Cell Growth Model - v0.8

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# Model Overview

## Features

* Gene expression models based biomolecular species classes:
  + Metabolic
  + Ribosome-associated
  + Housekeeping
* Translation models
  + Implicit polysomes formation
  + Elongation Complex formation dependent on cell energy levels
* Energy utilisation model
  + Utilised by Protein Synthesis process
  + Utilised by Elongation Complex Formation process
* Cell mass model:
  + Phenomenological
  + Logistic function shaped
  + Variable mass dependent on intracellular energy levels

## Version Modifications

* Derived from model v0.7
* Ribosome Assembly model
* Removed rRNA species

# Processes Models

## Transcription

## Translation Initiation Complex formation

|  |  |  |  |
| --- | --- | --- | --- |
| Assumptions | | | |
| * The association rate constant between ribosomes and rbs\_mRNAs is variable, while all classes exhibit the same dissociation kinetics. This simplification does not represent reality as experimental observation show both constant values can vary within an interval of 3 orders of magnitude (Gualerzi & Pon, 2015) but its implementation was necessary to reduce the search space and the number of dimensions in parameter fitting. | | | |
| Reaction | | | |
| Forward rate  Reverse rate | kb\_x  m\_x + ribo 🡨🡪 ic\_x  ku | | |
| Species | | | |
| m\_x  ribo  ic\_x | RBS of class x = {rib, met, hsk}  Ribosomes  Translation Initiation complex of class x = {rib, met, hsk} | | |
| Parameters | Description | Value | Units |
| kb\_x  ku | RBS/ribosome association rate  Initiation Complex dissociation rate |  | 1/(molecules\*minutes)  1/minute |
| Modifications to basic Model | | | |
| Assumptions | | | |
| * For rib class:   + The association rate of rbs\_mRNA with ribosome for the formation of ic\_rib is inhibited by a modulating function based on the amount of free ribosomal protein molecules in the cell, as negative feedback regulation at translation initiation stage is well established for the control of ribosomal protein expression (Nomura et al., 1980) | | | |
| Modulating function (rib class) |  | | |
| Parameters/Species | Description | Value | Units |
| p\_rib  Krepr | ribosomal proteins  repression threshold |  | molecules  molecules |
| Fluxes | | | |
| d(ic\_rib)/dt = +kb\_ribo \*ribo \*r\_rib \* ( 1 / ( 1 + ( ***p\_rib*** / Krepr ) ) )  -ku\*ic\_rib    d(ic\_met)/dt = +kb\_met \*ribo \* r\_cat  -ku\*ic\_cat  d(ic\_hsk)/dt = +kb\_others\*ribo \*r\_hsk  -ku\*ic\_hsk | | | |

## Translation Elongation Complex formation

## Translation Protein Synthesis

## mRNA degradation

## Ribosome Assembly

|  |  |  |  |
| --- | --- | --- | --- |
| Assumptions | | | |
| * Ribosomal proteins instantaneously form sets of ribosomal proteins of size equal to the total amino acid mass of an assembled ribosome * Ribosome Assembly is a single association event where a ribosomal proteins set forms an assembled ribosome | | | |
| Reaction | | | |
| Forward rate  Reverse rate | k\_form  p\_rib\_set 🡪 ribo | | |
| Species | | | |
| p\_rib  p\_rib\_set  ribo | Free ribosomal proteins  p\_rib\_set = ribosomal proteins / (lenRibo/lenR)  Ribosomes | | |
| Parameters | Description | Value | Units |
| lenRibo  lenR  k\_form | Size of ribosome with all its ribosomal proteins  Size of ribosomal protein  Rate constant for ribosome assembly |  | aa  aa  molecules/minute |
| Fluxes | | | |
| d(rib)/dt = - k\_form \* [p\_rib\_set] \* (lenRibo/lenR)  d(Ribo)/dt = + k\_form \* [p\_rib\_set] | | | |