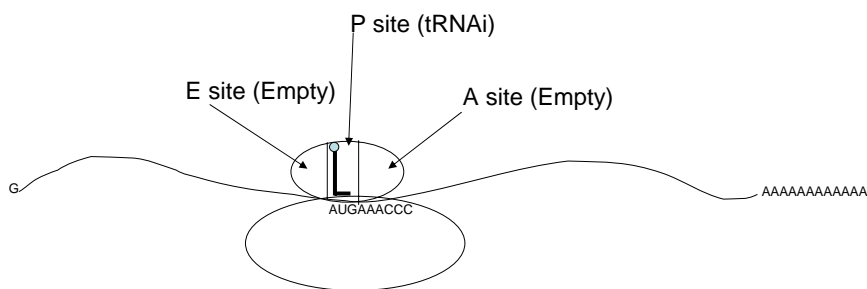


# Translation Elongation

1. Post Initiation Ribosome
2. Three Interlocking Cycles of Elongation
3. Role of eEF1 $\alpha$ 
  - Decoding/Proofreading/Delivery
4. Movement of tRNA through Ribosome
  - Hybrid site model
5. Role of eEF2
  - Molecular Mimicry
  - Binding and GTP Hydrolysis
6. Role of E site

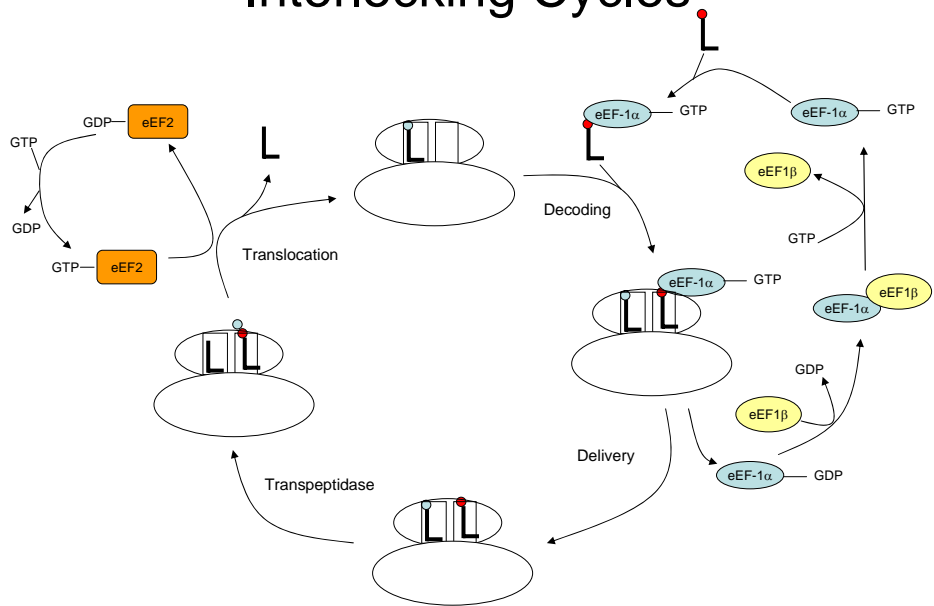
## Post Initiation Ribosome



### Four steps to Elongation

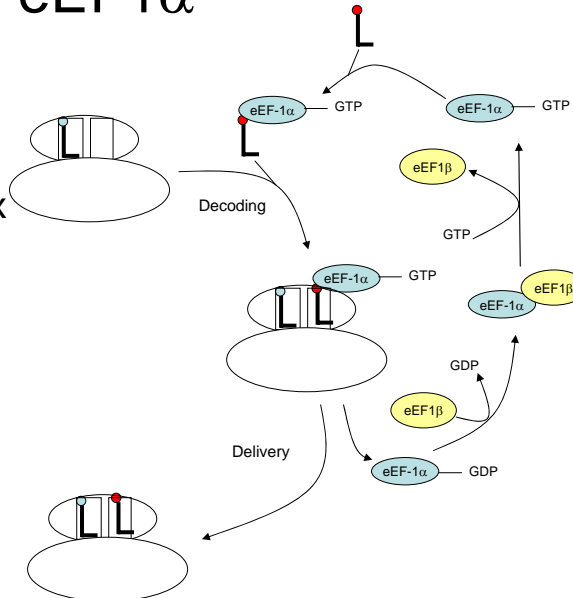
1. Decoding
2. Delivery of tRNA to A site
3. Transpeptidase Activity
4. Translocation

# Interlocking Cycles



## eEF1α

- eEF1α [EF-Tu]
- G protein
- Ternary Complex
  - Decoding Step
  - Delivery Step



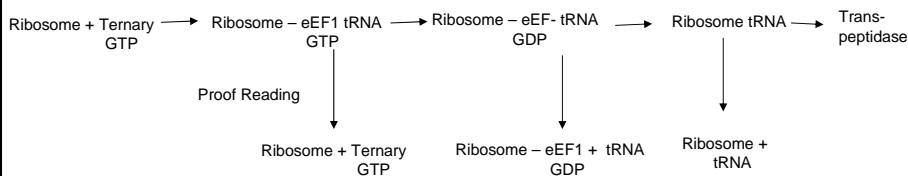
# Proof reading

## – Proofreading steps

- Decoding
  - Trigger GTP Hydrolysis
- Delivery
  - Second conformational check

## – Error rate

- 0.01% / amino acid added
- Probability of producing error free protein



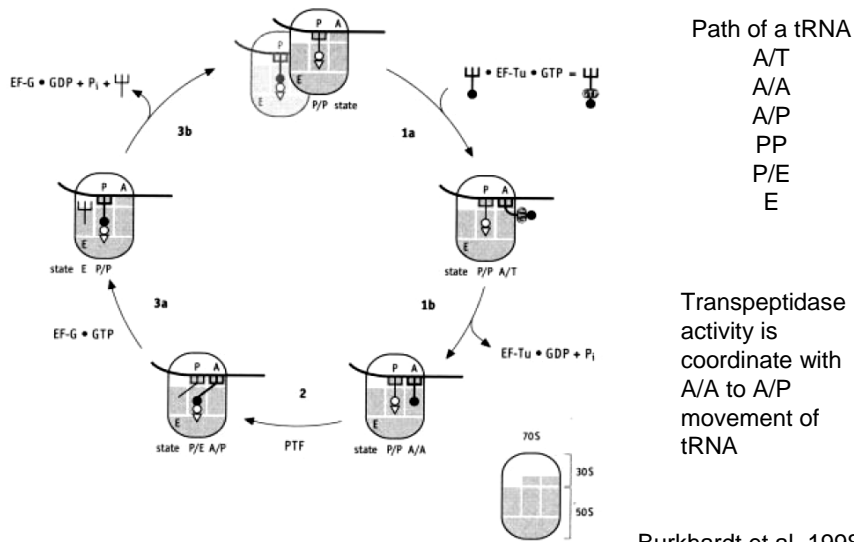
$$P = (1 - \text{Error Rate})^{\text{Number of amino acids}}$$

For average protein (300 amino acids)  $P = 97\%$

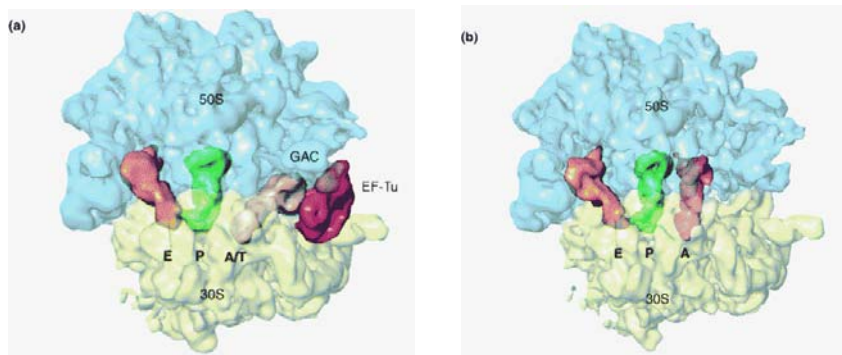
# Effect of Errors

- Alter one amino acid
  - compare to mis-sense mutation
- Most positions relatively insensitive to errors (Estimate 1 in 400 substitutions lethal to protein function)
- Conservative errors maybe favored
- Inverse relationship between speed of protein production and accuracy
- Streptomycin interferes with proofreading.

# Hybrid Site Model

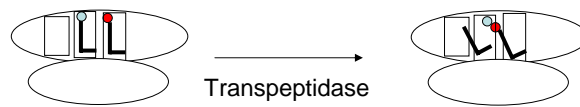


## eEF-1 $\alpha$

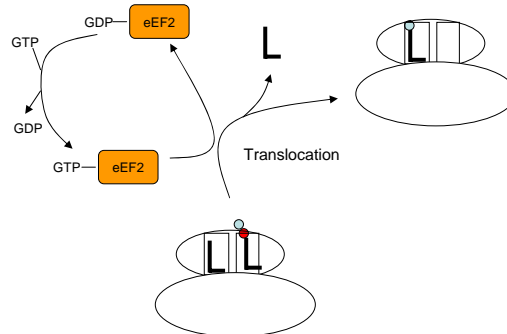


Nilsson and Nissen 2005

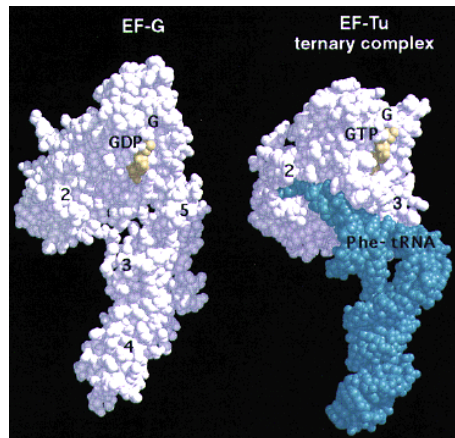
# Transpeptidase Activity



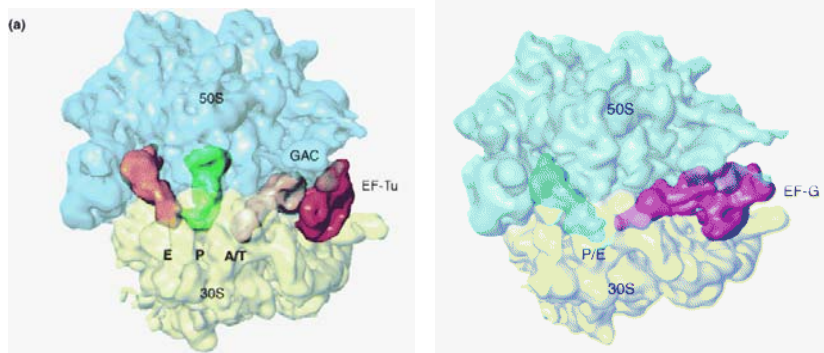
# Translocation



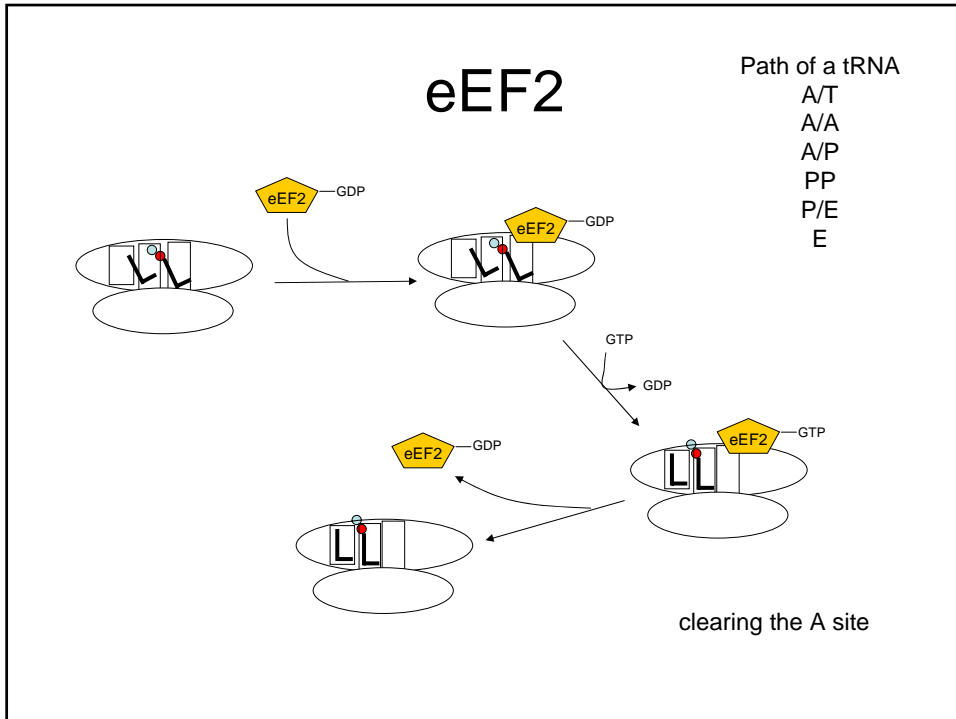
# Molecular Mimicry



# Molecule Mimicry



Nilsson and Nissen 2005



## Role of E-site in proofreading

- Allosteric communication with A-site
  - Occupied E site reduces affinity of the A-Site for Ternary complex. This low affinity may be necessary for proof-reading.
  - Antibiotics (edeine) and tRNA alterations which prematurely empty A site increase misincorporation.
  - Delivery of tRNA to A site results in emptying of E site.
  - Fungi have a separate EF (eEF3) required to clear E site.

## Role of E site in Frame Maintenance.

- Frame shifting is a severe ribosomal error.
- Binding of tRNA in E site limits frame shifting.
- Mechanism – Increase # H bonds?
- Loss of tRNA from E site increases frameshifts.