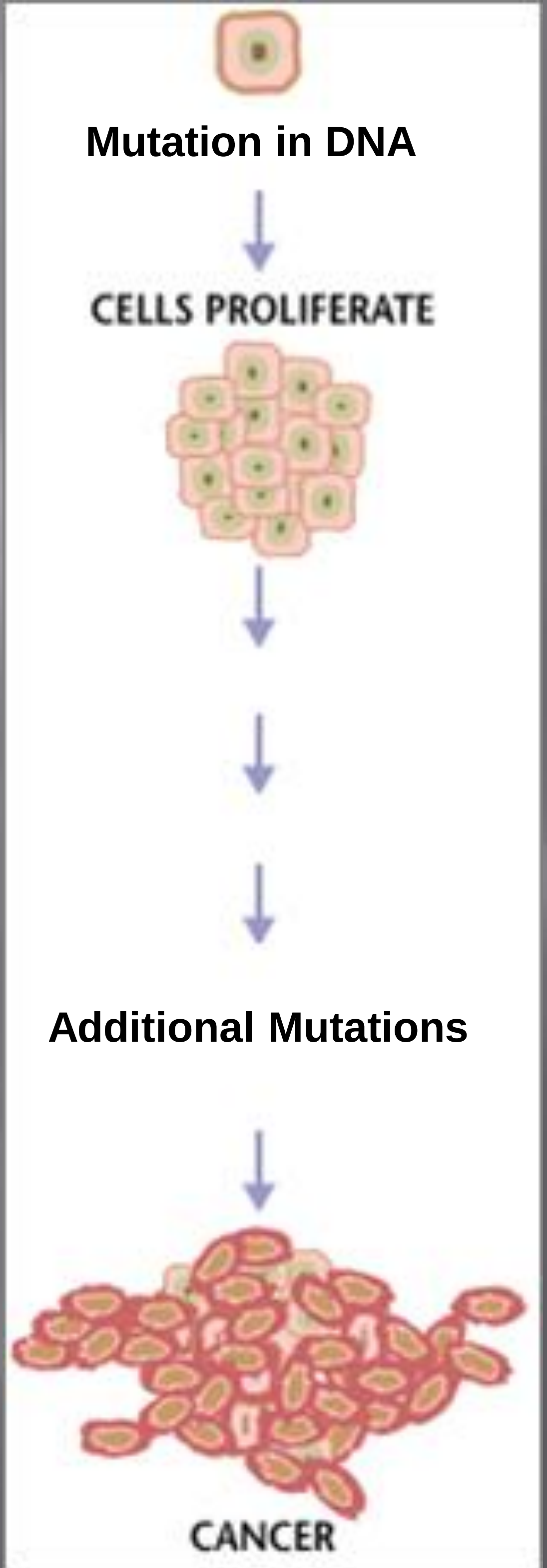
Modeling the role of cell fusion in cancer development

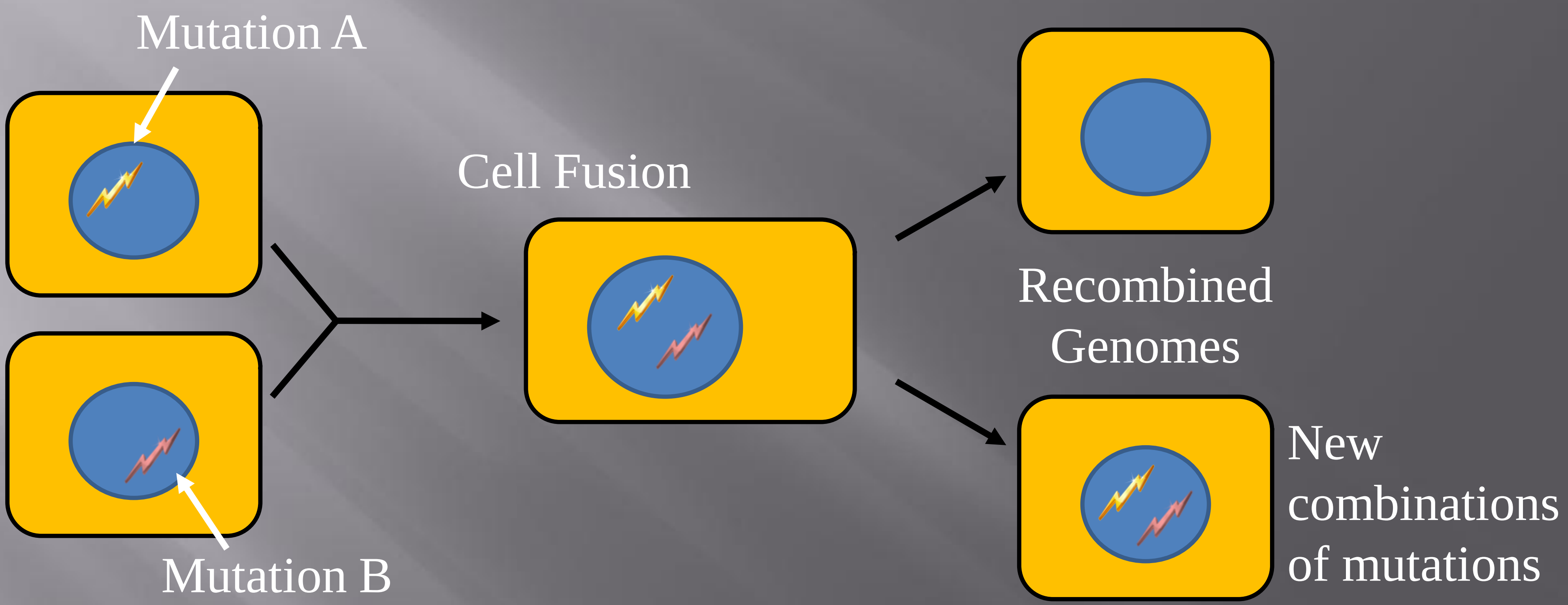
by Andrew Kim and Dash Elhauge

MIT PRIMES
May 21, 2011

Introduction



Why does cell fusion occur in cancer?



Hypothesis: Cell fusion allows for recombination of cancer causing genes from different cell lineages

Our Generic Cancer Model

The Goal: ***To get cancer to evolve from a population***

Homogeneous Population (size ~1000)

Apply Mutations (frequency ~ 10^{-6})

Apply Cell fusion (rate ~ 1%)

Apply Evolutionary Advantage to Most Cancerous Cells

Next Generation

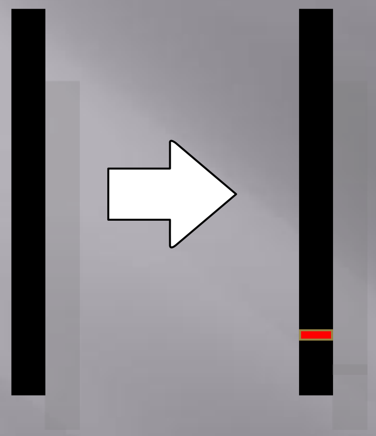
Is cancer found?

NO

YES

FINISH

Mutation:

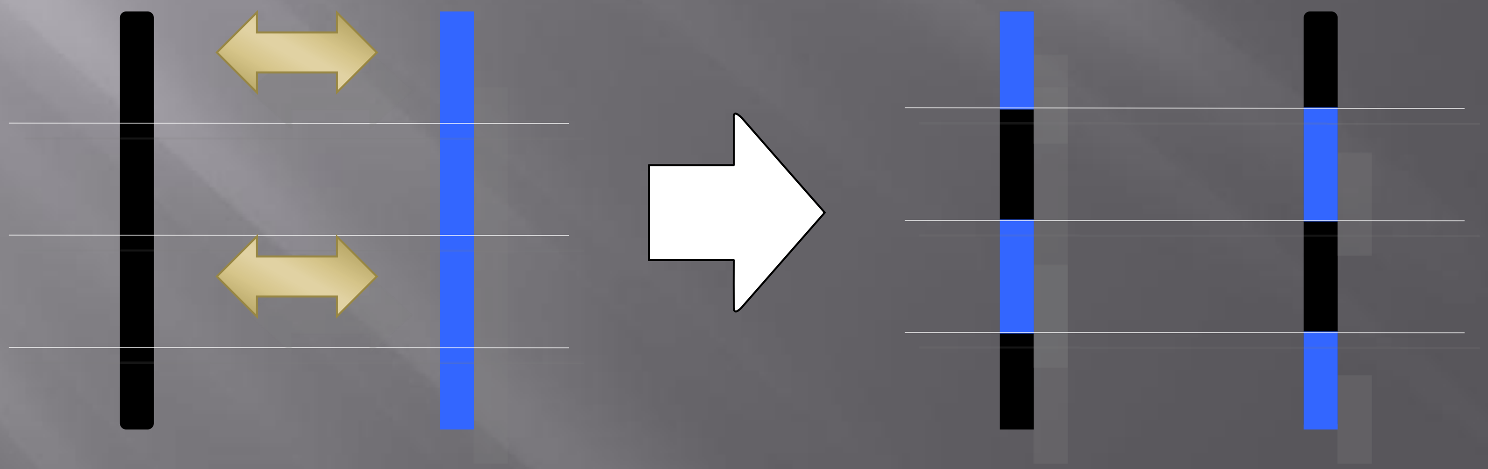


0 0 1 0 1 1 0 1 …

0 0 1 0 1 0 0 1 …

Cell Fusion:

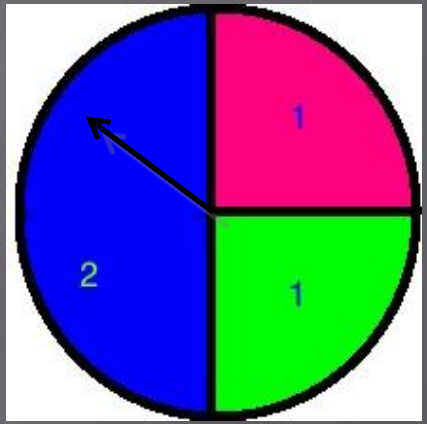
- -Cell fusion occurs with randomly selected partner cell
- -Genomes are each split into chromosomes *of equal length*
- -Chromosomes matchup, and have a 50% chance of trading



What defines advantage?

-Each generation, select cells for the next generation randomly with probability proportional to cell's fitness, keeping population size constant

Sum Fitness: 4



Spin 3 times: Blue, Blue, Green

What defines fitness?

-multiply by a constant *s* every step towards cancer, i.e.:

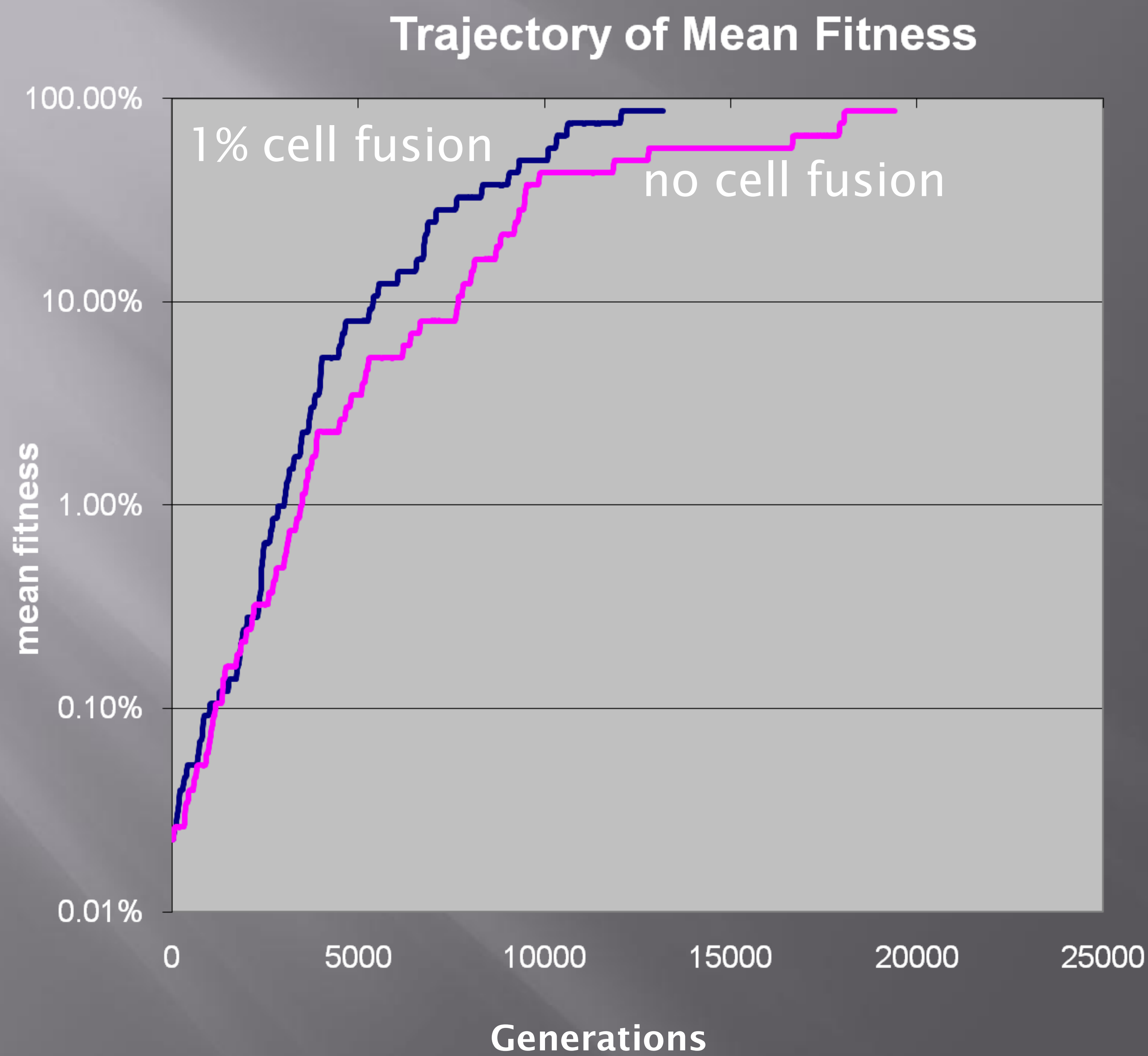
$$fitness \propto e^{-Const*(distance\ to\ cancer)}$$

Distance is number of discrepancies:

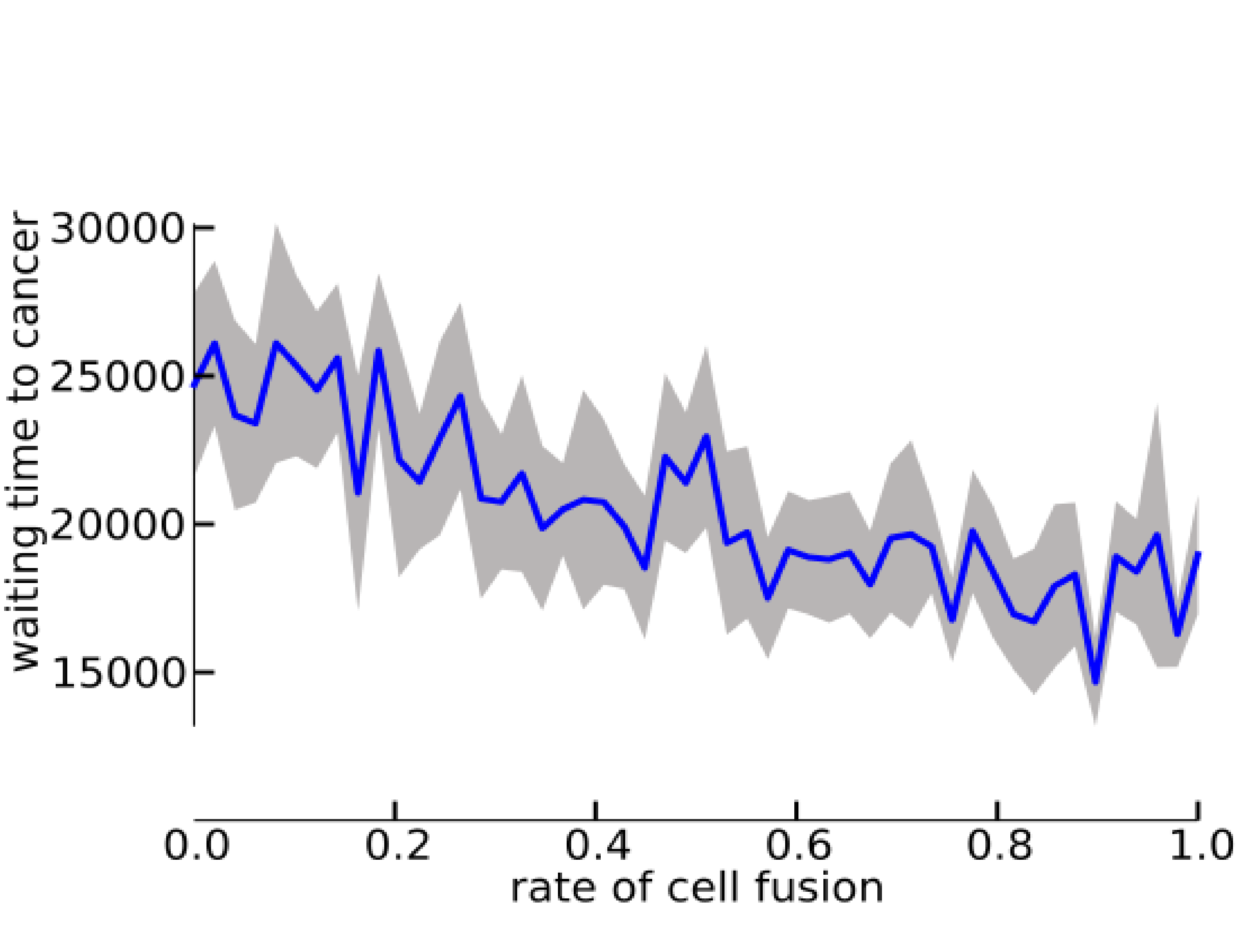
Cancer: 0 0 1 1 0 1 0

Cell: 1 0 0 1 0 1 1

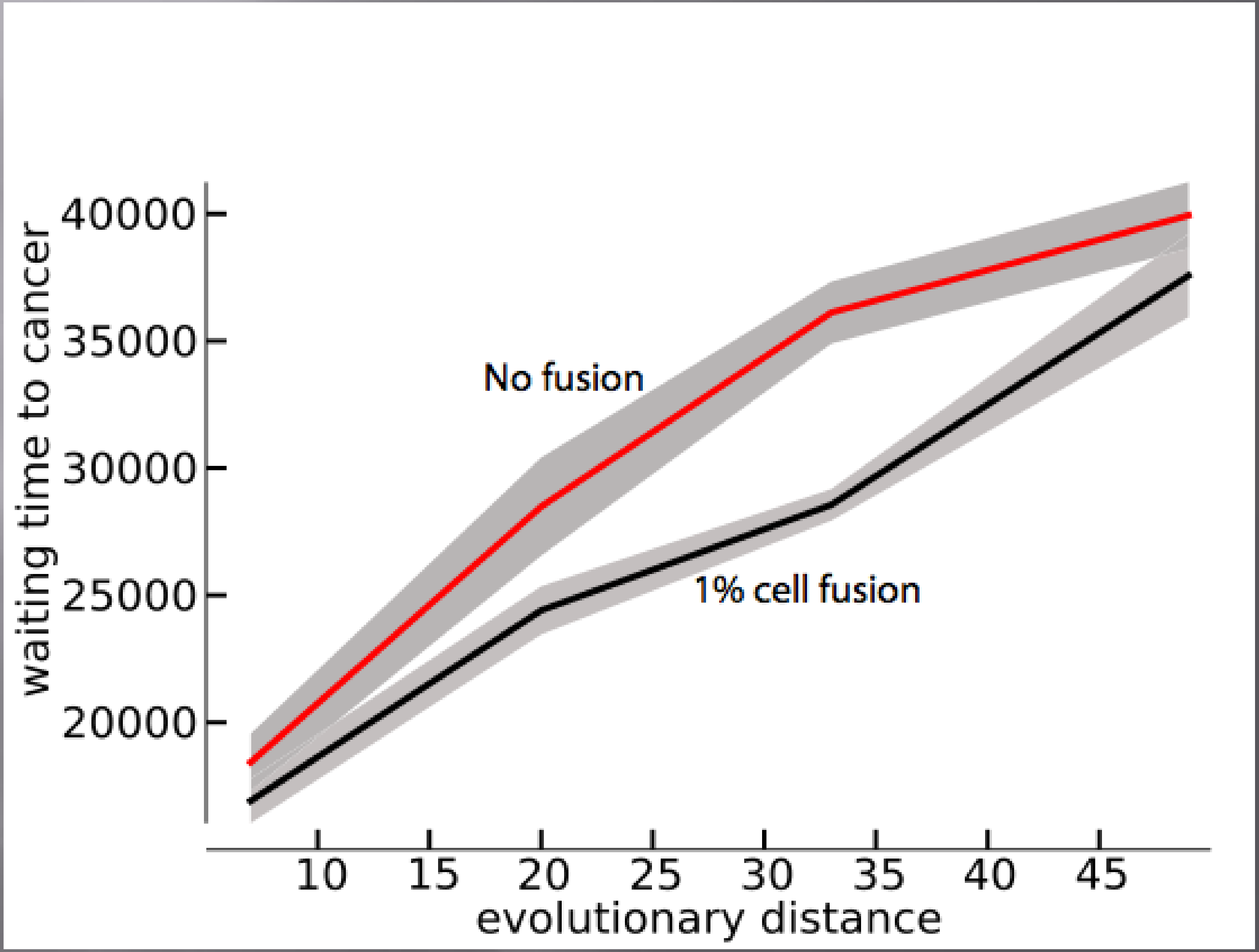
= 3


Trajectory of Mean Fitness
100.00%
10.00%
1.00%
0.10%
0.01%
mean fitness
1% cell fusion
no cell fusion
0
5000
10000
15000
20000
25000
Generations

Waiting time to cancer decreases as rate of cell fusion increases

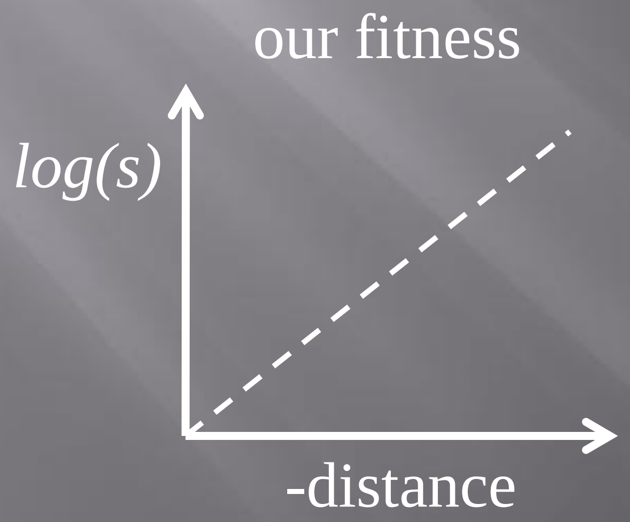


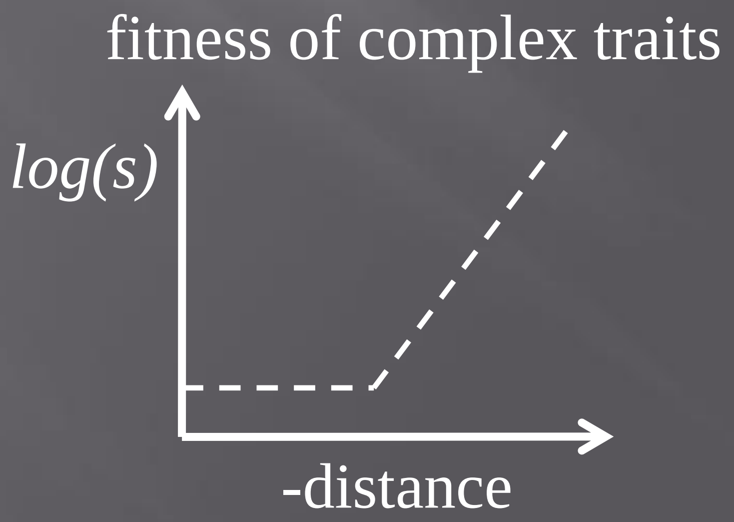
Evolutionary distance between starting population and cancer state affects waiting time



Interpreting and Future Studies

-Genetic recombination is universally important in evolution
-Introduction of more environmental, spacial factors
-Limiting the number of assumptions
-Try different cell fusion methods
-Redefining fitness to be more realistic and model complex traits





Acknowledgments

The MIT PRIMES Program
Our mentor: Christopher McFarland
Our project advisor: Dr. Leonid Mirny
Our parents and family