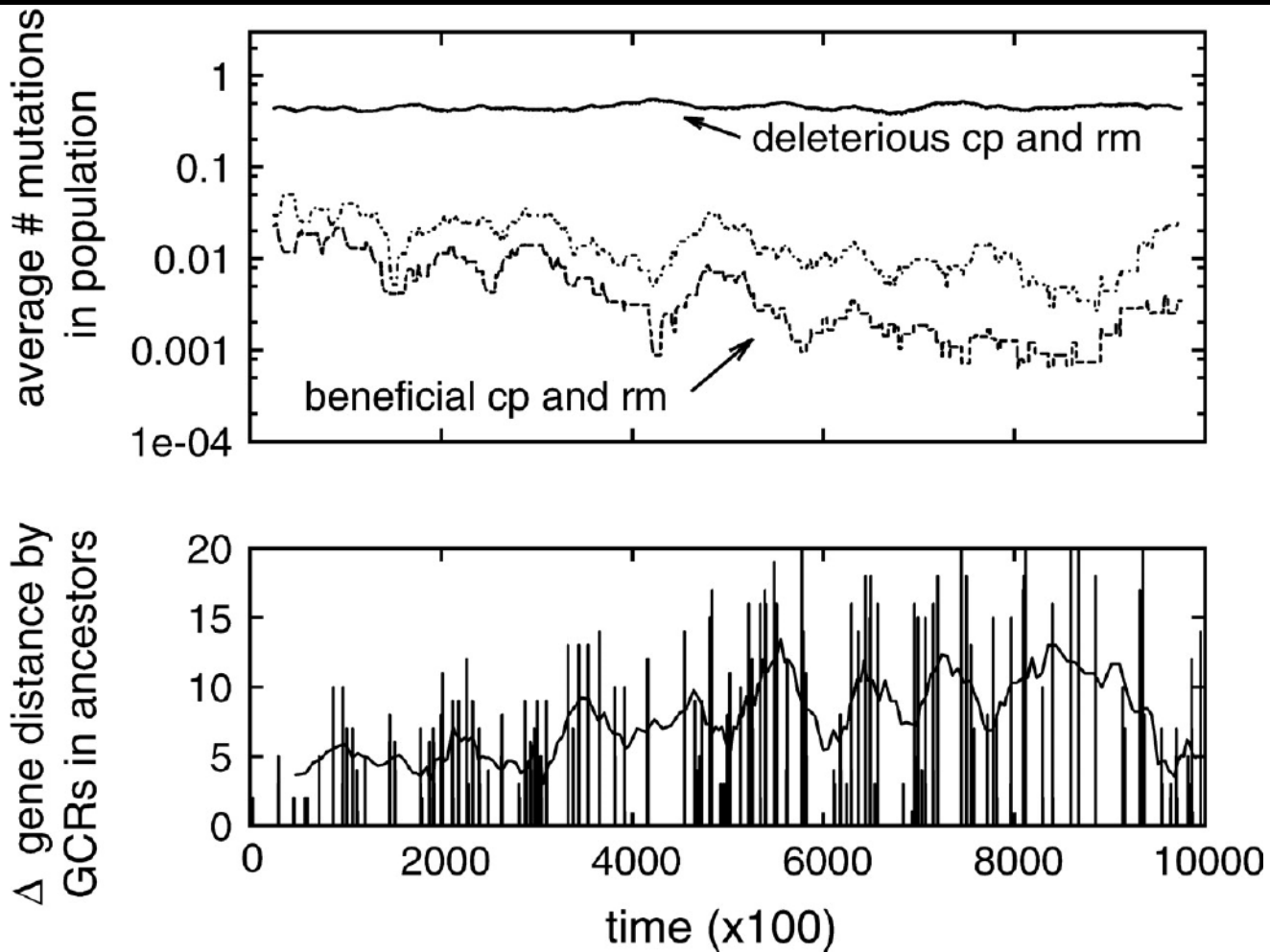
- Evolved genome, grouping of genes as a side effect:



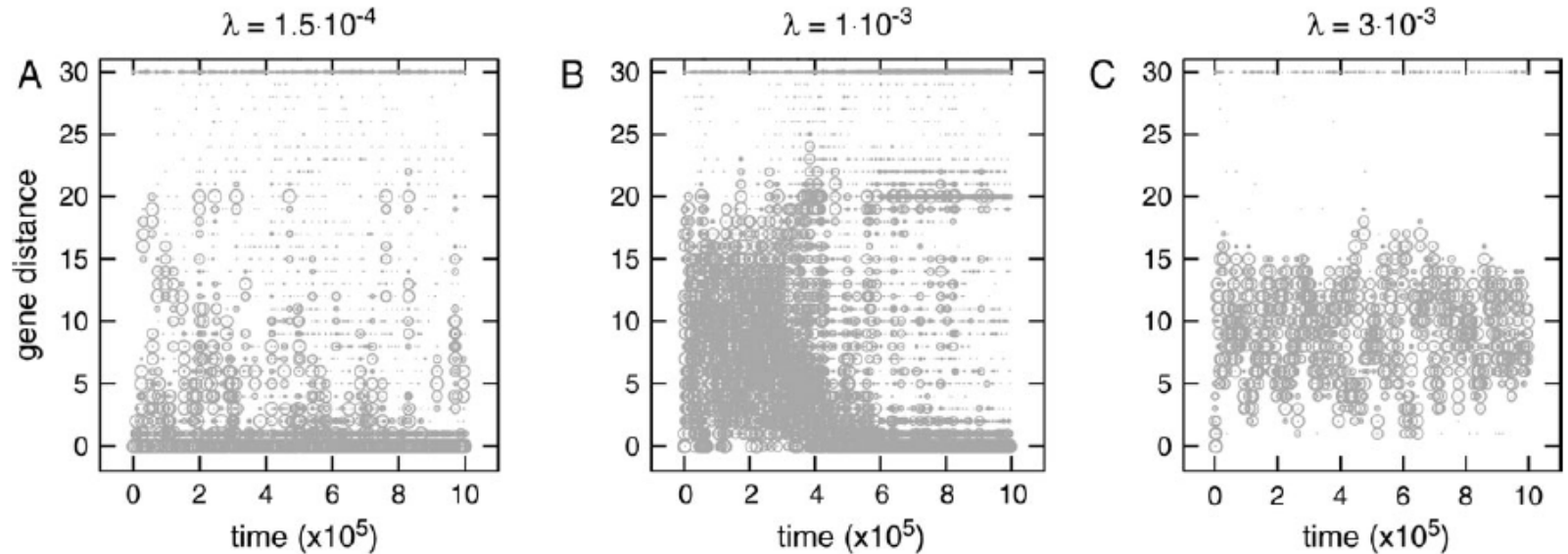
## genome organization over time



# mutations over time



# Evolution of evolvability: timescales



genome organization evolves when no adaptation is possible  
- and so enables adaptation

## conclusions

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Very simple demonstration of mutational priming through genome structuring

Yeast example also transposon remnants on breakpoints

Much pattern analysis research:

islands of transposable elements, variable and important for adaptations

(e.g. Michael Seidl in fungi; also studied in ants etc.

# Evolution of Regulation based mutational priming

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## network dynamics and fitness

Network update:

fitness:

$$s_i^{t+1} = \begin{cases} 0 & \text{if } \sum_j w_{ij}s_j^t < \theta_i \\ s_i^t & \text{if } \sum_j w_{ij}s_j^t = \theta_i \\ 1 & \text{if } \sum_j w_{ij}s_j^t > \theta_i \end{cases} \quad f = \left(1 - \frac{D}{D_{max}}\right)^p$$

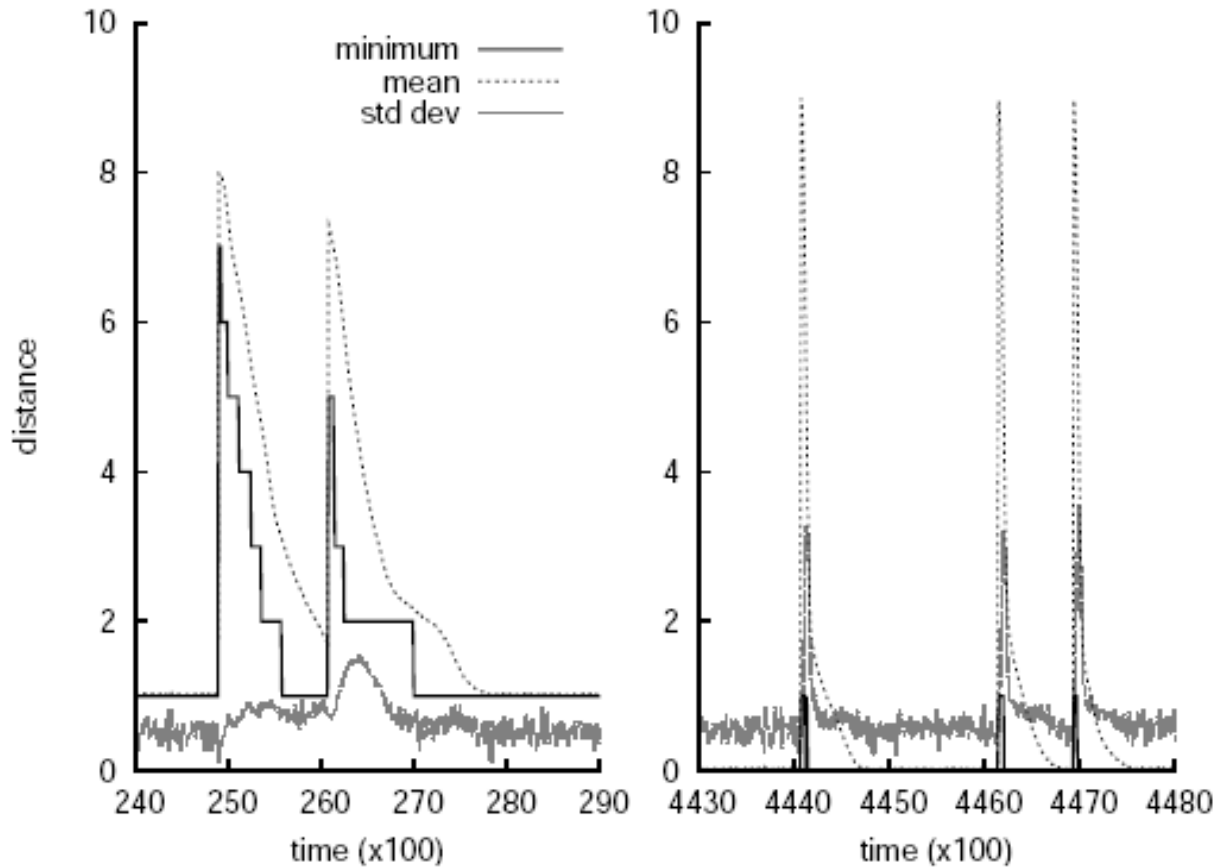
Switching environment

Gene expression in attractor of GRN defines fitness  
each environment defines in terms of target gene expression



# improved (faster) evolvability observed

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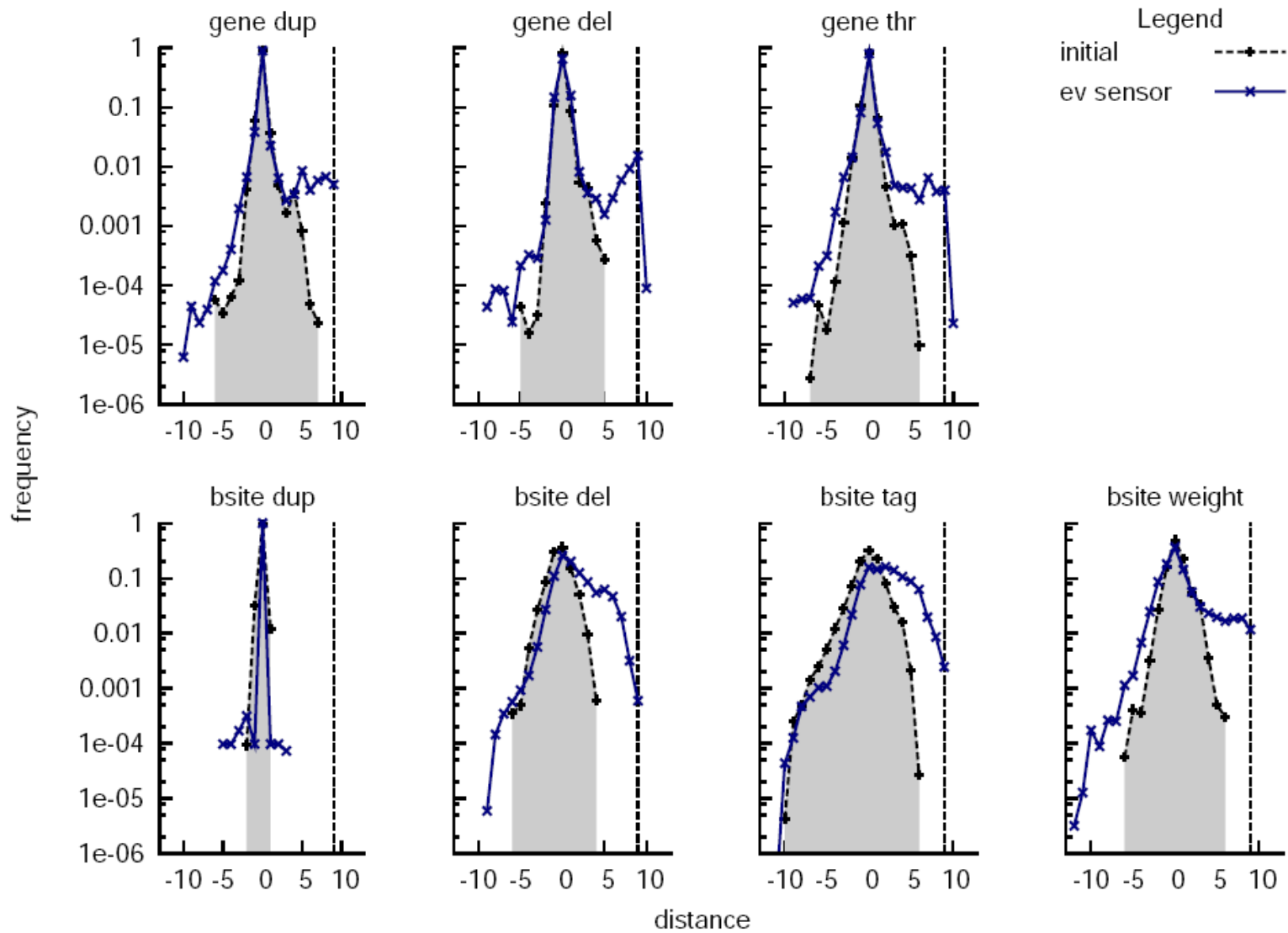


## **Hamming distance improvement to opposite target**

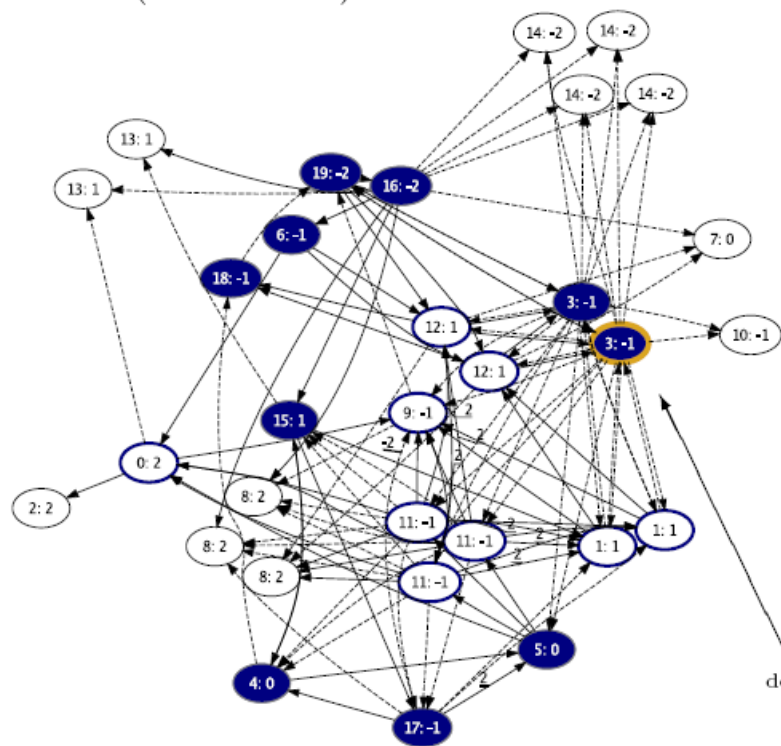
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### **Regulatory Mutational Priming:**

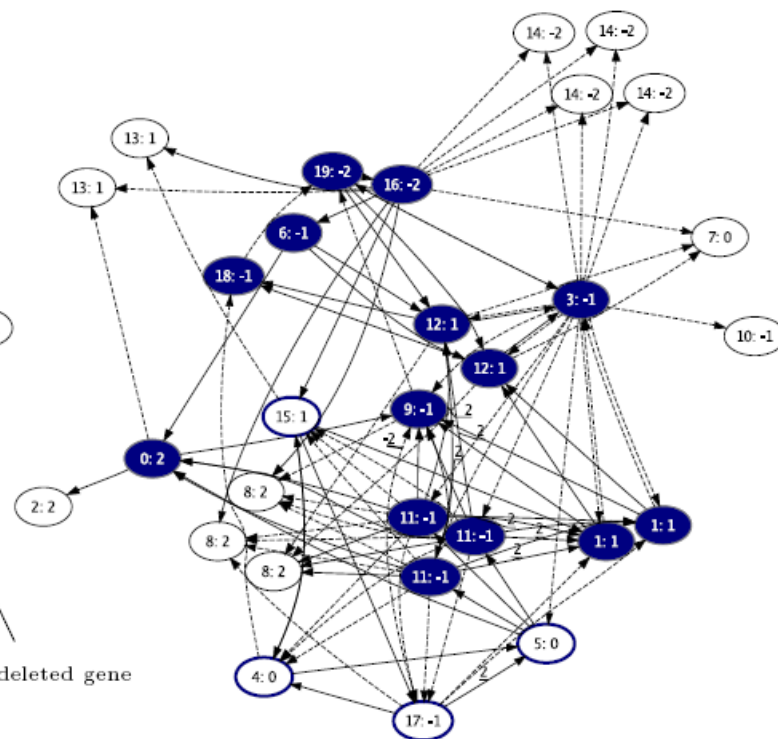
Many different mutations lead to “beneficial” adaptation

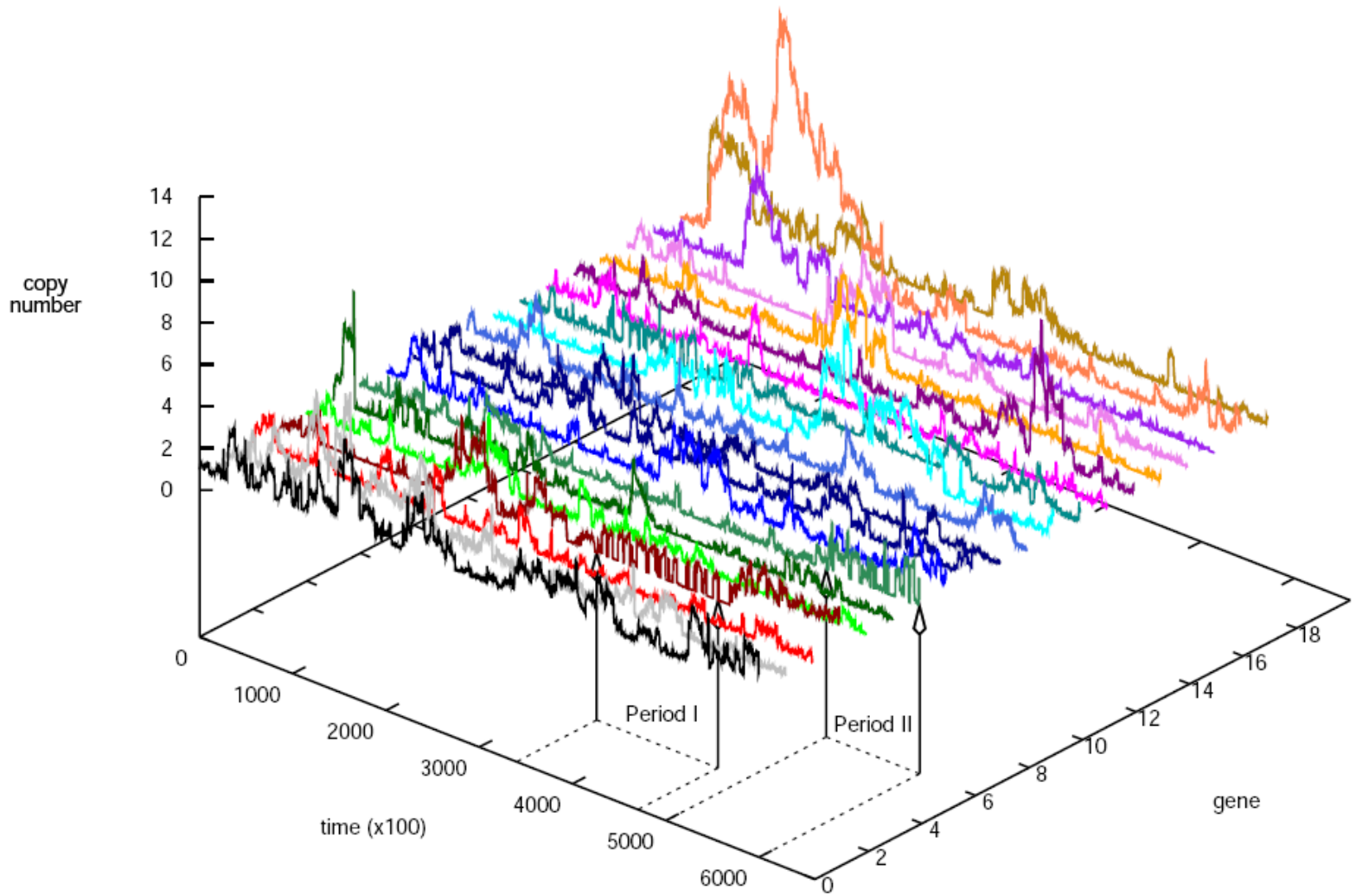


Parent (t = 457 755):



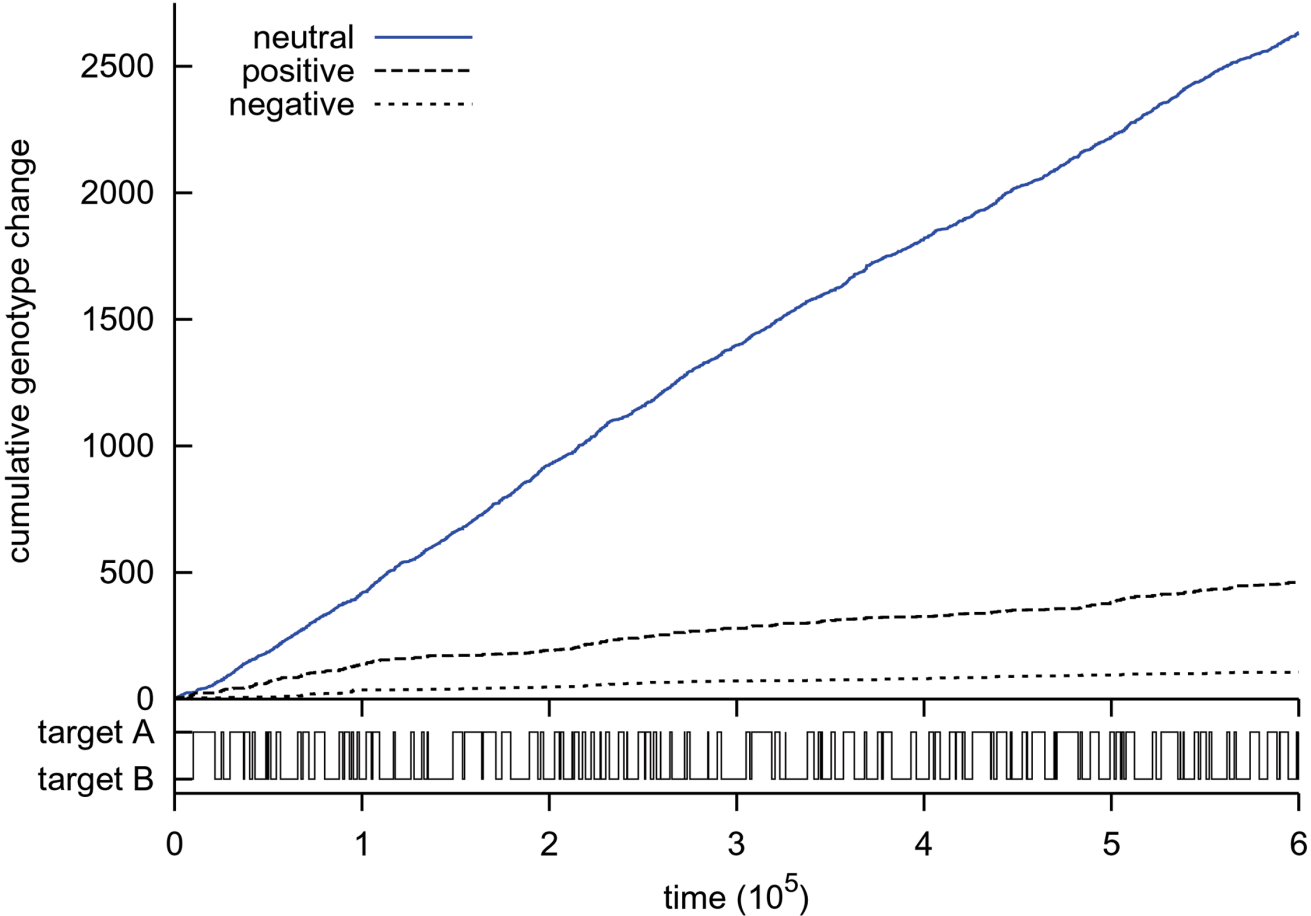
Child (t = 457 758):





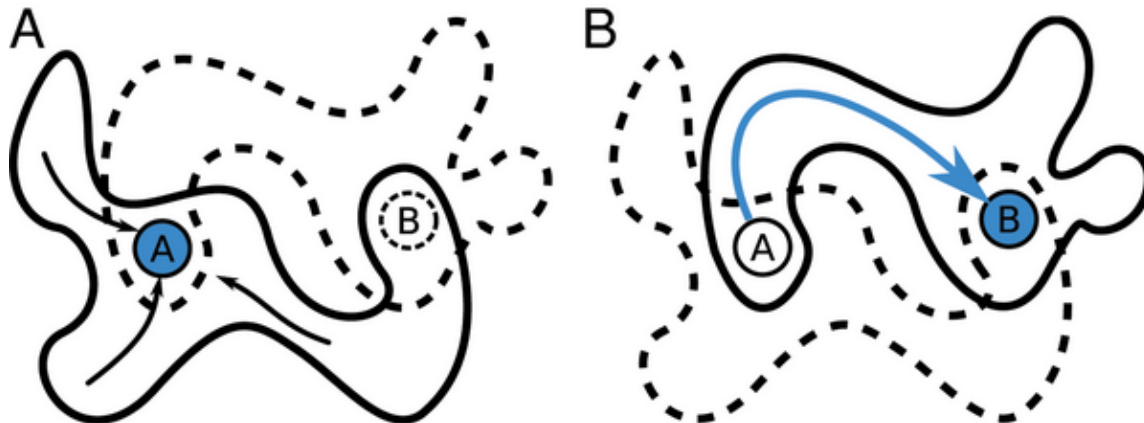
**“evolutionary sensor”**

# Neutral drift far greater than adaptive change!



## evolution of evolvability and bases of attraction

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single/few Mutations destabilize attractor of env 1  
and becomes state in domain of attraction of of env 2

## conclusions

# Evolution of genomes and gene regulatory networks evolution of evolvability

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*Random mutations are not “random”  
in EVOLVED genomes*

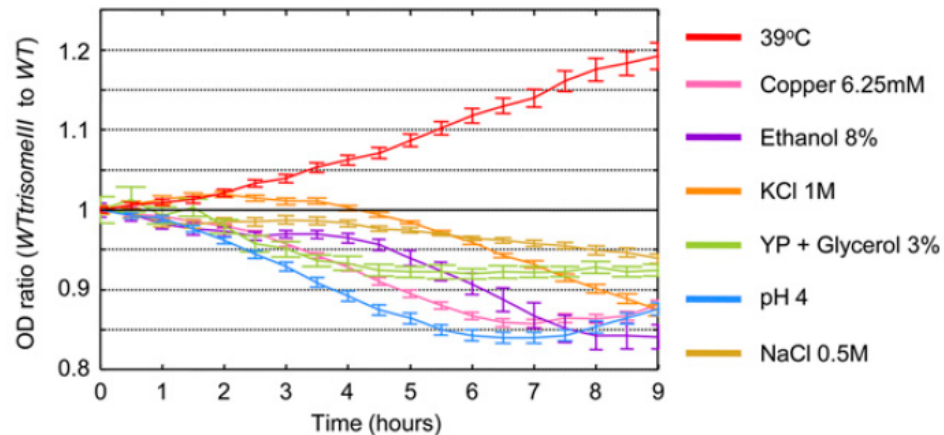
- Transposon dynamics structures genomes creating hotspots for mutations and genome ordering. Long term evolution leads to genome structures such that short term evolution is facilitated
- Genotype to phenotype mapping through gene regulatory networks evolves such that (advantageous) attractor switching occurs (blow up of single mutations to large scale effects)
- State space may remain very similar despite attractor switch, but can also change drastically
- *“individual vs population based” evolution of evolvability*



## Mutational Priming in Yeast: Genome organization and regulation adaptation to high temperature: short term vs long term effects

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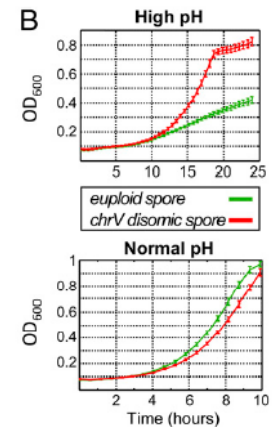
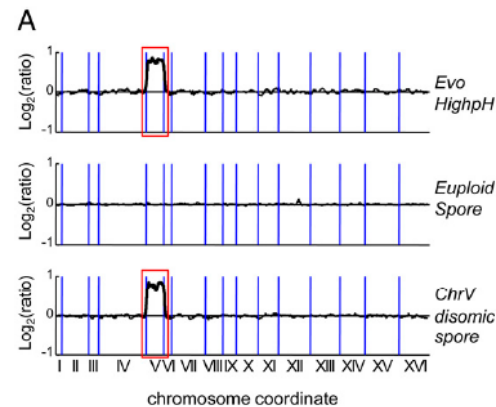
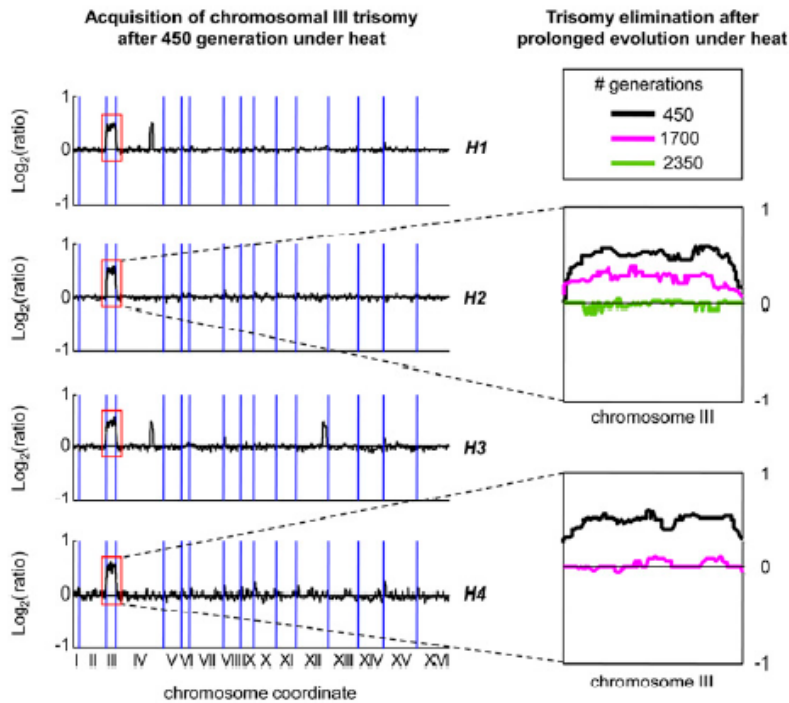
Diploid yeast adapted to 'normal' temperature of 30 C placed in 39 C. After 450 generations:  
Increased growth rate (specific for temperature)



Next continued at 39 C

Yona et al, PNAS 2012: Chromosomal duplication is a transient evolutionary solution to stress

# Yeast adaptation to high temperature by duplication of resp chromosome 3 ( and at high ph chromosome 5 )



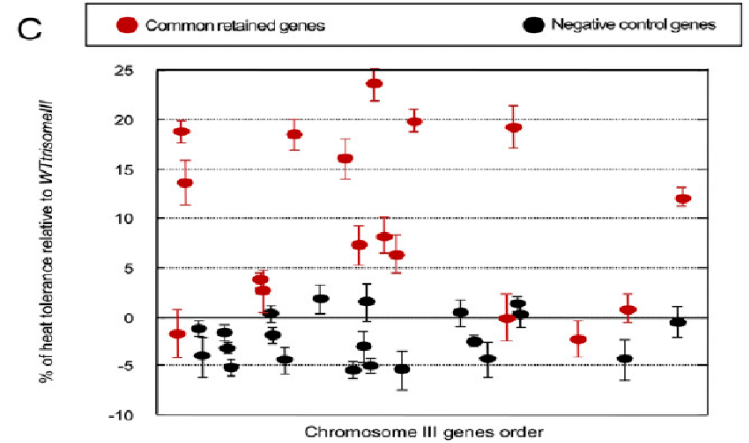
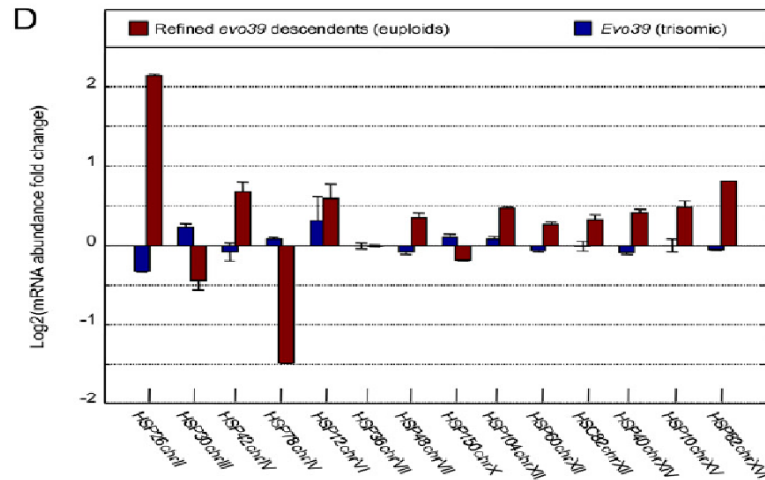
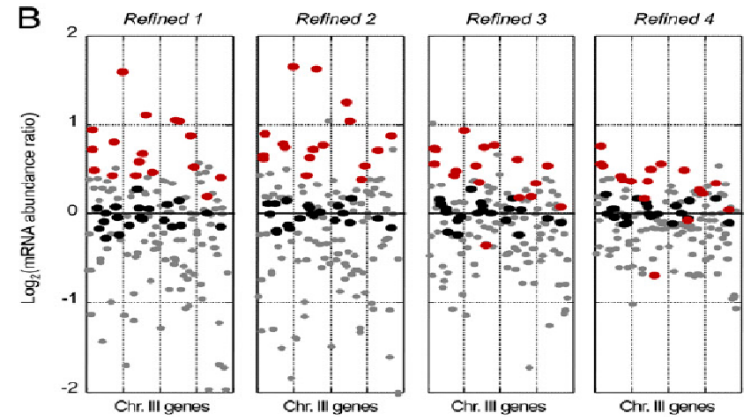
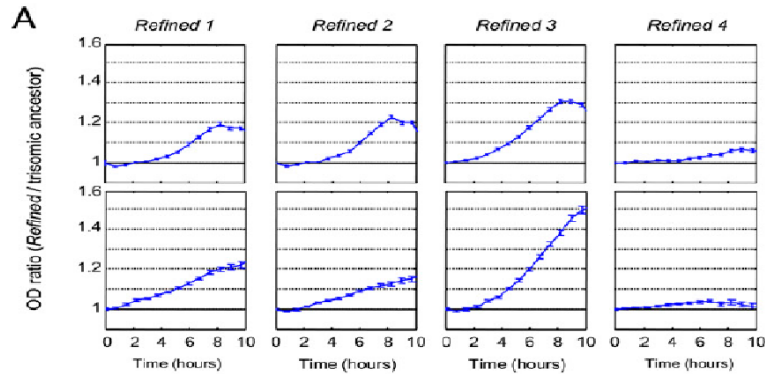
trisomy not retained

Yona et al, PNAS 2012: Chromosomal duplication is a transient evolutionary solution to stress

# chromosomal duplication is followed by regulatory adaptation

continued increase growthrate

overexpression retained of some genes

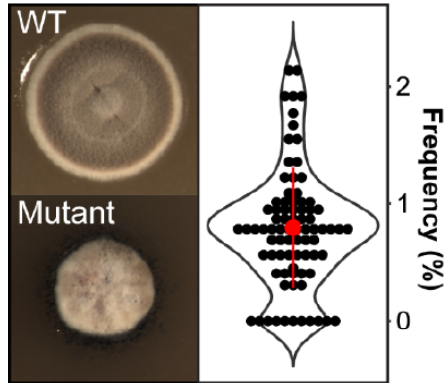


overexpression HSP only later

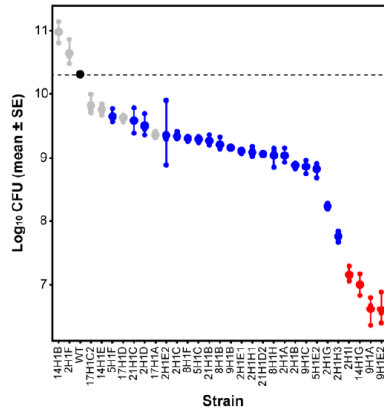
retained genes increase growthrate in ancestor

# Mutational priming in *Streptomyces*: quasispecies

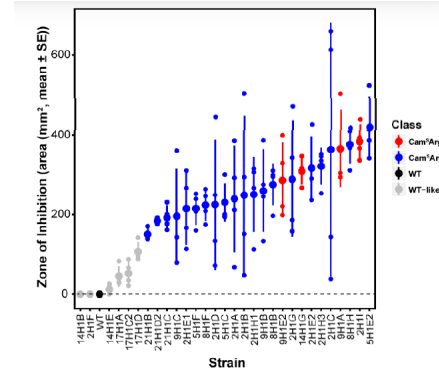
*Antibiotic production in Streptomyces is organized by a division of labor through terminal genomic differentiation. Zhang ...Rozen 2020*



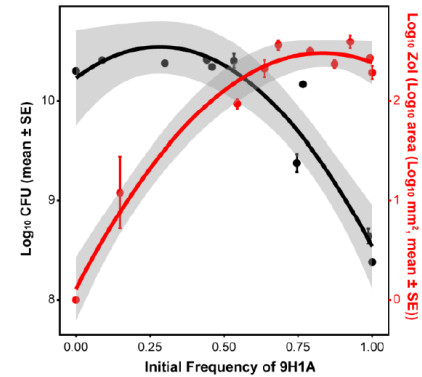
High Mut. Rate



Mut. fitness

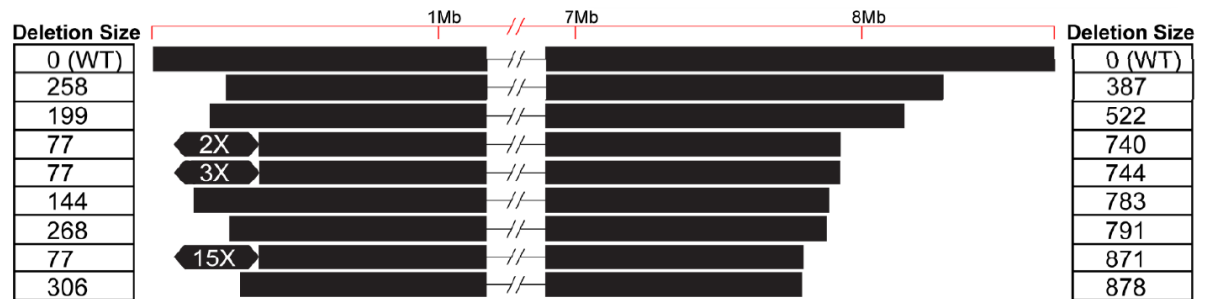
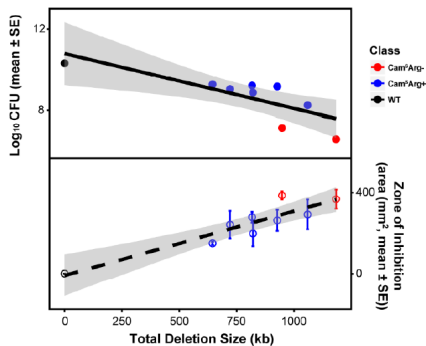


antibiotics production



QS fitness

only > 50% of mutants lowers colony fitness



Genome structure and targeted mutations