

# Appendix

The source code is available on our Github.

The full functions and parameters are listed in the following appendix PDF.

## RNAi

$$\left\{
 \begin{aligned}
 \frac{dpri\_miRNA}{dt} &= \alpha_{pri\_miRNA} \cdot gene - \frac{V_{max,Drosha\&DGCR8,pri\_miRNA}}{K_{m,Drosha\&DGCR8+pri\_miRNA}} - d_{pri\_miRNA} \cdot pri\_miRNA \\
 \frac{dpre\_miRNA}{dt} &= \frac{V_{max,pri\_miRNA}}{K_{m,RNAPoly+pri\_miRNA}} - v_{exp} \cdot pre\_miRNA - d_{pre\_miRNA} \cdot pre\_miRNA \\
 \frac{dpre\_miRNAs_{out}}{dt} &= v_{exp} \cdot pre\_miRNA - \frac{V_{max,DICER,pre\_miRNAs_{out}}}{K_{m,DICER+pre\_miRNAs_{out}}} \\
 &\quad - d_{pre\_miRNAs_{out}} \cdot pre\_miRNAs_{out} \\
 \frac{dds\_miRNA}{dt} &= \frac{V_{max,DICER,pre\_miRNAs_{out}}}{K_{m,DICER+pre\_miRNAs_{out}}} - d_{ds\_miRNA} \cdot ds\_miRNA \\
 &\quad - v_{as,RISC} \cdot ds\_miRNA \cdot RISC + v_{dis,RISC} \cdot Ago\&RISC\&miRNA \\
 \frac{dmRNA}{dt} &= \alpha_{mRNA} \cdot gene \\
 &\quad - v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA + v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
 &\quad - d_{mRNA} \cdot mRNA \\
 \frac{dRISC\&miRNA}{dt} &= v_{as,RISC\&miRNA} \cdot ds\_miRNA \cdot RISC \\
 &\quad - v_{dis,RISC\&miRNA} \cdot Ago\&RISC\&miRNA \\
 &\quad - v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA + v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
 \frac{dRISC\&miRNA\&mRNA}{dt} &= v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA - v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
 &\quad - d_{RIM} \cdot RISC\&miRNA\&mRNA
 \end{aligned}
 \right.$$

Notation	Meaning	Value
$g$	gene copies	200 from our assumption
$\alpha$	transcription rate for kinds of RNA	$1.5 \times 10^{-3}$ [2]
$\beta$	translation rate for kinds of mRNA	0.000162 [3]
$k_m$	Kinetic constant of Miltonian equation	$1.2 \times 10^3 nM$ [4]
$v_{max}$	Kinetic constant of Miltonian equation	$0.246 nM/s$ [4]
$d_{mRNA}$	decomposition rate of mRNA	$3.3 \times 10^{-3}$ [6]
$d_{protein}$	decomposition rate of protein	$5.22 \times 10^{-3}$ [7]
$d_{siRNA}$	decomposition rate of siRNA	$8.887 \times 10^{-4}$ [8]
$v_{as}, v_{dis}$	association and disassociation rate	$1 \times 10^{-3}$ (Estimated)
$v_{trans}$	transport rate of exportin5	$2 \times 10^{-3}$ [5]

Table. 1: RNAi parameters

## Specific proliferation

$$\left\{
\begin{aligned}
\frac{dpri\_miRNA}{dt} &= \alpha_{pri\_miRNA} \cdot gene - \frac{V_{max,Drosha\&DGCR8,pri\_miRNA}}{K_{m,Drosha\&DGCR8+pri\_miRNA}} - d_{pri\_miRNA} \cdot pri\_miRNA \\
\frac{dpre\_miRNA}{dt} &= \frac{V_{max,pri\_miRNA}}{K_{m,RNAPoly+pri\_miRNA}} - v_{exp} \cdot pre\_miRNA - d_{pre\_miRNA} \cdot pre\_miRNA \\
\frac{dpre\_miRNA_{out}}{dt} &= v_{exp} \cdot pre\_miRNA - \frac{V_{max,DICER,pre\_miRNA_{out}}}{K_{m,DICER+pre\_miRNA_{out}}} \\
&\quad - d_{pre\_miRNA_{out}} \cdot pre\_miRNA_{out} \\
\frac{dds\_miRNA}{dt} &= \frac{V_{max,DICER,pre\_miRNA_{out}}}{K_{m,DICER+pre\_miRNA_{out}}} - d_{ds\_miRNA} \cdot ds\_miRNA \\
&\quad - v_{as,RISC} \cdot ds\_miRNA \cdot RISC + v_{dis,RISC} \cdot Ago\&RISC\&miRNA \\
&\quad - v_{as,siRNA\&sponge} \cdot dssiRNA \cdot Sponge + v_{dis,siRNA\&sponge} \cdot siRNA\&sponge \\
\frac{dmRNA}{dt} &= \alpha_{mRNA} \cdot gene \\
&\quad - v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA + v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
&\quad - d_{mRNA} \cdot mRNA \\
\frac{dRISC\&miRNA}{dt} &= v_{as,RISC\&miRNA} \cdot ds\_miRNA \cdot RISC \\
&\quad - v_{dis,RISC\&miRNA} \cdot Ago\&RISC\&miRNA \\
&\quad - v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA + v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
\frac{dRISC\&miRNA\&mRNA}{dt} &= v_{as,RIM} \cdot RISC\&miRNA \cdot mRNA - v_{dis,RIM} \cdot RISC\&miRNA\&mRNA \\
&\quad - d_{RIM} \cdot RISC\&miRNA\&mRNA \\
\frac{dSponge}{dt} &= \alpha_{Sponge} \cdot gSponge - d_{Sponge} \cdot Sponge \\
&\quad - v_{as,siRNA\&sponge} \cdot dssiRNA \cdot Sponge + v_{dis,siRNA\&sponge} \cdot siRNA\&sponge \\
\frac{dSponge\&siRNA}{dt} &= v_{as,siRNA\&sponge} \cdot dssiRNA \cdot Sponge - v_{dis,siRNA\&sponge} \cdot siRNA\&sponge \\
&\quad - d_{Sponge\&siRNA} \cdot Sponge\&siRNA
\end{aligned}
\right.$$

Notation	Meaning	Value
$\alpha_{sponge}$	transcription rate for sponge	$1.5 \times 10^{-3}$
$v_{as,sponge\&siRNA}$	the association rate of sponge and siRNA	$1 \times 10^{-3}$ from assumption
$v_{dis,sponge\&siRNA}$	the disassociation rate of sponge and siRNA	$1 \times 10^{-3}$ from assumption
$d_{sponge}$	The decomposition rate of sponge	$8.887 \times 10^{-4}$ from mRNA estimates
$d_{sponge\&siRNA}$	The decomposition rate of sponge	$8.887 \times 10^{-4}$ from mRNA estimates

Table. 2: Specific Proliferation Parameters

## Automata

Assume  $v_1, v_2, v_3$  represent free virus, virus infecting normal cells, virus infecting cancer cells respectively and  $c_1, c_2$  represent normal cells and cancer cells respectively.

$$\left\{ \begin{array}{l} v_{1,t+1} = -d \cdot v_{1,t} - \alpha \cdot v_{1,t} + r_1 \cdot v_2 + r_2 \cdot v_3 \\ v_{2,t+1} = -d \cdot v_{2,t} + \frac{c_1}{c_1+c_2 \cdot spi} \cdot \alpha \cdot v_{1,t} \\ v_{3,t+1} = -d \cdot v_{3,t} + \frac{c_2 \cdot spi}{c_1+c_2 \cdot spi} \cdot \alpha \cdot v_{1,t} \\ c'_{1,t} = \max(1, c_{1,t} - k_1 \cdot v_{2,t}) \\ c'_{2,t} = \max(1, c_{2,t} - k_2 \cdot v_{3,t}) \\ c_{1,t+1} = \frac{c'_{1,t}}{c'_{1,t}+c'_{2,t}} \cdot N \\ c_{2,t+1} = \frac{c'_{2,t}}{c'_{1,t}+c'_{2,t}} \cdot N \end{array} \right.$$

Notation	Meaning	Value
$N$	total number of cells	20000
$d$	decomposition rate of virus	0.1
$\alpha$	infection ratio of virus	0.3
$spi$	Specific infection parameter	5
$r_1$	replication rate of virus in normal cell	0.05
$r_2$	replication rate of virus in cancer cell	0.2
$k_1$	killing rate of virus in normal cell	0.02
$k_2$	killing rate of virus in cancer cell	0.2

Table. 3: Automata concept model parameters

## References

- [1] Eytan Zlotorynski. Insights into the kinetics of microRNA biogenesis and turnover. *Nature Reviews Molecular Cell Biology*, 2019.
- [2] Heather A Ferguson, Jennifer F Kugel, and James A Goodrich. Kinetic and mechanistic analysis of the RNA polymerase II transcription reaction at the human interleukin-2 promoter edited by K. Yamamoto. *Journal of Molecular Biology*, 314(5):993–1006, 2001.
- [3] Shlomi Reuveni, Isaac Meilijson, Martin Kupiec, Eytan Ruppin, and Tamir Tuller. Genome-scale analysis of translation elongation with a ribosome flow model. *PLOS Computational Biology*, 7(9):1–18, 09 2011.
- [4] D.N. Fouillen A. et al. Bouvette, J. Korkut. High-yield production of human dicer by transfection of human HEK293-EBNA1 cells grown in suspension. *BMC Biotechnol* 18, 76 (2018)., 2018.

- [5] Nancy J. Pokrywka and David S. Goldfarb. Nuclear export pathways of tRNA and 40S ribosomes include both common and specific intermediates. *Journal of Biological Chemistry*, 2021/10/02.
- [6] Antoine et al Baudrimont. Multiplexed gene control reveals rapid mRNA turnover. *Science advances*, 3, 2017.
- [7] Rafał Krzysztoń, Daniel Woschée, Anita Reiser, Gerlinde Schwake, Helmut H. Strey, and Joachim O. Rädler. Single-cell kinetics of siRNA-mediated mRNA degradation. *Nanomedicine: Nanotechnology, Biology and Medicine*, 21:102077, 2019.
- [8] Jiajia Guo, Jianjun Wang, and Genxing Xu. Pharmacokinetic perspective and the delivery of siRNA in vivo. *Pharmaceutical and Clinical Research*, 18(4):363–365, 2010.