# Modelling RNA devices in a cellular context

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Winterseminar, Bled 2015



## RNA devices (RNAdevs)

- ON/OFF switches
  - Transcriptional
  - Translational
- Direct/Induced

- Direct binding to RBS/Antiterminator
- Binding triggers riboswitch



## Ordinary Differential Equations (ODEs) systems

- Cellular context is necessary for RNAdev functionality
- Core system modelling transcription, translation and degradation adapted from Keasling Lab (Carothers et al. 2011)
- Expanded core to model RNAdev regulation
- Extensive research for meaningful rates
- Calculation of sequence dependent rates



#### Core System



#### Let's solve the equation!



#### Translational ON/OFF switch



### Translational OFF switch solved





#### Sequence dependent rates

- Complex formation rate (k30)
- Complex dissociation rate (k40)
- Translation initiation rate mRNA (k4)
- Translation initiation rate complex (k4')



### **RBS** accessibility rates

Translation initiation rates (k4, k4')
 k4 = P(RBS unbound) \* k4<sub>original</sub>

$$P(\text{RBS unbound}) = 1 - \frac{\sum_{\forall i \in \text{RBS}} \sum_{0 \le j \le n}^{j \ne i} P_{ij}}{|RBS|}$$

- ON switches: k4 (mRNA) << k4' (complex)</li>
- OFF switches: k4 >> k4'



(1)

 $sRNA \cap + mRNA$ 

#### **Complex formation rate**

$$\bigotimes_{R} + \bigcap_{F} + \bigcap_{k_{40}} \bigoplus_{C_{long}} \bigvee_{C_{long}} \times$$

$$R + F \rightleftharpoons C_{long} : k_{30}/k_{40} \tag{1}$$

$$K = \frac{[R \cdot F]}{[R][F]} = \frac{Z^{RF}}{Z^R \cdot Z^F}$$
$$Z^{RF} = Z^{cofold} - Z^R \cdot Z^F$$

(2)

$$Z = e^{-\frac{\Delta G}{RT}}$$
$$K = e^{-\frac{G_{cofold} - (G_R + G_F)}{RT}} - 1 = \frac{k_{30}}{k_{40}}$$

$$k_{40} = e^{-\frac{(-1)\cdot\Delta G_{Binding}}{RT}}$$

$$k_{30} = K \cdot k_{40}$$
(3)
(3)



## Outlook

- Sensitivity Analysis
- Collaboration partner to verify/improve rates
- Verify model using existing RNAdev sequences
- Benchmark prediction ability of new designs
- Use models in RNA design objective function
- These models are available on Github in the popular SBML exchange format:

https://github.com/ribonets/rnadev-models/



### Thanks to...

- Sven Findeiß
- Christoph Flamm
- Ivo Hofacker
- Stefanie Hertel
- Ribonets Team
- TBI Colleagues

#### https://github.com/ribonets/rnadev-models/













