Does God play dice with the cell?

Overview

Our team, enlightened by the idea of gambling machines, aims to construct a synthetic device - the Randomizer - which could generate randomness. The core part of the device relies on the random but exclusive binding of T7 polymerase to a pair of overlapping T7 promoters to generate a logic signal of 0 or 1 - in this case, either green or red fluorescence - which is then stabilized by reciprocal repression of the two T7 promoters.

Randomizer

"Kicking Start"

Success of the randomizer depends on a controllable T7 polymerase production by inducible pBAD/araC promoter. Low copy number of T7pol reduces T7 polymerase firing frequency, which can benefit our design.

The origin of randomness arises from T7 polymerase’s random but exclusive binding to an overlapping T7 promoter pair. The identical promoter sequence could potentially cause random binding of polymerase. This design can also reduce extrinsic and intrinsic noise to minimum.

Optimally the first binding and transcription event could effectively generate repressors which silences the opposite promoter thus stabilizing randomizing outcome.

Simulation

For the total pool of cells, define:

- SuccessRate = \# of distinct cells / \# of total cells

Each cell is defined as distinct if:

- r ≤ 0.1 or r ≥ 0.9

Sample run of the simulation program:

- Single Variable Plots
  - plus series: semi-double-variable
  - Polymerase binding time intervals, repression, action delay, promoter bias, repressor asymmetry

Promoter & parts tests

- T7 polymerase production test
- GFP test with intact T7 promoter
- Translated promoter test
- Leftward induction test
- Adjacent biased promoters test
- Reciprocal inhibition test

Design extension

Memorizer + Reporter

The output of the Randomizer could potentially be read by a Memorizer and Reporter, which compares two successive logic signals and reports a jackpot hit. Memorization could be achieved by E. coli/two hybrid toggle switch. While AD-BD act as antagonists which couldn’t stably co-exist. Thus non-interacting AD-BD could serve as memory molecules.

Reporter could work by transient AD-BD activation followed by self activation.

References

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