Modeling the role of cell fusion in cancer development

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Introduction

Mutation in DNA

CELLS PROLIFERATE

Additional Mutations

CANCER
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?

FINISH

YES

NO
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.

What defines fitness?

- Multiply by a constant $s$ every step towards cancer, i.e.:

\[ \text{fitness} \propto e^{-\text{Const} \times (\text{distance to cancer})} \]

Distance is number of discrepancies:

<table>
<thead>
<tr>
<th>Cancer:</th>
<th>0 0 1 1 0 1 0</th>
<th>Sum Fitness: 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell:</td>
<td>1 0 0 1 0 1 1</td>
<td>Spin 3 times: Blue, Blue, Green</td>
</tr>
</tbody>
</table>

Distance: $3$
Trajectory of Mean Fitness

1% cell fusion

no cell fusion

mean fitness

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

\[
\text{our fitness} = \log(s)
\]

\[
\text{fitness of complex traits} = \log(s)
\]
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