

# *In Silico* Evolution of Attenuated Parasites in Catalytic Regulatory Networks

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Bled, some day in February 2007

# Outline

- 1 Introduction
- 2 The Model
- 3 Methods
- 4 Results
- 5 Conclusion



# RNA World - "Molecular Biologist's Dream"

[Joyce and Orgel, 1999]

*de novo* origin ...

- ① prebiotic synthesis of nucleotides
- ② prebiotic synthesis of polynucleotides
- ③ emergence of RNAs catalyzing their own replication
- ④ evolution of primordial replicases to more efficient ones
- ⑤ **emergence and evolution of other catalytic RNAs**



# The Model

- regulatory network
- based on RNA
- life cycle simulation of a RNA virus

Question:

emergence & behavior of parasites within the model

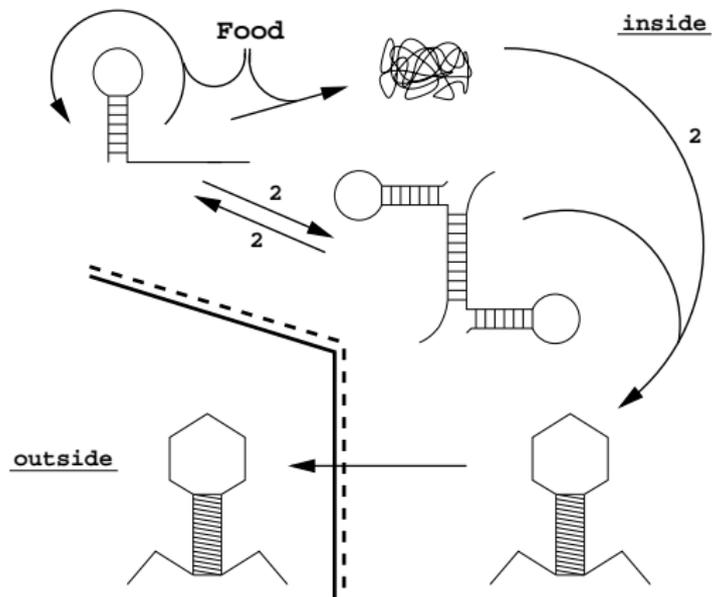
# The Model

- regulatory network
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# The Model



# Basic assumptions

- 2D surface      ~→
- 40mers of RNA      ~→
- decreasing amount of "food"
- target structure
- parallel populations

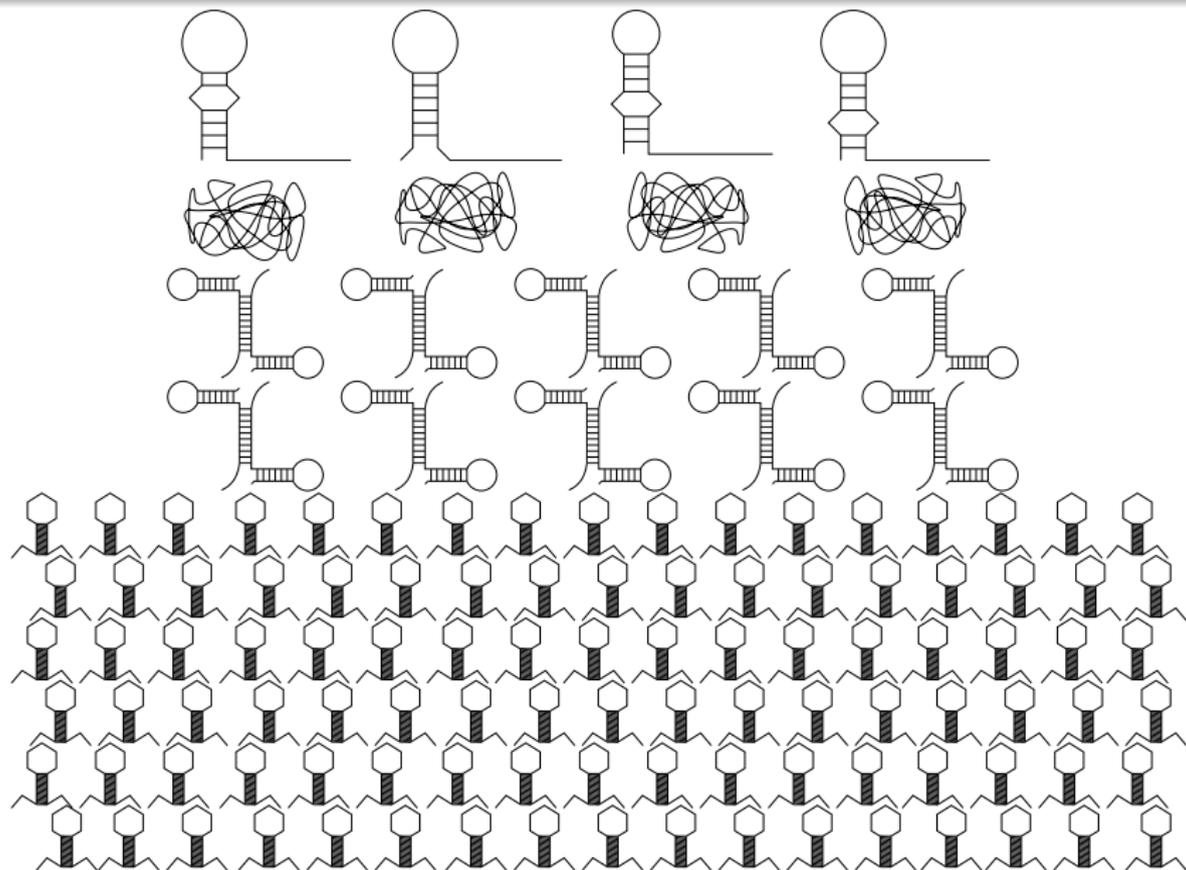
e.g. Montmorillonite

*"The generation of RNAs with chain lengths greater than 40 mers would have been long enough to initiate the first life on Earth."*

[Joyce and Orgel, 1999; Szostak and Ellington, 1993]

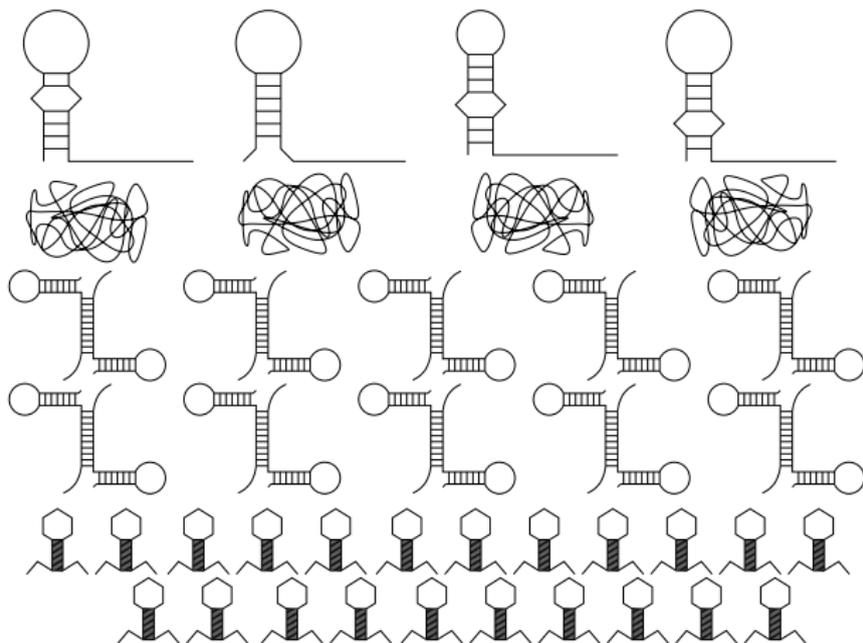
## Combinatorial Explosion

$$\binom{n+1}{2}^2 = \frac{n^4 + 2n^3 + n^2}{4}$$



## Simplification

$$\frac{3n^2 - n}{2}$$



# The Reactions



$$Z \in \{X \equiv X; X \equiv Y; Y \equiv Y\}$$



## Dimerization (reversible)

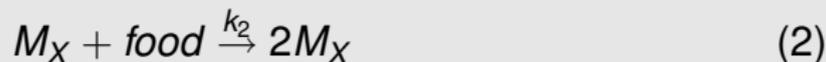


$$h = \sum_{(i,j) \in T_D} (1 - p_{ij}) + \sum_{(i,j) \notin T_D} (1 - p_{ij})$$

$$k_1 = 10^{-5}$$

$$k_{-1} = \frac{k_1}{K} \quad \left[ K = \frac{Z}{Z_A * Z_B} \right]$$

# Translation & Replication

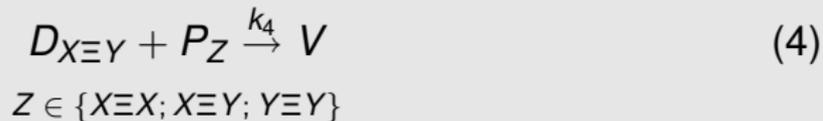


$$k_2 = \sum_{(i,j) \in T_M} (1 - p_{ij}) + \sum_{(i,j) \notin T_M} (1 - p_{ij})$$

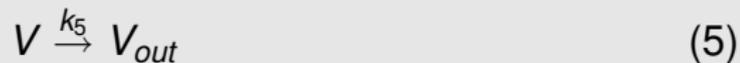


$$k_3 = 1 - k_2$$

# Encapsulation & Removal



$$k_4 = \text{const} * k_1$$



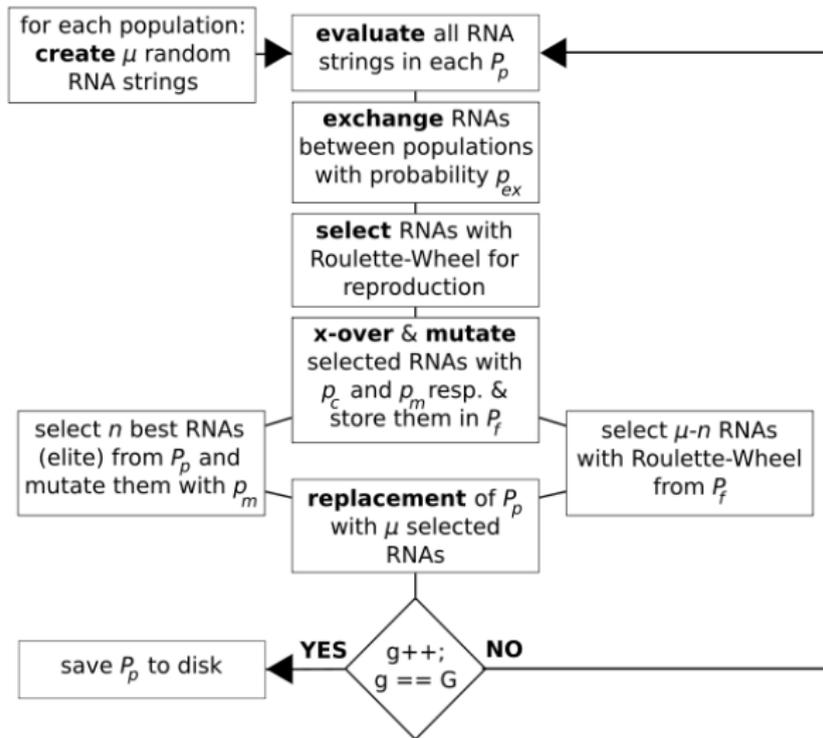
$$k_5 = \text{const}$$

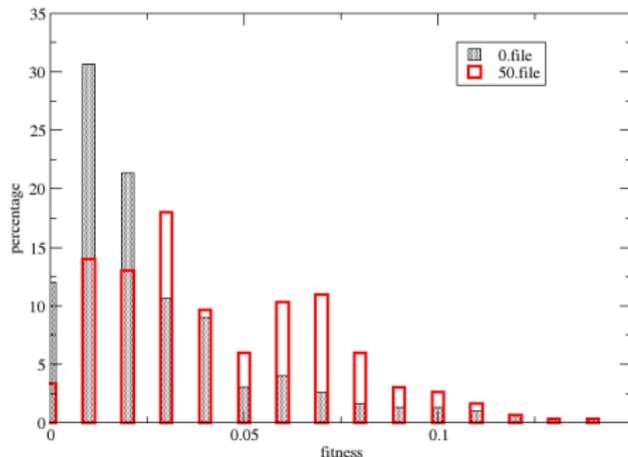


# Tools

- libSBML  
Systems Biology Markup Language
- Vienna RNA Package
- SOSlib  
SBML ODE Solver Library
- GA

# The GA





generations: 50  
 replacement: keep the best

$\rho$  : 6

$\mu$  : 10

$\lambda$  : 12

$\tau$  : 4

$p_{1-point-xover}$  : 0.2

$p_{2-point-xover}$  : 0.2

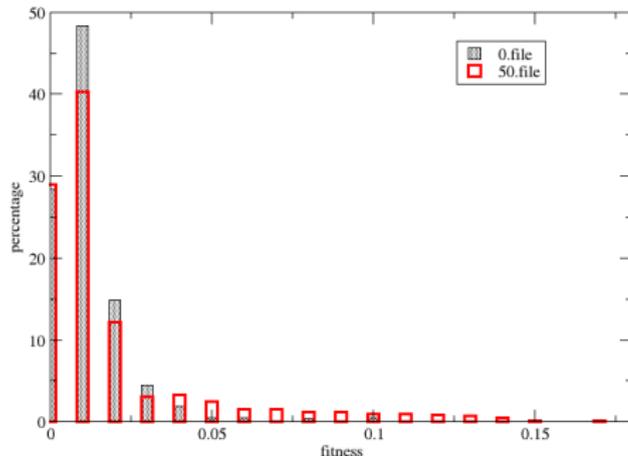
$p_{n-point-xover}$  : 0.2

$p_{bitmutation}$  : 0.01

$p_{transloc-mutation}$  : 0.05

$p_{reverse-mutation}$  : 0.05

$p_{xchange}$  : 0.05



generations: 50  
replacement: elitism

$\rho$  : 6

$\mu$  : 20

$\lambda$  : 24

$\tau$  : 4

$p_{1-point-xover}$  : 0.2

$p_{2-point-xover}$  : 0.2

$p_{n-point-xover}$  : 0.2

$p_{bitmutation}$  : 0.01

$p_{transloc-mutation}$  : 0.05

$p_{reverse-mutation}$  : 0.05

$p_{xchange}$  : 0.05

# Conclusion

- homodimeric RNAs
- heterodimeric RNAs with homodimeric protein coats
- no real parasitism
- combinatorial explosion
  
- rate parameters
- tracking history

# Acknowledgment

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