



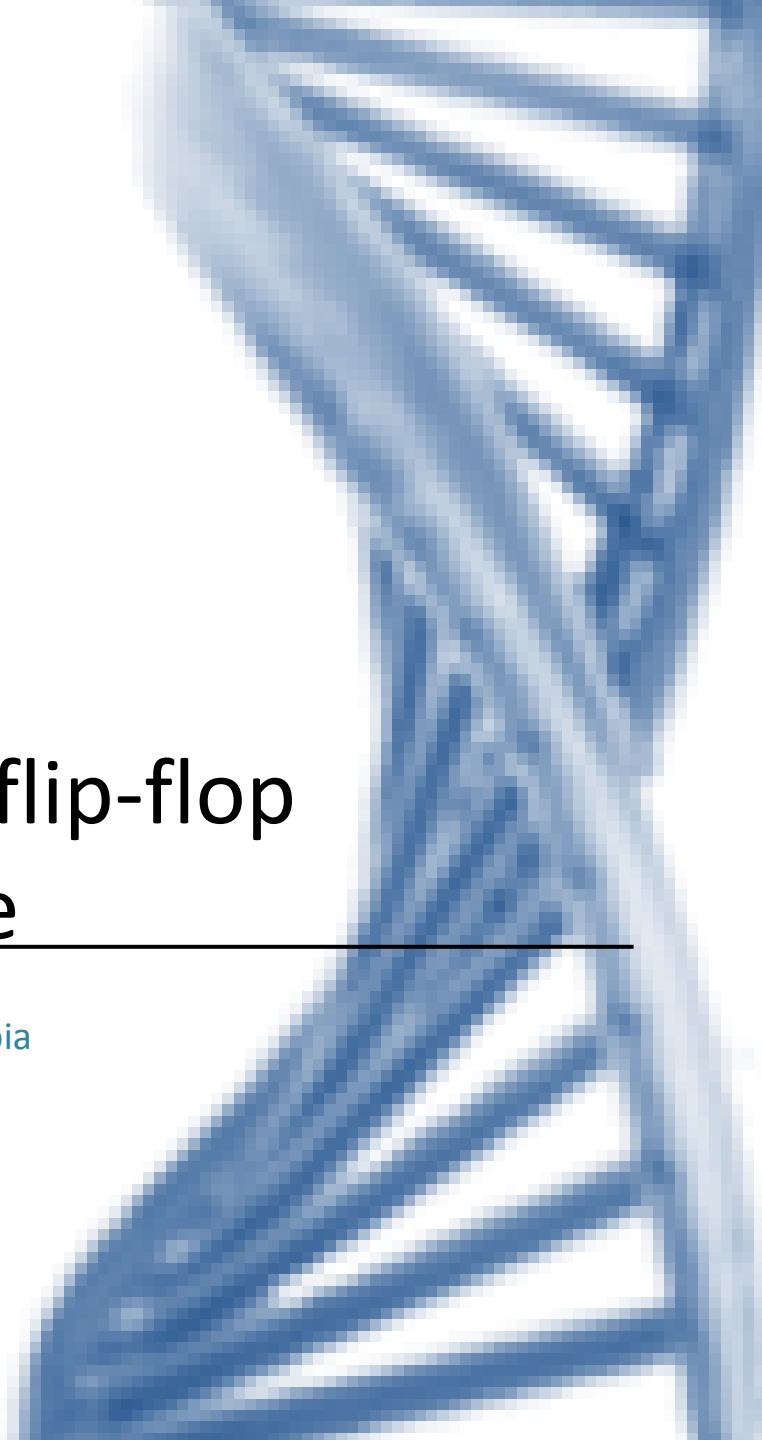
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THE UNIVERSITY OF BRITISH COLUMBIA

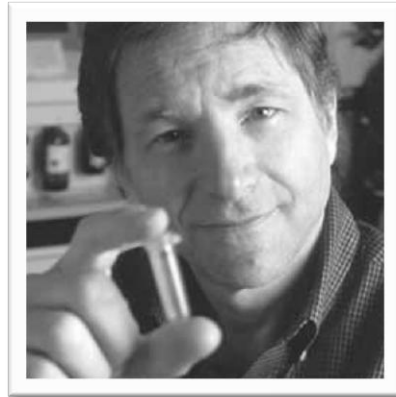
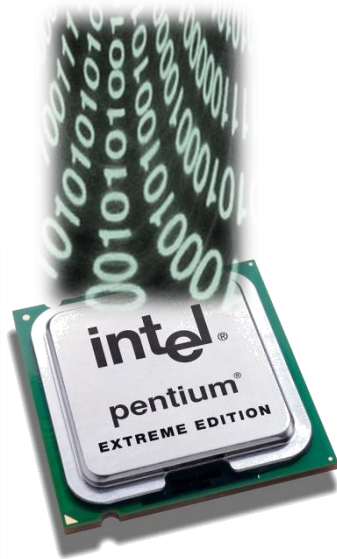
# Modelling a biomolecular flip-flop based on RNA interference

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Department of Computer Science, University of British Columbia



# Biomolecular Computing



Leonard Adleman  
1994

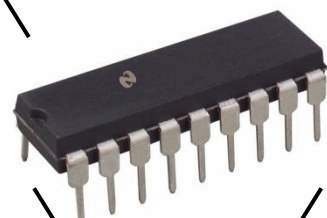
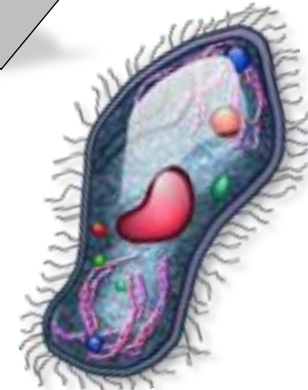
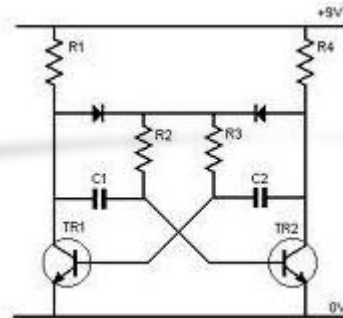


Paradigm: Biomolecules for storing and enzymes for manipulating information  
Unique strength: Biocompatibility, i.e. computation inside living cells

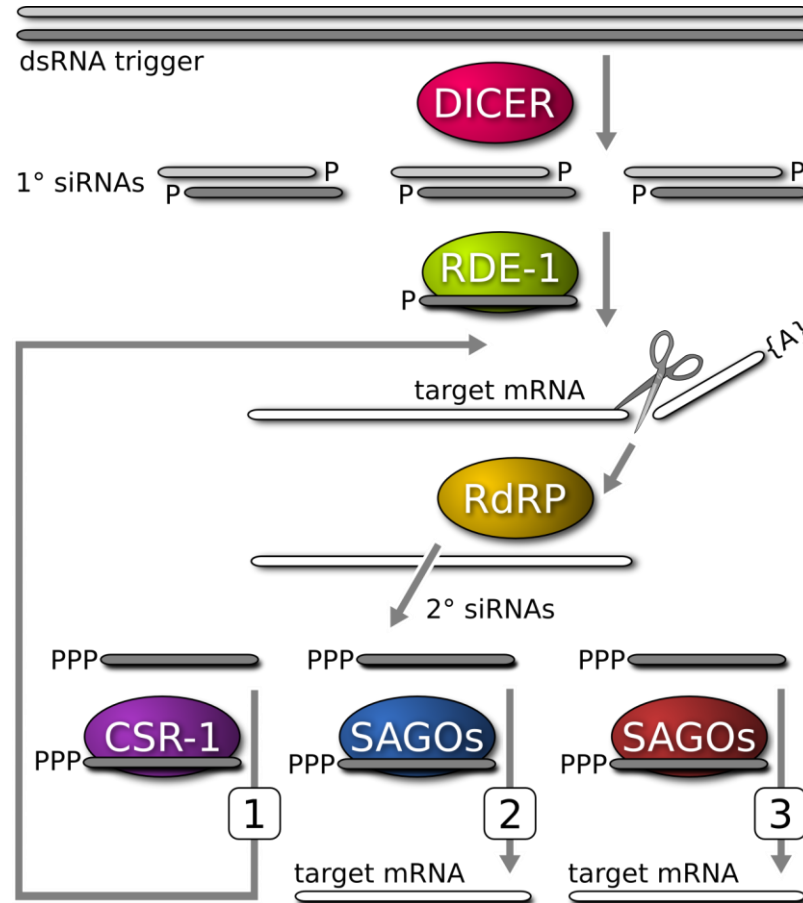
# Flip-flop: A universal memory unit

Silicon

Carbon



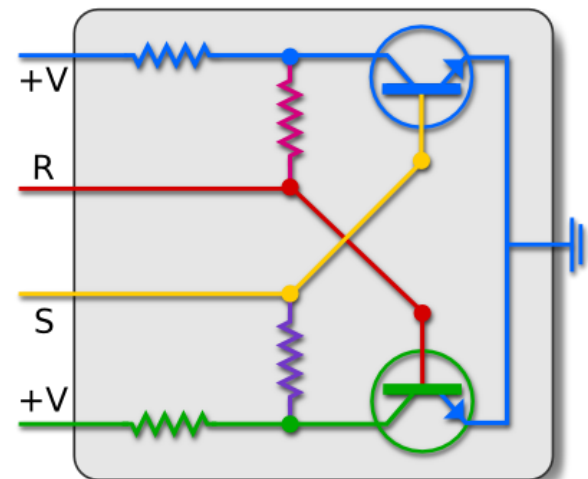
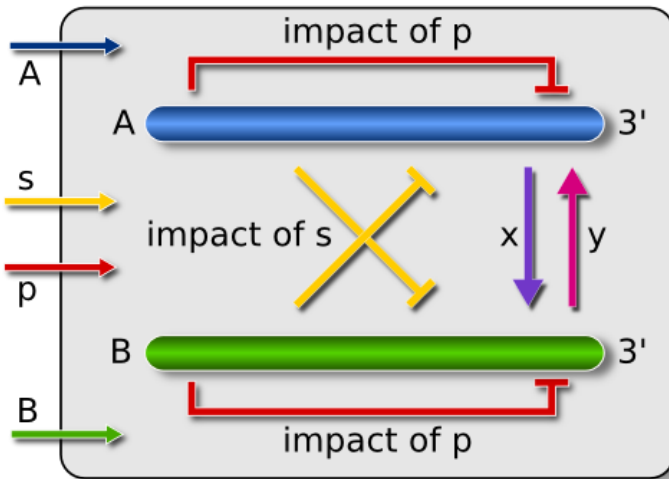
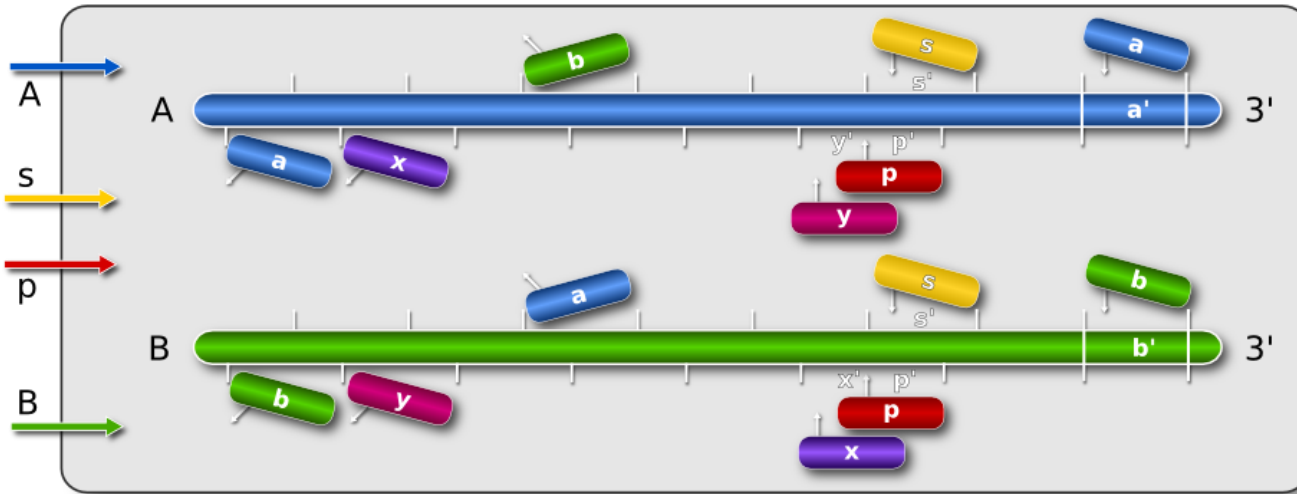
# RNA interference



siRNA-programmable universal protein machinery

Manipulates information encoded in mRNA concentrations

# Flip-flop design scheme

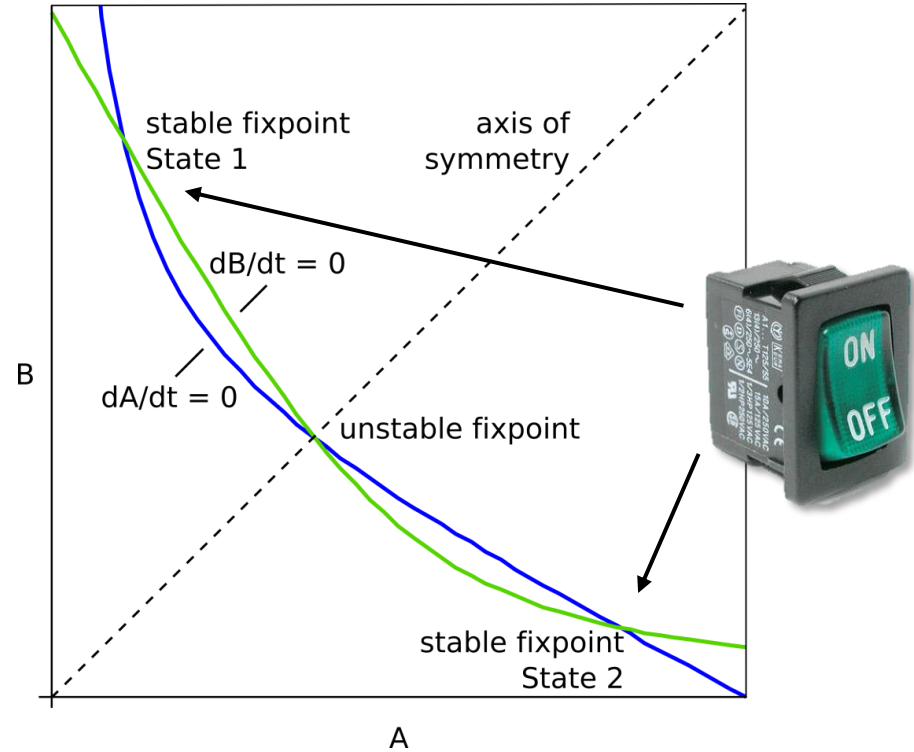
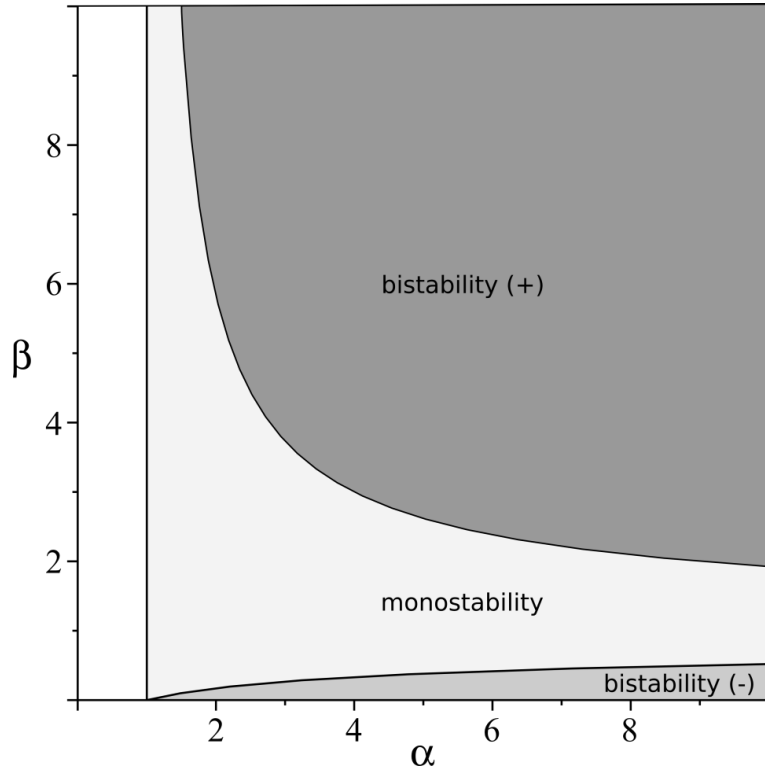


# RNAi flip-flop model

$$\begin{aligned} \frac{\partial A}{\partial t} &= \tau - \gamma A - \phi a A - \mu y A + \delta A_b \\ \frac{\partial B}{\partial t} &= \tau - \gamma B - \phi b B - \mu x B + \delta B_b \\ \frac{\partial a}{\partial t} &= \omega B - \epsilon a - \rho a A + \xi f_t A \\ \frac{\partial b}{\partial t} &= \omega A - \epsilon b - \rho b B + \xi f_t B \\ \frac{\partial x}{\partial t} &= \xi f_t A - \epsilon x - \mu x B + \delta B_b \\ \frac{\partial y}{\partial t} &= \xi f_t B - \epsilon y - \mu y A + \delta A_b \\ \frac{\partial A_b}{\partial t} &= \mu y A - \delta A_b \\ \frac{\partial B_b}{\partial t} &= \mu x B - \delta B_b \end{aligned}$$

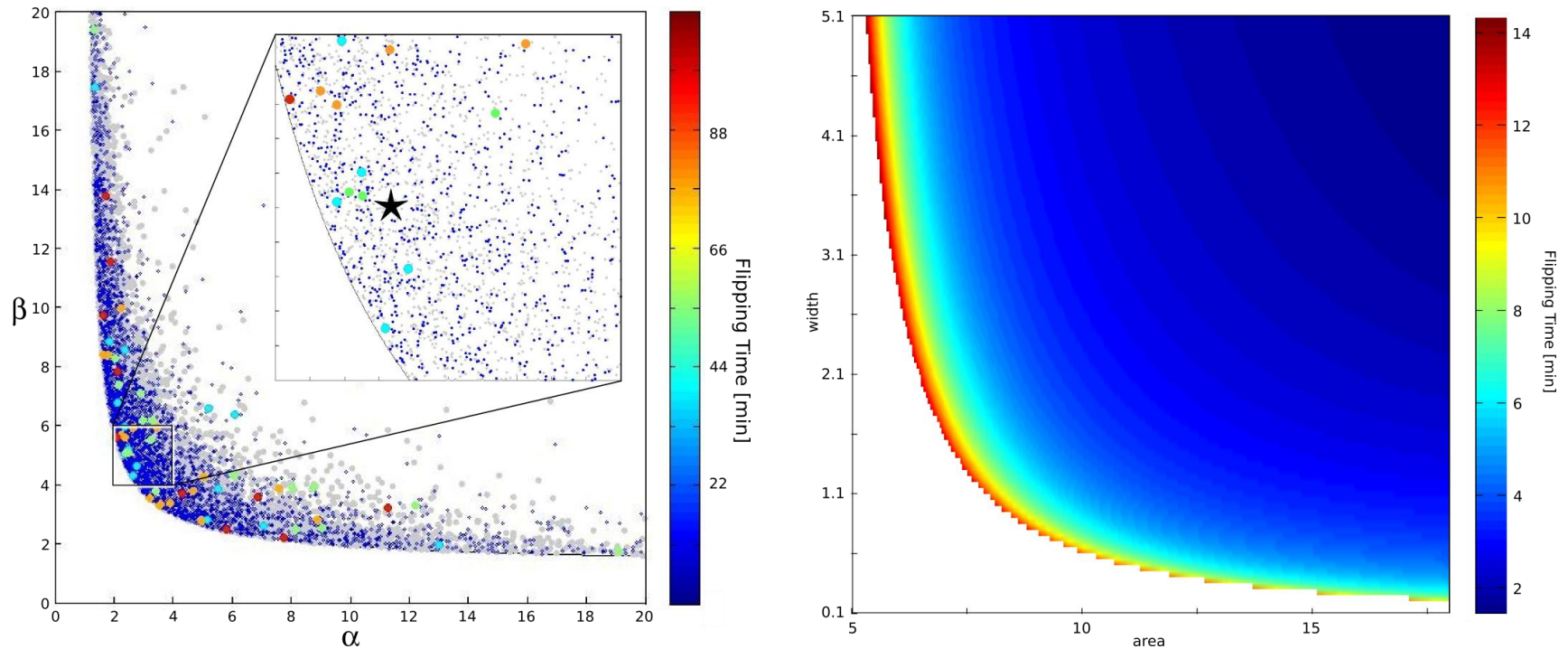
Parameter	Description
$\tau$	mRNA transcription rate
$\gamma$	unspecific mRNA degradation rate
$\phi$	RNAi-based mRNA consumption rate
$\mu$	hybridization-based mRNA blocking rate
$\delta$	mRNA-siRNA deblocking rate
$\omega$	steady siRNA production rate
$\epsilon$	unspecific siRNA degradation rate
$\rho$	RNAi-based siRNA consumption rate
$\xi$	trigger-mediated siRNA production rate

# Static properties of the model



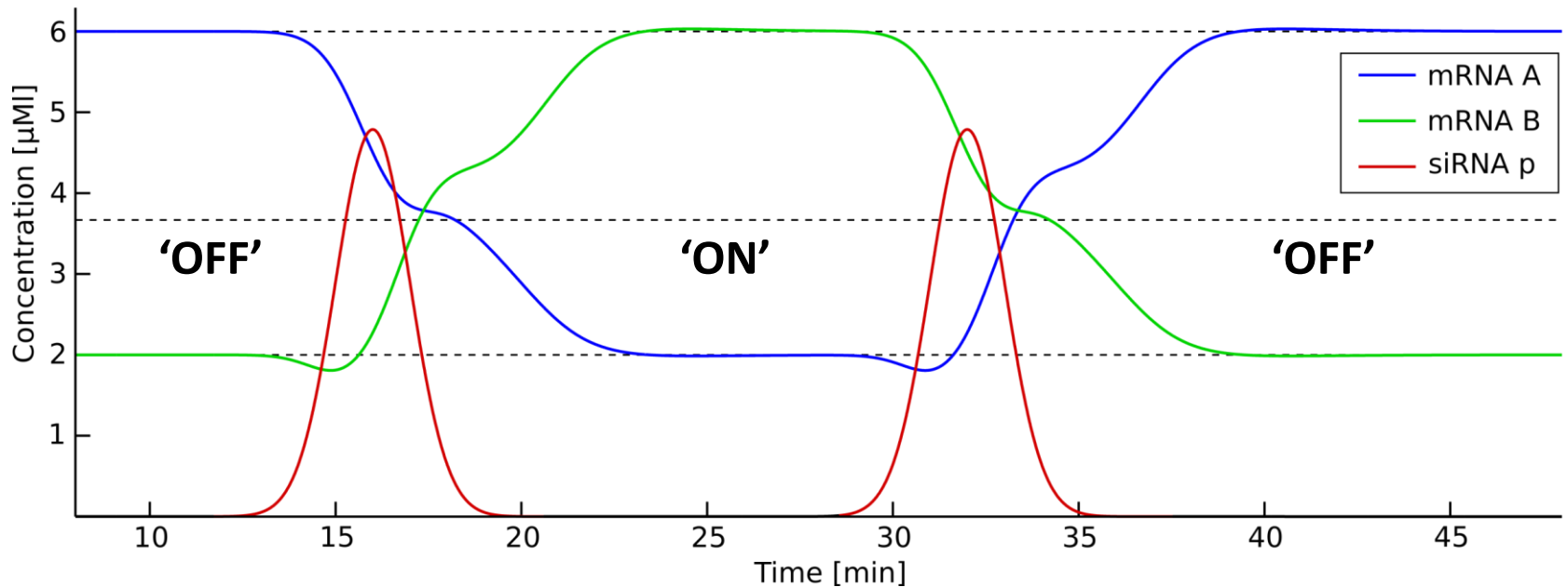
Model exhibits desired bistability characteristics for certain parameters

# Dynamic properties of the model



Robust flipping can be achieved over large parameter ranges

# Simulation of the RNAi flip-flop



Optimized flip-flop with switch-like behaviour between discrete states

# Potential applications



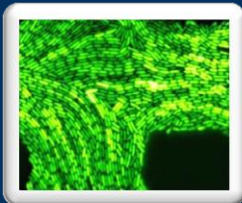
## Biomolecular Computing

- Sequential logic
- Synchronize computations



## Biology & Medicine

- Monitor cellular events
- Diagnose disease conditions



## Synthetic Biology

- Incorporate in more complex systems
- Universal memory device

# Acknowledgment

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Dr. Eldon Emberly



Bioinformatics Training Program

