1 Set up

This model is designed to capture the burden effects of shared resources within a cell. It was originally based of the work in https://www.nature.com/articles/s41467-020-18392-x written by Guy-Bart Stan and Velia Siciliano.

The original model aimed to capture the burden effects of shared resources by deriving an effective rate constant. For example, consider the following two-step translation reaction:

$$\mathrm{A}_i + \mathrm{R} \underset{\mathrm{k}_i^-}{\overset{\mathrm{k}_i^+}{\rightleftharpoons}} \mathrm{C}_i \xrightarrow{\mathrm{k}_i^{\mathrm{cat}}} \mathrm{A}_i + \mathrm{B}_i + \mathrm{R} \tag{1}$$

All i number of these reactions will be coupled with the shared resource R, and thus the larger the number of reactions i, the more scarce the resource R will be. The burdening effect of this can be approximated as described in the nature article.

$$\mathrm{A}_i \xrightarrow{\mathrm{k}_i^{\mathrm{eff}}} \mathrm{B}_i, \qquad k_i^{eff} = k_i^{cat} R^{total} \frac{k_{m_i}^{-1} A_i}{1 + \sum_{j=1}^{n} k_{m_j}^{-1} A_j} \tag{2}$$

This is an incredibly useful approximation. However, due to assumptions made in its derivation, it does not consider the burden effects on the shared resources themselves. This is the unique niche that this model aims to capture.

The additional effect that this model must capture, is the effect of miRNA regulation. When transcribed, both 3' and 5' miRNA are able to selectively bind to mRNA, thereby recruiting exoribonucleases for degradation. 5' miRNA have an additional effect of blocking translation initiation due to steric hindrance.

Therefore, the model must be able to capture two effects:

- Temporary consumption of shared cellular resources.
- Competitive binding between ribosomes and 5'miRNA.

To capture point 1, the model must have a species that represents the number of elongating ribosomes. To capture point 2, the model must have a mRNA binding site with a capacity of 1, and that can be by bound by either a 5'miRNA or a ribosome.

2 Introduction

To capture all the effects summarised, the following general reaction framework was created for translation:

$$\mathrm{m}_{j,u} + \mathrm{R} \underset{\mathrm{k}^-}{\overset{\mathrm{k}^+}{\rightleftharpoons}} \mathrm{m}_{j,b} \xrightarrow{\mathrm{k}} \mathrm{m}_{j,u} + \mathrm{R}_j, \qquad \mathrm{R}_j \xrightarrow{\widehat{\mathrm{k}^{\mathrm{cat}}}} \mathrm{R} + \mathrm{P}_j \tag{3}$$

This reaction framework shows a temporary occupying of the mRNA binding site, $mj,u- > mj,b- > mj,u$, and a temporary bound elongating state for the ribosomes.