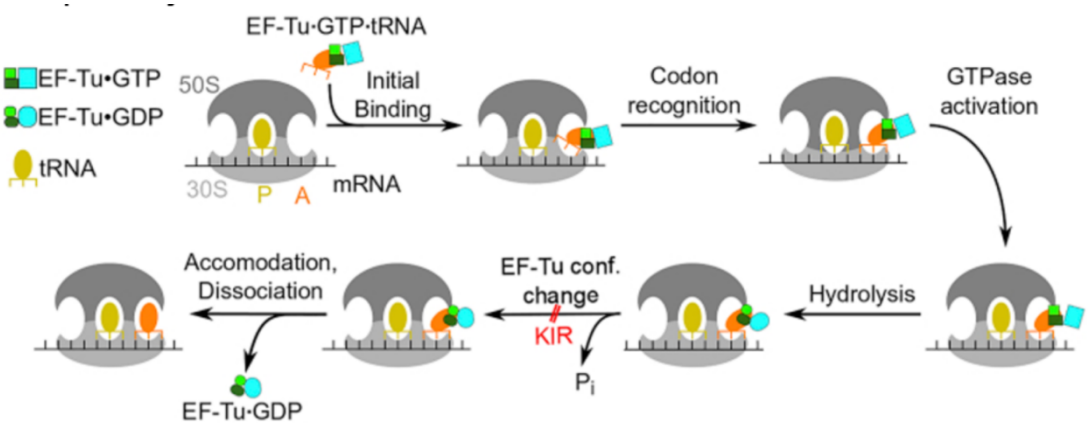
BIOENG-320
Gene circuits
Week 2

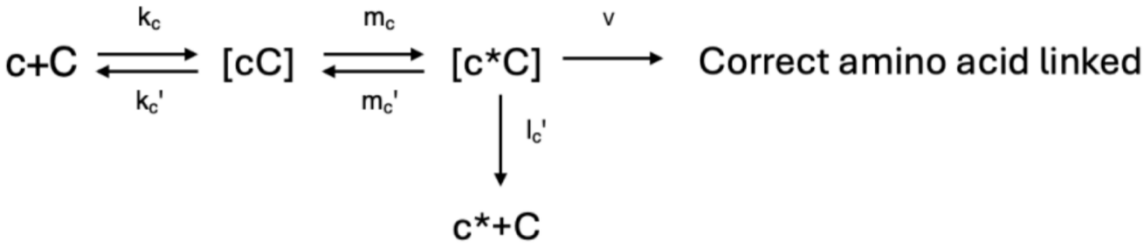
Q1. Kinetic proofreading

Protein translation involves the interaction of many molecular players in the cell. Although we have studied this process in the past decades, there are still many aspects to be discovered such as intermediate states or interactions due to the complexity and fast dynamics of this process. A summary of the steps required for tRNA-ribosome-mRNA recognition in prokaryotes is shown below:



During this week's lecture, you learned about a simplified model of the tRNA-ribosome-mRNA interaction. It was mentioned during class that an additional control step (kinetic proofreading) during translation was the modification of the tRNA (c*). In the diagram above, you can observe that the tRNA forms a ternary complex with the elongation factor thermo-unstable protein (EF-Tu) and GTP. Upon recognition of the anticodon-codon, EF-Tu undergoes conformational changes to allow the GTPase domain to become active resulting in the hydrolysis of GTP to GDP and inorganic phosphate (P_i). The hydrolysis changes again the conformation of EF-Tu reducing its binding affinity to the tRNA, which results in the dissociation of the complex. GTP hydrolysis leads to a near irreversibility due to the shift in the equilibrium of the process.

For the purpose of this exercise, consider the translational kinetic proofreading model of reversibility for the modified tRNA:



Where c: correct tRNA; C: Codon; [cC] and [c*C]: intermediate states of unmodified and modified tRNA.

a) Derive an expression for the rate of correct incorporation. Note: The kinetic coefficient v is not negligible for this exercise.
b) Derive an expression for the error rate of incorporation. Note: Consider different kinetic constants containing w, as subscripts for the wrong incorporation (i.e. k_w, l_w, m_w). Also consider that the v constants are equal for wrong and correct incorporation of amino acids.