Algorithm:

The transition probabilities are calculated in a recursive fashion: if a ribosome moves, and there was a ribosome directly behind it on the same mRNA, then the transition rate of the second ribosome is reset from zero to the local translation elongation rate ('local' referring to the fact that the ribosome place might contain a slow codon, so it needs to be checked to make sure that the correct translation elongation rate is assigned). When a ribosomebinds to an mRNA, then the initiation rate for that mRNA is set to zero. Is that ribosome moves from the ribosome binding site to the next ribosome place, then the initiation rate for the mRNA is reset to its normal value. We also need to consider the transition rates for the moving ribosome: if there is another ribosome directly in front of it (after it has moved to its new place), then we need to set its transition rate to zero. Otherwise, its transition rate is the normal local elongation rate. If the ribosome detaches from the mRNA (by reaching a slow codon), then it can be randomly chosen to bind to an mRNA when initiation is the next state transition. If initiation is the next state transition, we also need to choose which type of mRNA (R, E, Q or H) the ribosome attaches to. The type is chosen randomly, but on average it is proportional to the initiation rate of the type.

Dilution:

Dilution is bound to happen when a new protein is produced due to the finite proteome (finite mass) constraint of our system. To keep the mass of the cell constant at 10^8 amino acids, when the new protein is produced, we calculate the ratio between the new mass (after the protein is produced) and the old mass (before the protein is produced) and divide the number of proteins by this ratio. To give an example, suppose that we have the following number of proteins in one cell: 5740 R proteins, 7840 E proteins and 181980 Q proteins (numbers are taken from Table 1 in Results). Using the values from Weiße et al. [6], we know that R proteins have 7500 amino acids, and E and Q proteins have 300 amino acids. If one R protein is produced, the ratio between the old and new mass becomes:

$$ratio = \frac{5741 * 7500 + 7840 * 300 + 181980 * 300}{5740 * 7500 + 7840 * 300 + 181980 * 300}$$

Taking the constraint into account, the number of proteins is then given by:

$$\frac{(5741\ \ 7840\ \ 181980)}{ratio} = (5740.6\ \ 7839.4\ \ 181966.4)$$

Since the number of ribosomes (equalling the number of R-proteins as defined by Weiße et al. [6]) has to be an integer number so that we can use it in the translation model, the current number of ribosomes is given by the current number of R proteins rounded to the nearest integer. Since dilution also affects energy, the number of transcripts as well as the number of internalised nutrients, these values are also divided by the ratio as calculated above. The number of transcripts (of each type) also need to be integer numbers, so they are also rounded to their nearest integer in the translation model (however, we keep track of their fractional values). Note that dilution does not happen when a heterologous protein is produced. This is simply because,by definition, the heterologous protein has no benefit to the cell, hence it does not help it in its division process.

Explanation of variables:

State_array: has length equal to the number of ribosomes; describes which ribosome footprint the ribosome is translating at the moment; if ribosome is free, the respective number is one, if ribosome is at the beginning of the transcript, its state is two and if it is at the n^{th} position, its state is n+1. Note: this does not cause an issue, because if transcript has length n, beta array (see below) of that transcript is n+1 long, so protein is produced when the state is equal to the length of the corresponding beta array!

Location_array: has length equal to the number of ribosomes; describes which mRNA the ribosome is on, if the ribosome is free, the respective number is zero

Time_P_cell: cellular array, which has length equal to the number of types of mRNAs; the respective arrays store the times when a protein type was made from a given mRNA type

P_count_vec: has length equal to the number of protein types; the respective elements store the total number of proteins of the corresponding type

Betas: cellular array, which has length equal to the number of types of mRNAs; the respective arrays store the local elongation speed for each ribosome footprint on a given mRNA starting with initiation speed and hence have the length of the length of the mRNA plus one (because of initiation speed) Note: initiation rate should be reflected both in beta_array_cell and in temp!

Transition_array – as it is created when number of input arguments is 12: array, which has number of rows equal to the number of mRNAs and number of columns equal to the number of ribosomes; each row stores the current elongation speeds associated with the ribosomes that are on the respective mRNA, otherwise the element is zero

Transition_array – after merge and sum: 1D array, which has length of the number of ribosomes plus eight. The first element (created using an array called temp) corresponds to the total transition rate of the free ribosomes to any of the mRNAs, whereas the following elements (each element corresponding to one ribosome) correspond to the transition rate of a ribosome to the next position on the mRNA; if the ribosome is free, the element is zero. The seven last elements correspond to R transcription rate, E transcription rate, Q transcription rate, H transcription rate, degradation rate, nutrient transport rate and nutrient metabolism rate, respectively.

Temp: array, which has length equal to the number of mRNAs. Each element corresponds to the current initiation rate of the mRNAs taking into account that if the RBS site is occupied the current initiation rate is zero

Type_idx_array: array, which has length equal to the number of mRNAs. Each element denotes which type the corresponding mRNA belongs to.