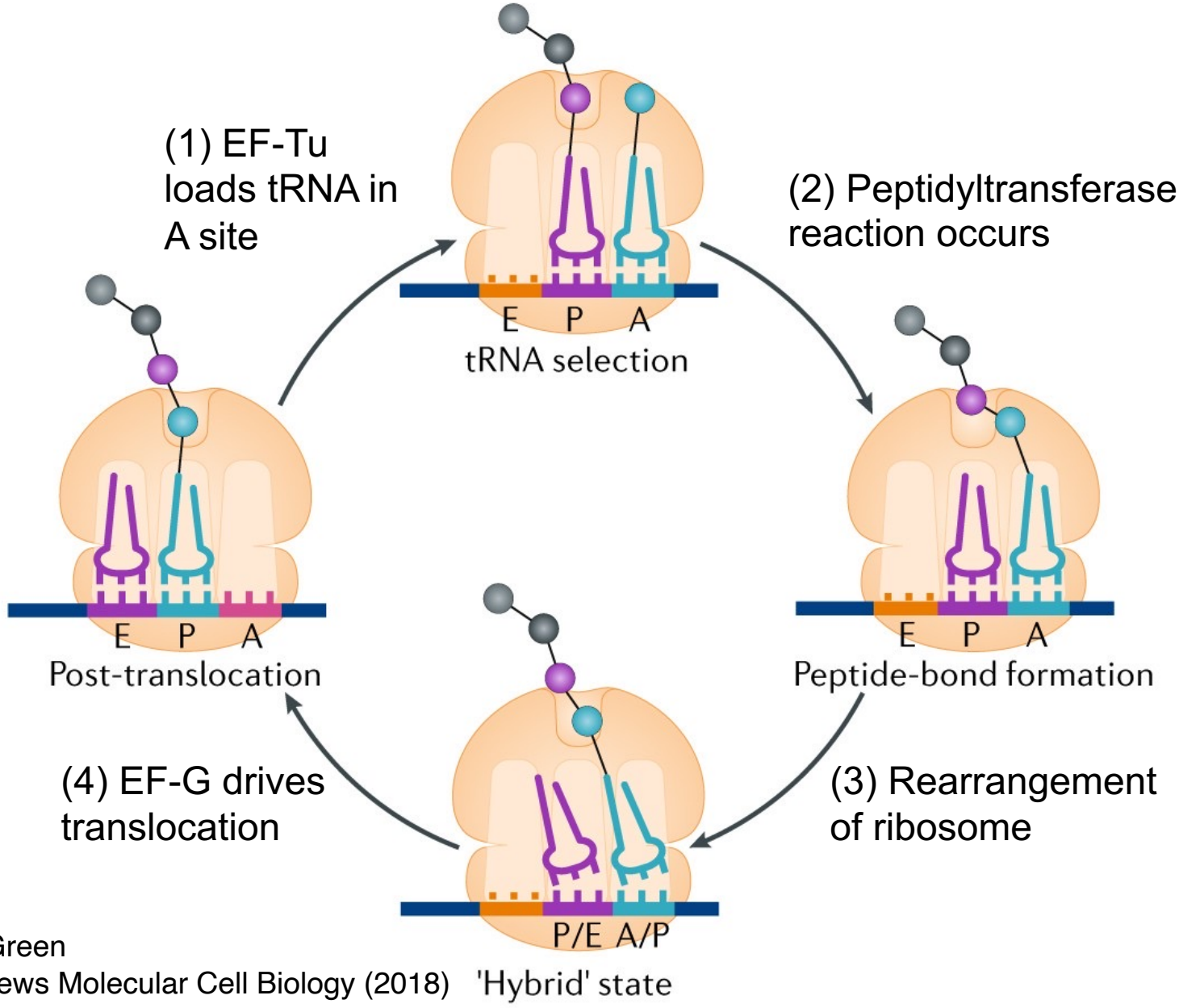
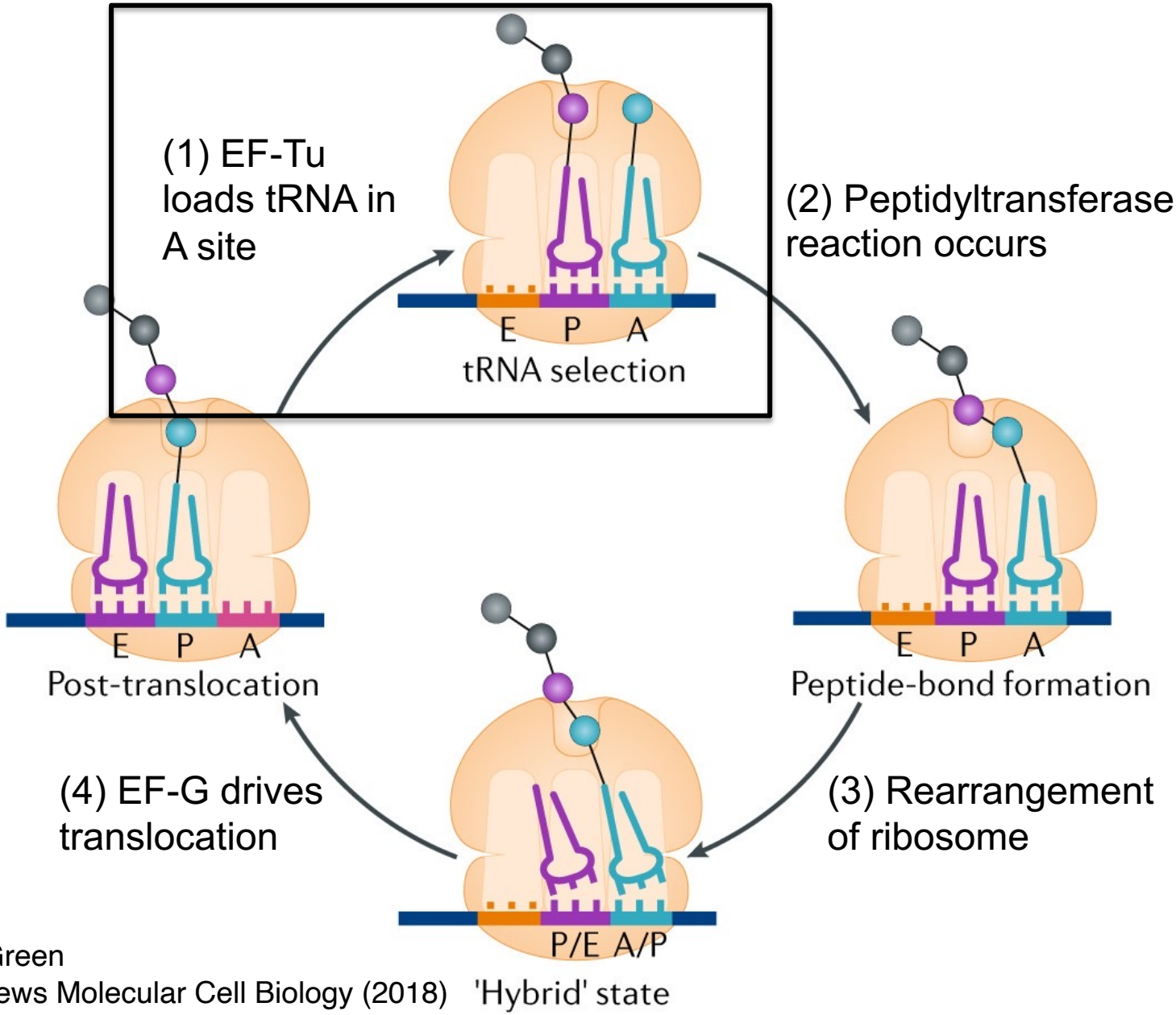
- **1% extra credit on your final grade (= 10 points on your lower midterm grade) for submitting an online evaluation for the course by the campus deadline**
- **Final exam next Wednesday at 8am in CS24**
- **Final exam is cumulative**
- **You will have all 3 hours**
- **I will have my final office hours on Monday (2pm)**
- **The TAs have extra office hours today and Saturday**
- **Review session Monday evening at 6pm**

Summary of translation elongation (similar in bacteria and eukaryotes, bacterial names shown)



Schuller & Green
Nature Reviews Molecular Cell Biology (2018)

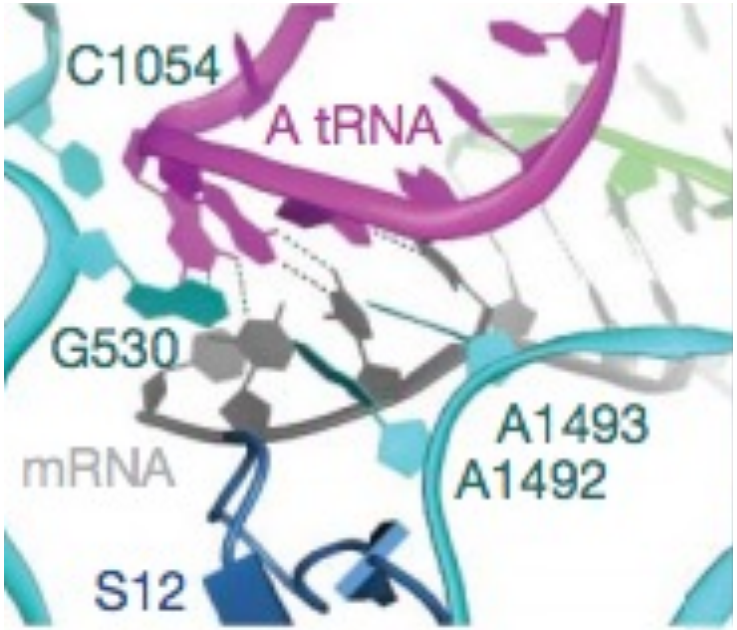
Summary of translation elongation (similar in bacteria and eukaryotes, bacterial names shown)



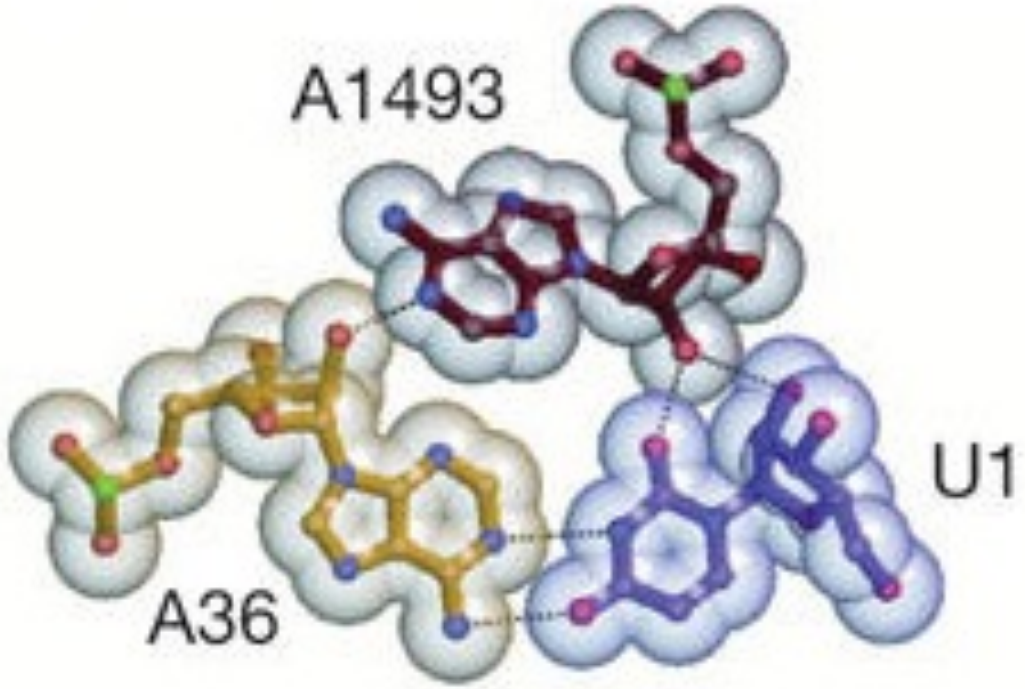
Schuller & Green
Nature Reviews Molecular Cell Biology (2018)

The codon/anticodon interaction is stabilized in the A site through interactions with the 16S rRNA

5´-U1 U2 U3-3´ **codon**
| | •
3´-A_{36} A_{35} G_{34}-5´ **anticodon**



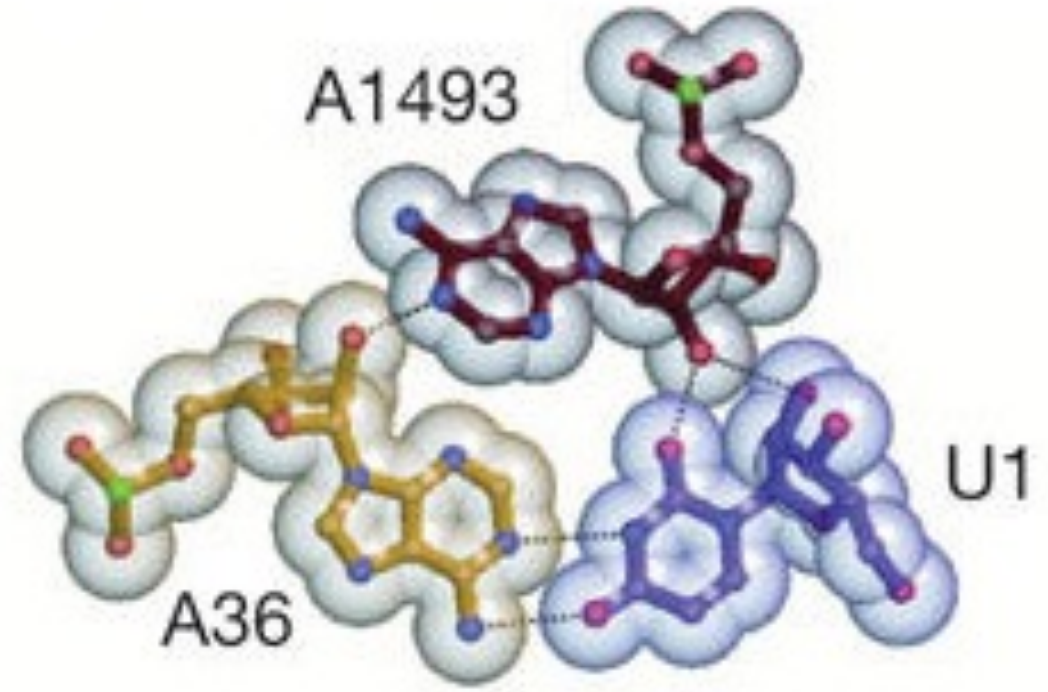
Schmeing & V. Ramakrishnan
Nature 2009



A-Minor interaction between A1493 of 16S rRNA and the first codon/anticodon base-pair

Moore &
Steitz
Nature 2002

Is this interaction specific to the codons containing a U at position 1?



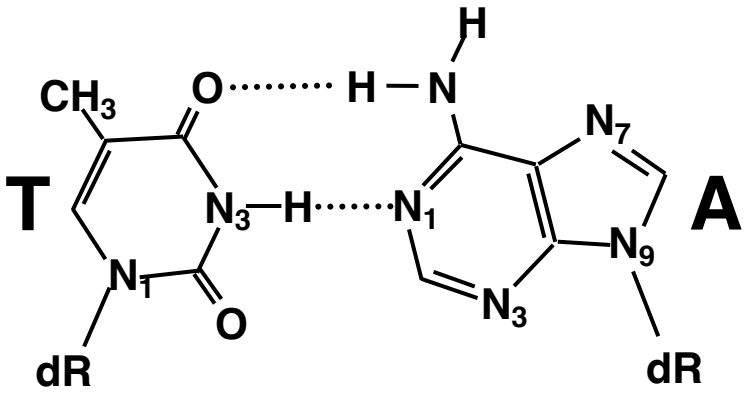
A: Yes because it involves the carbonyl of U in the minor groove

B: No because it involves the 2´OH of both codon and anticodon

C: Yes because a G instead of the U would sterically clash with A1493

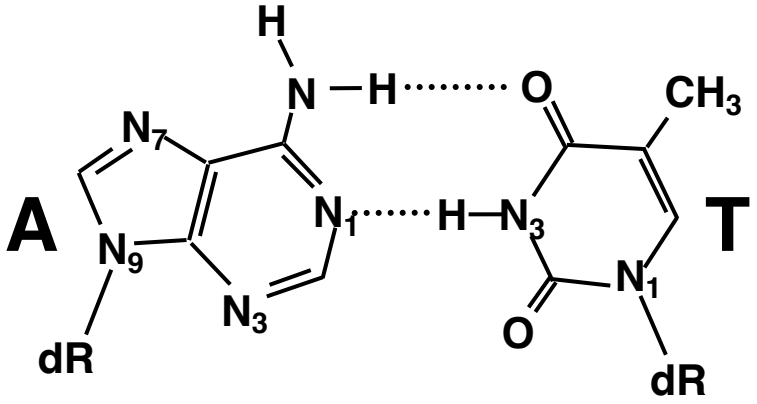
D: No because you could form interactions with the H-bond acceptor in the minor groove and the 2´-OH regardless of the sequence

Recognition of Specific sequences by DNA-binding proteins



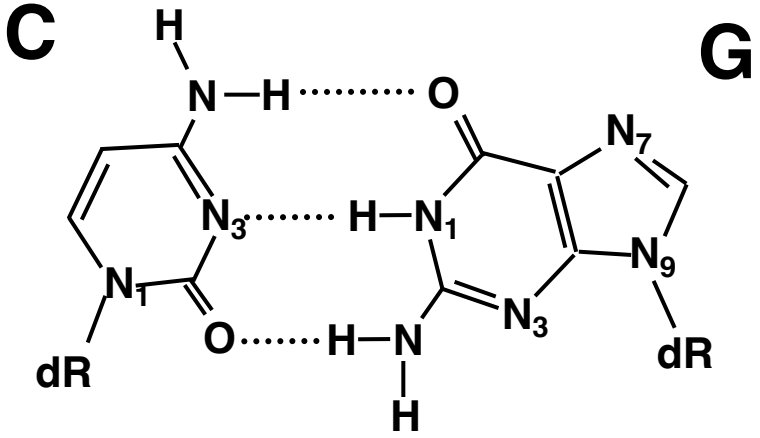
Distribution of H-bonds Donors (D) Acceptors (A) and Hydrophobic groups (H) available for recognition

D
H A A
Major groove
Minor groove
A A



D
A A H
Major groove
Minor groove
A A

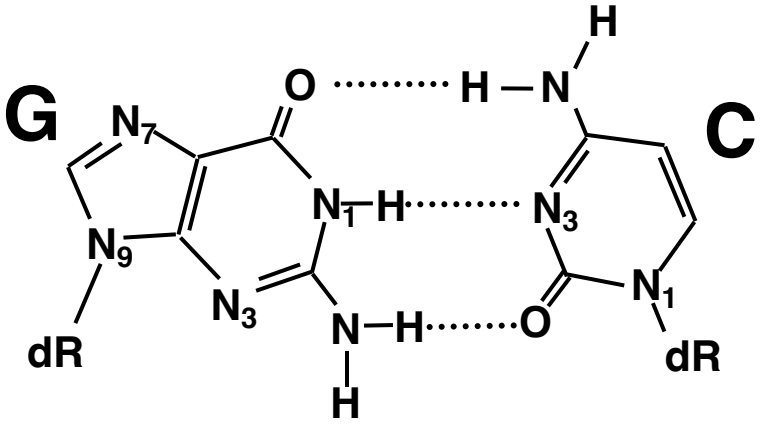
Recognition of Specific sequences by DNA-binding proteins



Patterns of H-bonds Donors (D), Acceptors (A), and Hydrophobic groups (H) available for recognition

D A A — Major groove

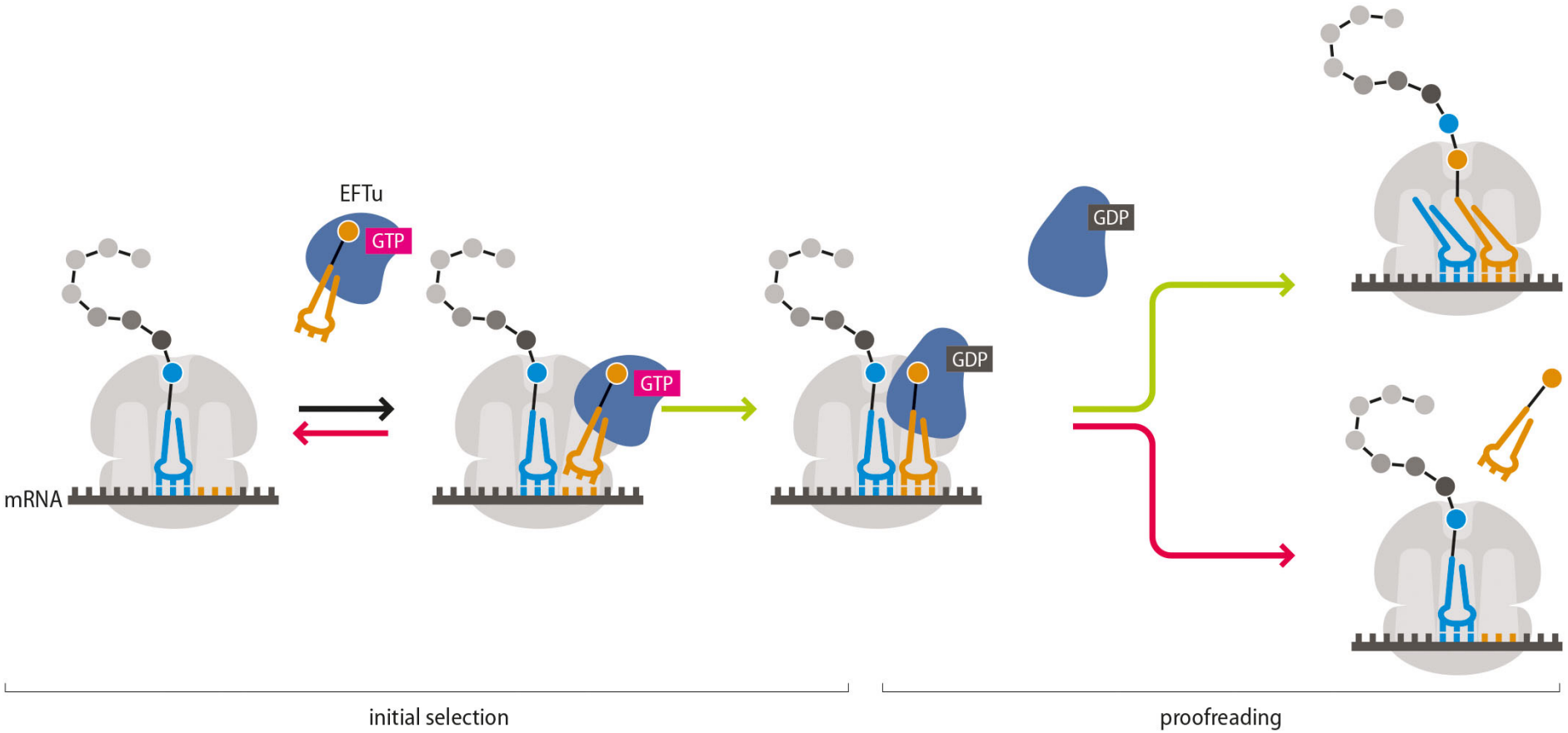
A A D — Minor groove



D A A — Major groove

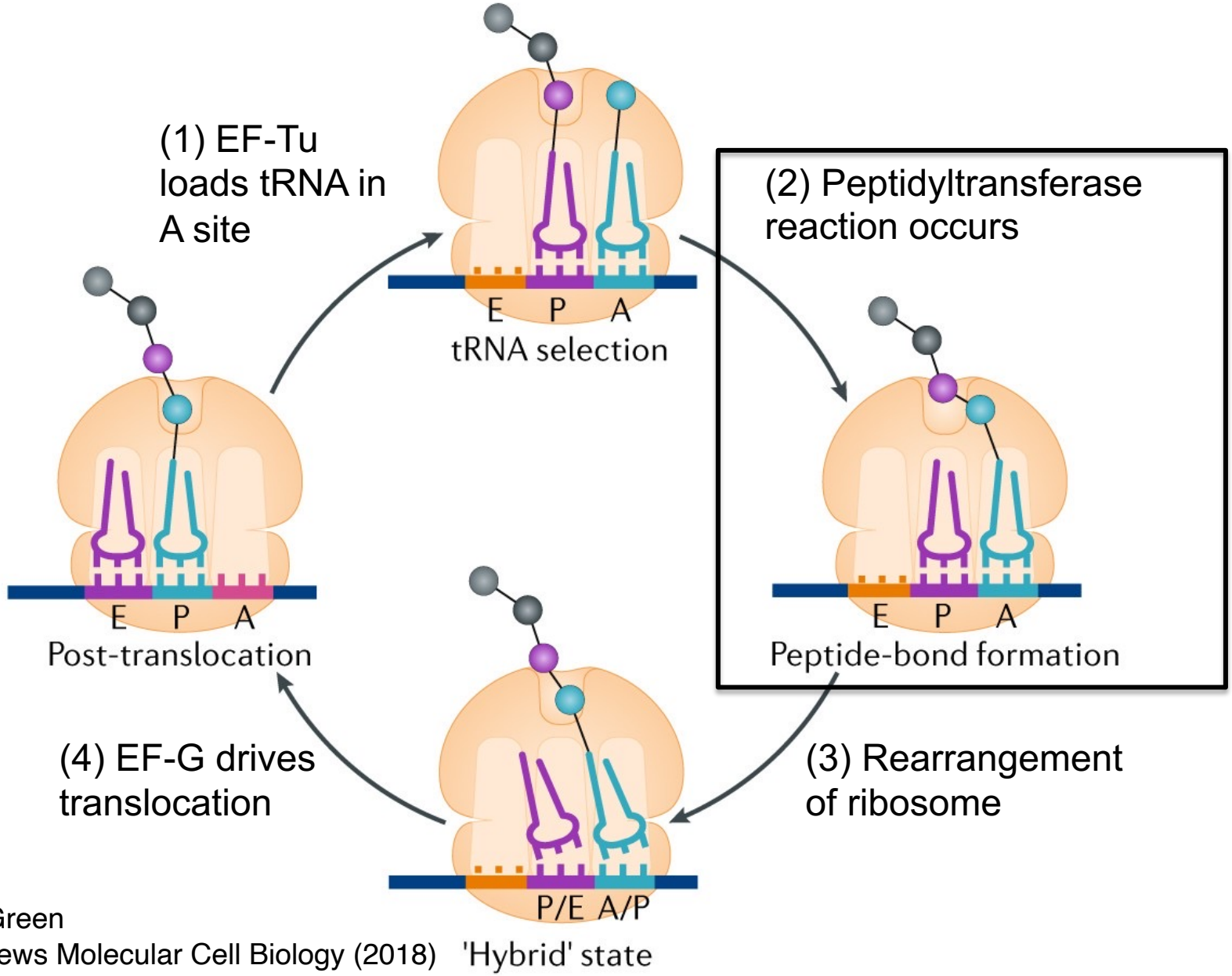
A A D — Minor groove

Fidelity of A-site codon/anticodon interaction is sensed numerous times in elongation (kinetic proofreading)



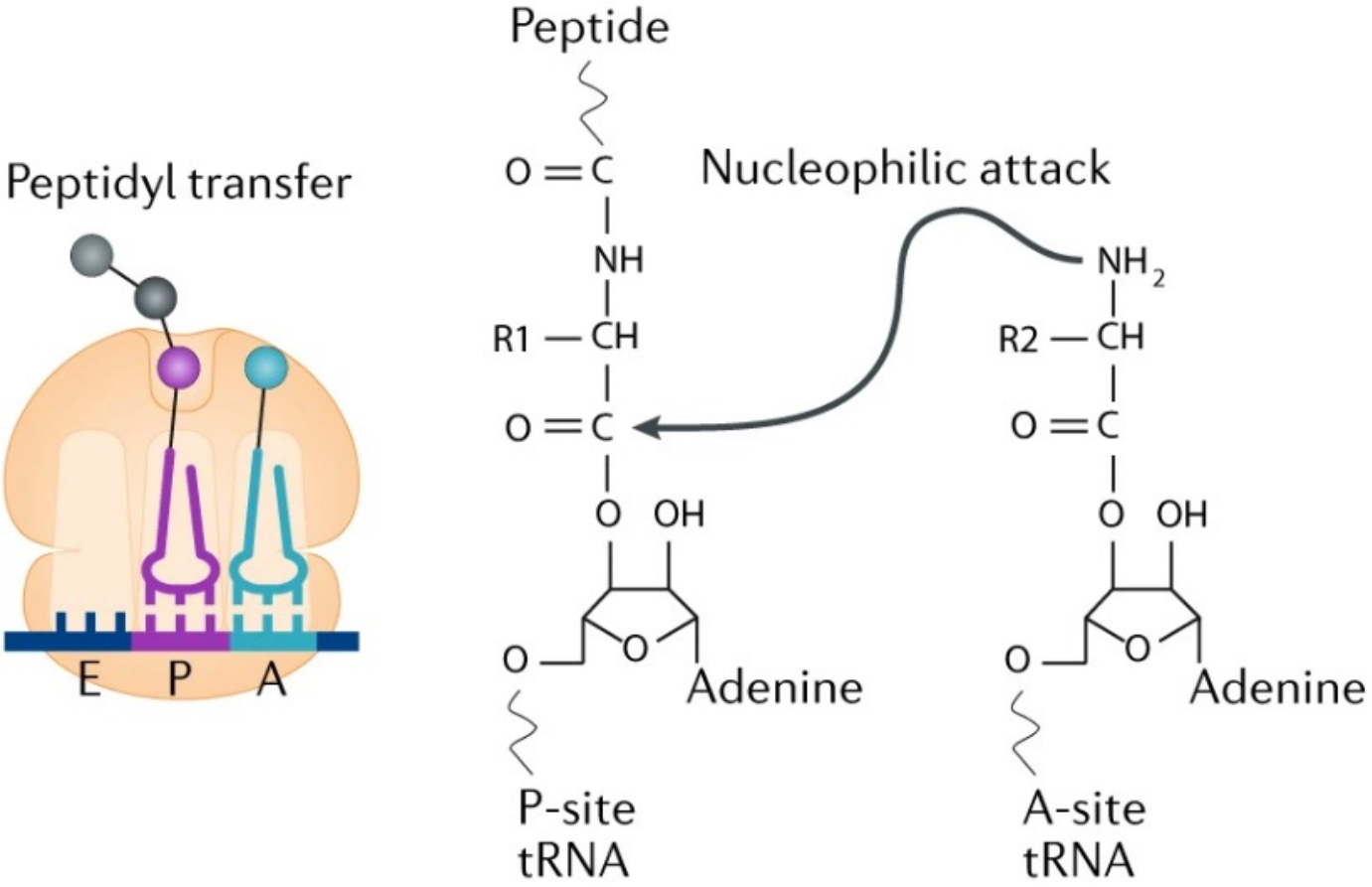
From Molecular Biology, Principles of Genome Function

Summary of translation elongation (similar in bacteria and eukaryotes, bacterial names shown)



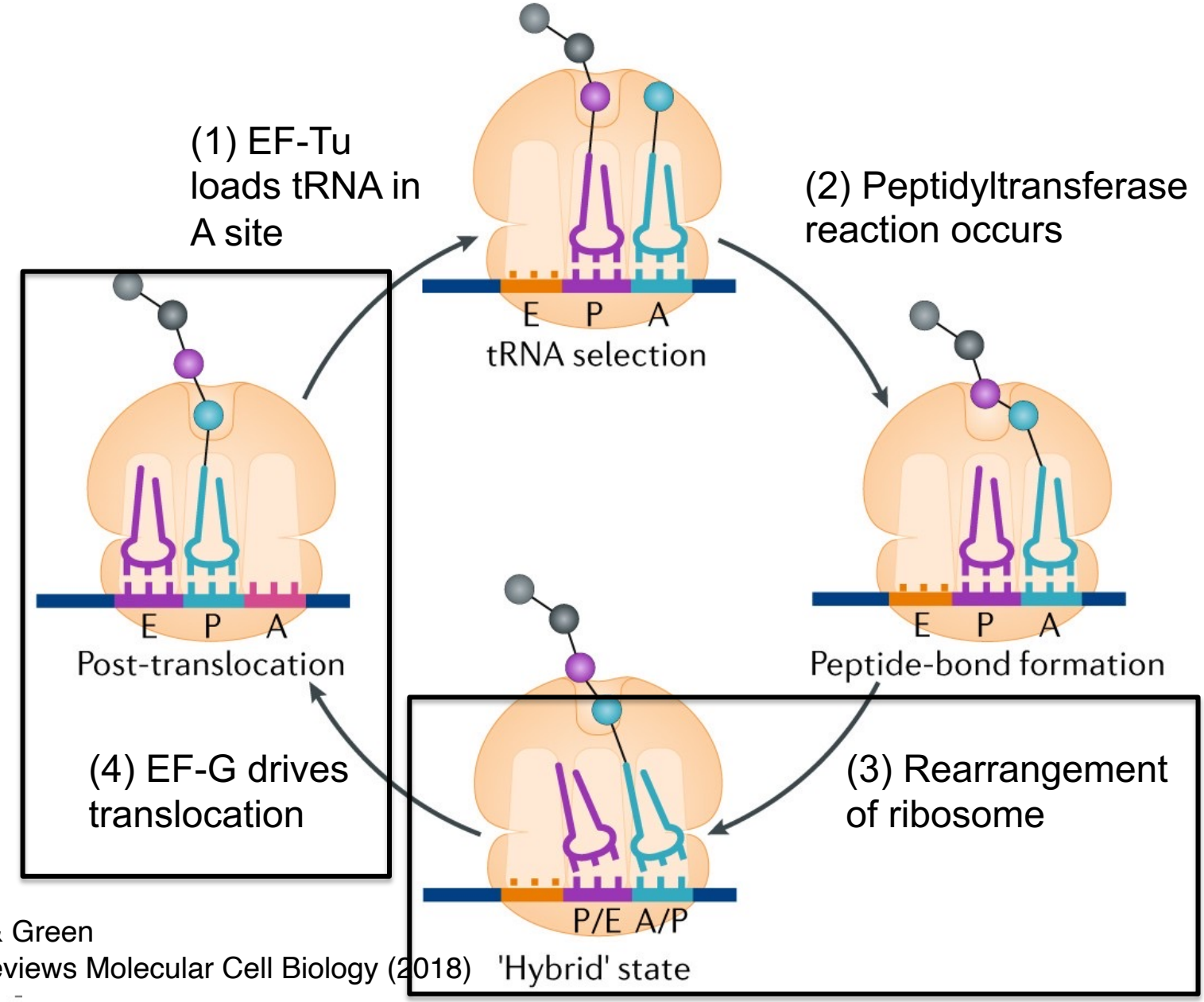
Schuller & Green
Nature Reviews Molecular Cell Biology (2018)

The peptidyl transferase reaction



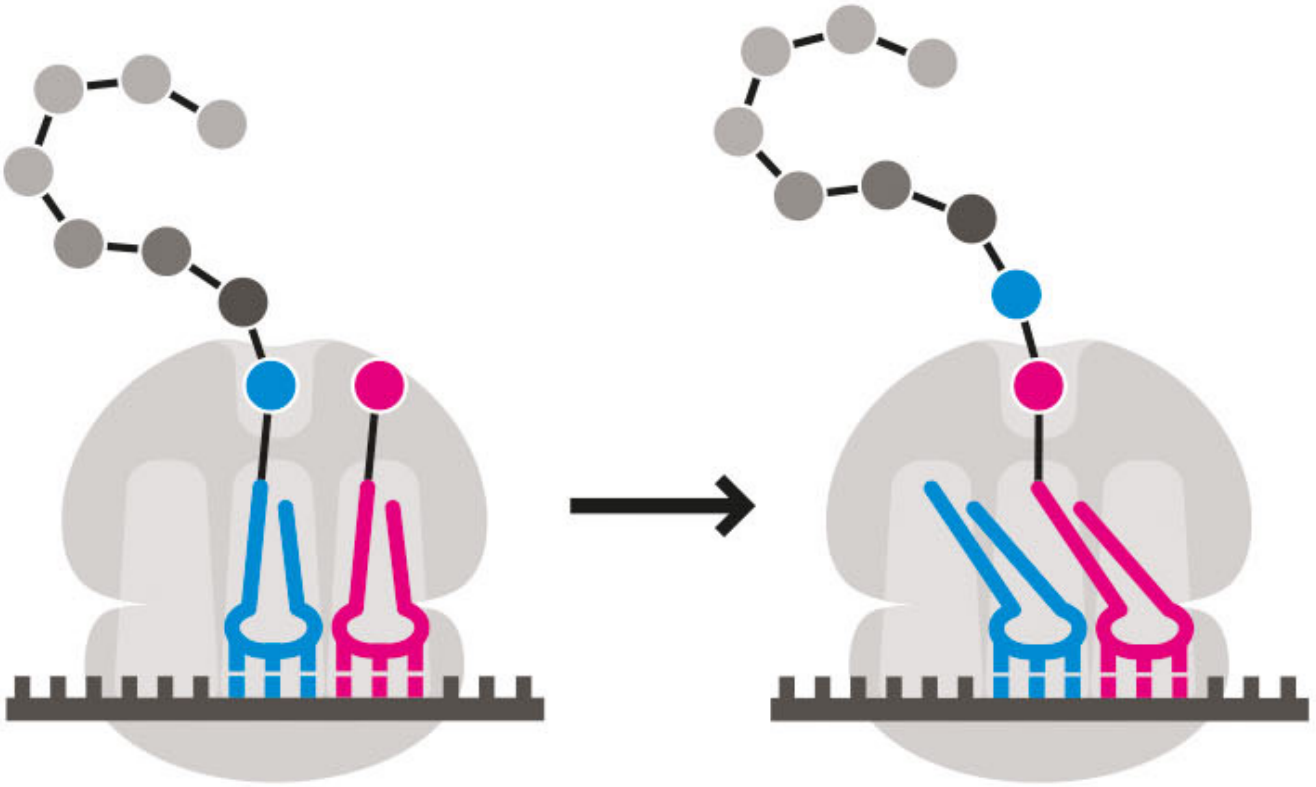
Schuller & Green
Nature Reviews Molecular Cell Biology (2018)

Summary of translation elongation (similar in bacteria and eukaryotes, bacterial names shown)



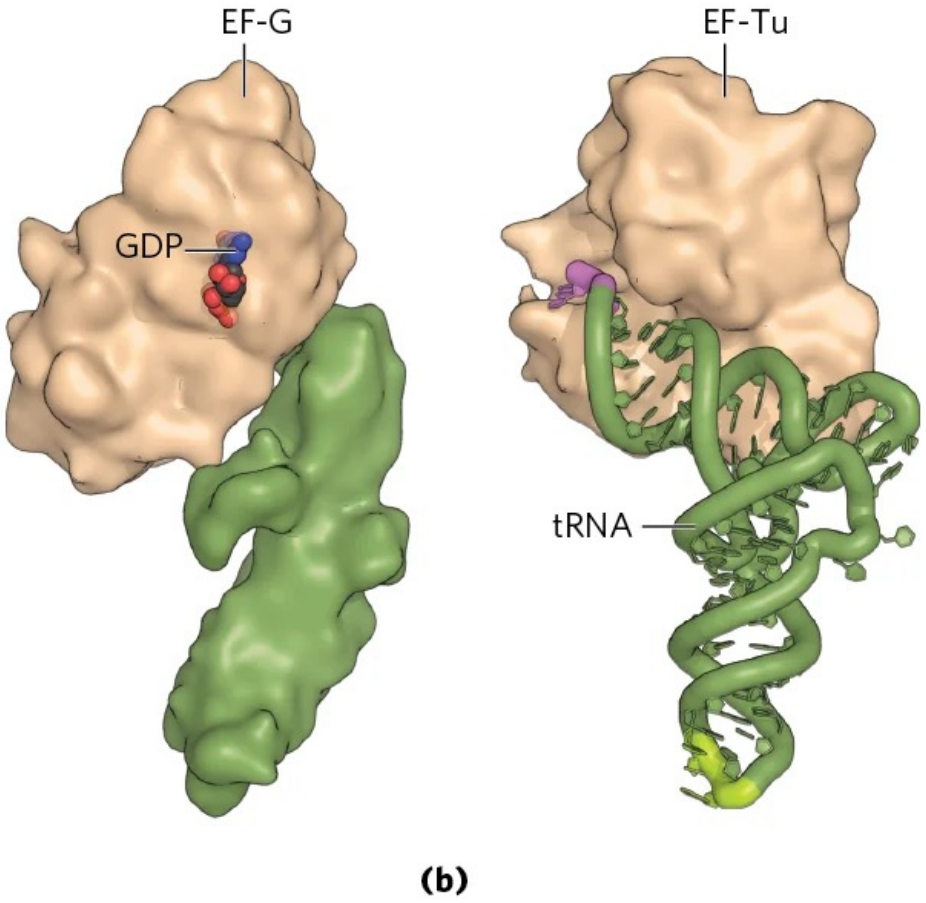
Schuller & Green
Nature Reviews Molecular Cell Biology (2018)

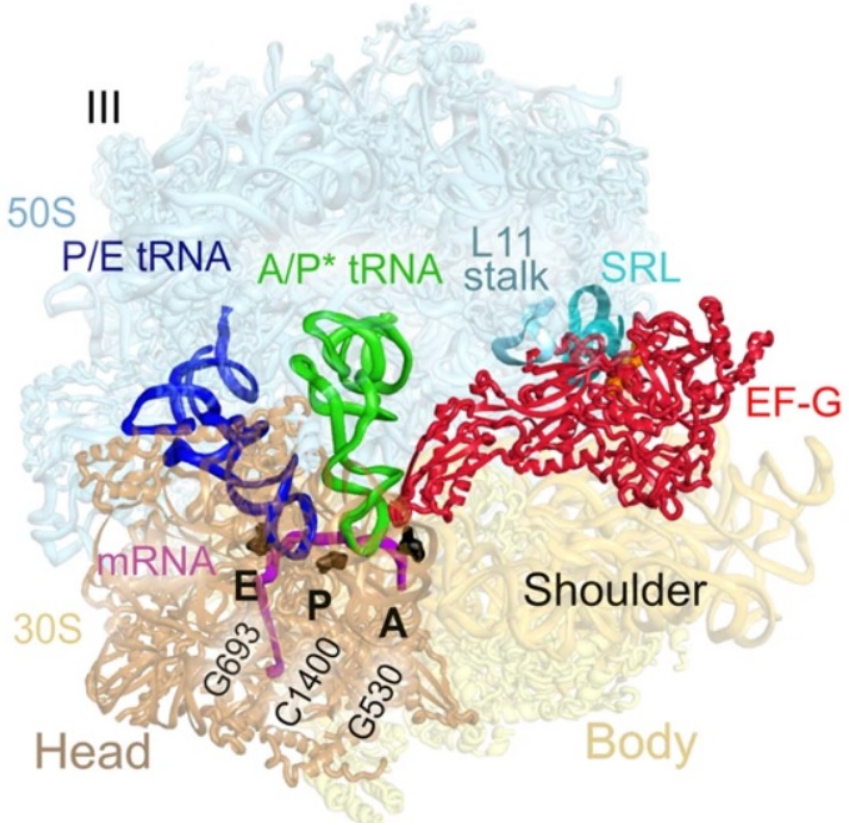
Rearrangement to the hybrid state occurs concurrently with peptide bond formation



EF-G drives translocation of tRNAs through the ribosome

EF-G is a GTPase that mimics a tRNA-EfTu complex, drives forward movement of tRNAs through ribosome





Termination of translation (figure shows bacterial factors)

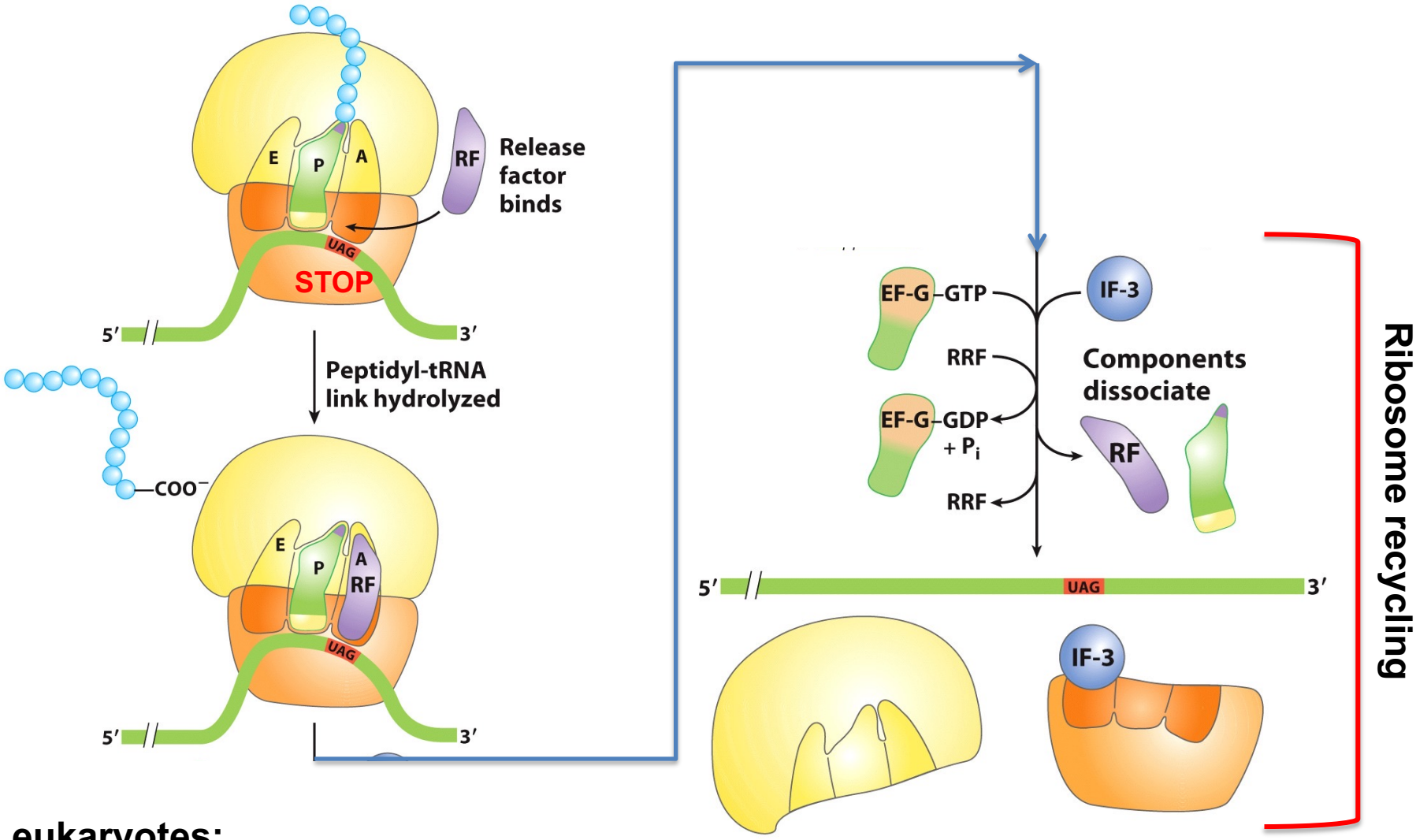
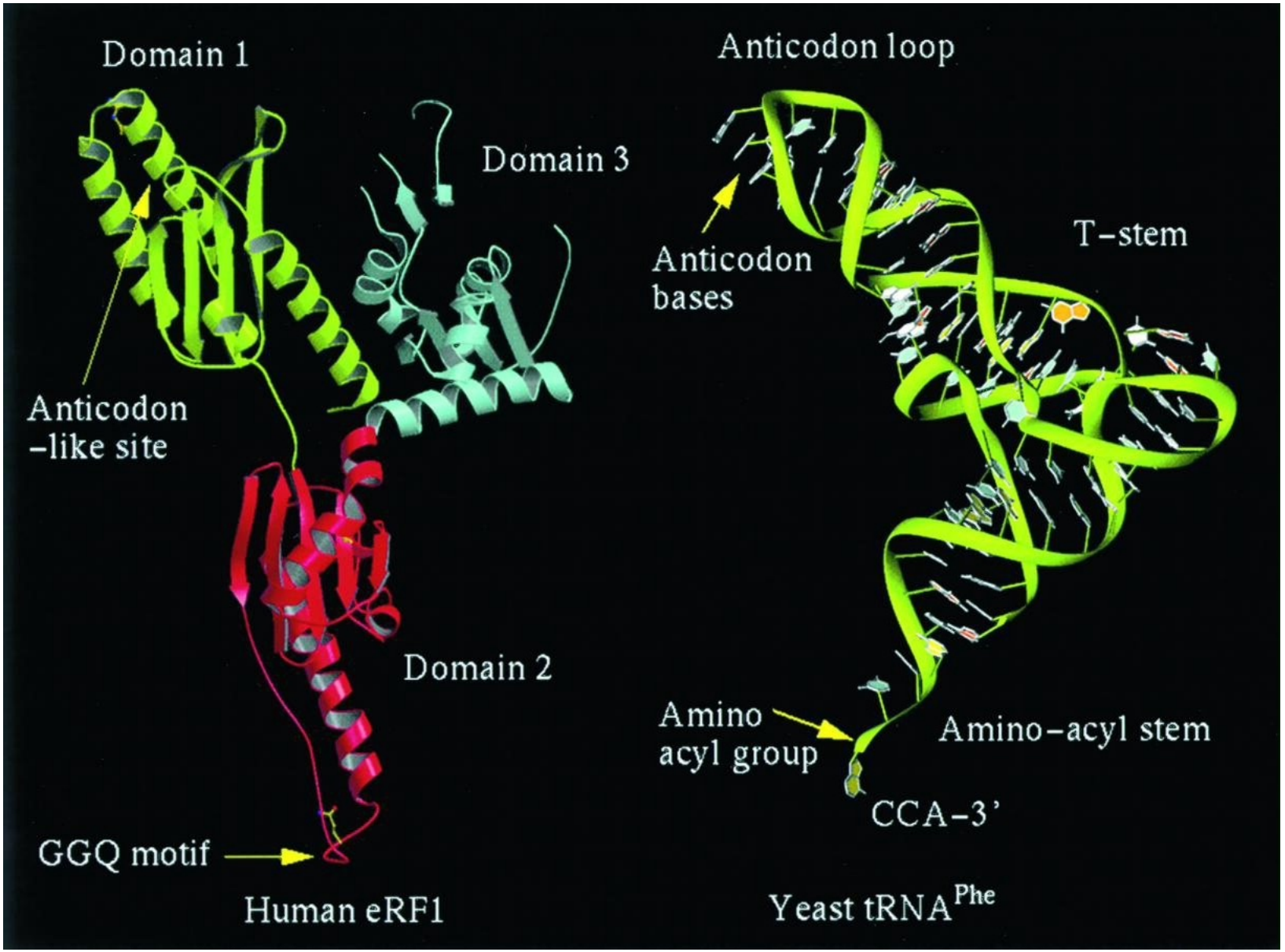


Figure 27-32
Lehninger Principles of Biochemistry, Sixth Edition

In eukaryotes:

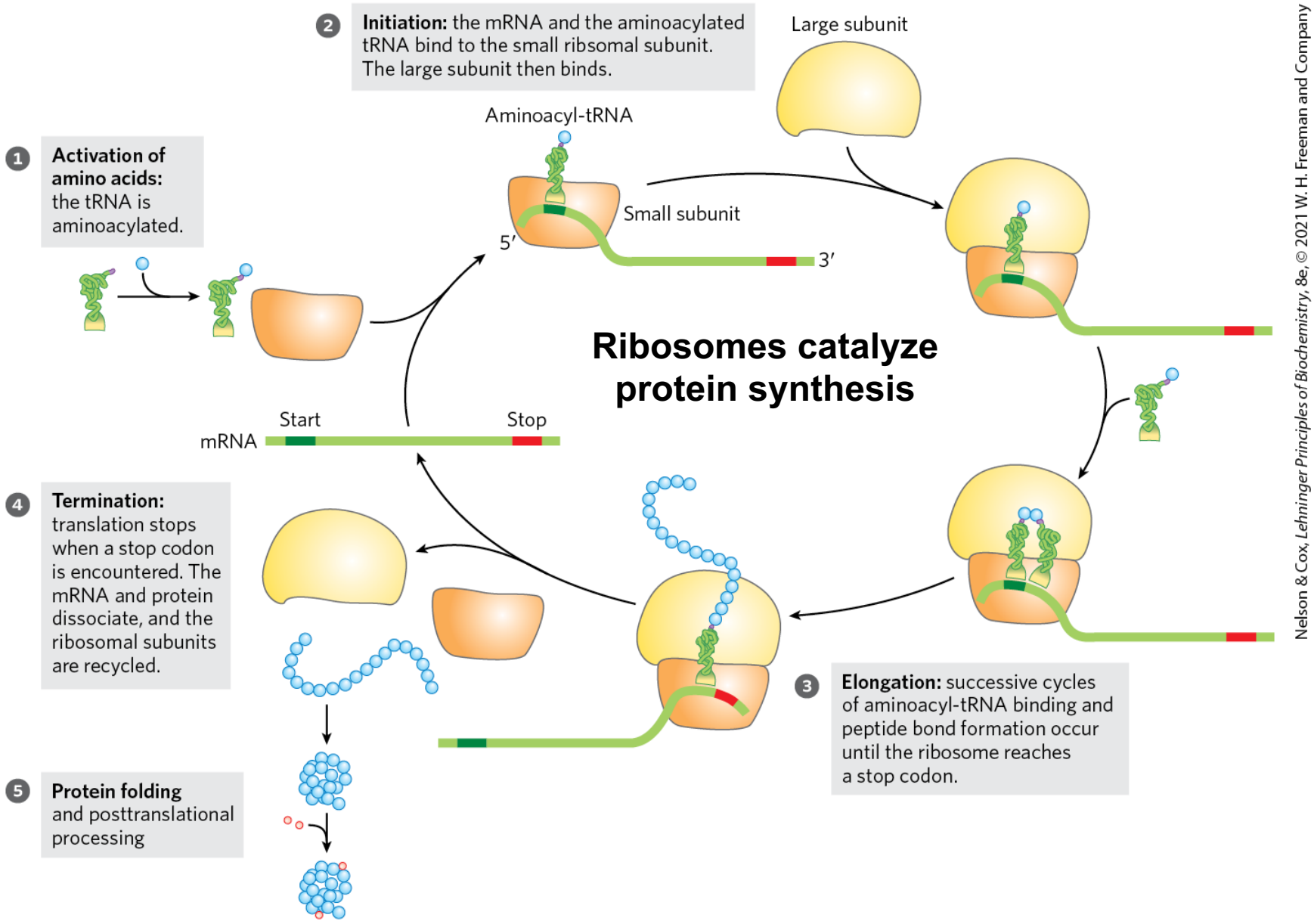
- **eRF1 catalyzes peptidyl-tRNA bond cleavage (hydrolysis reaction)**
- **eRF3 is a GTPase that assists eRF1**

eRF1 looks just like a tRNA!!



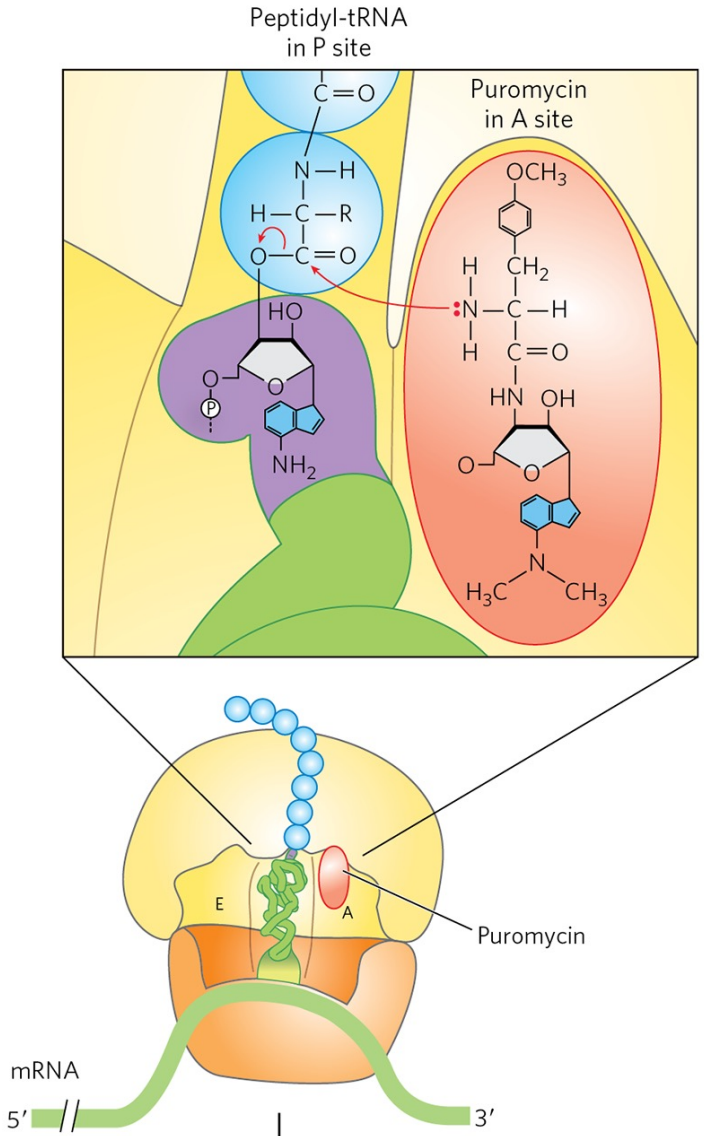
Song et al. Cell 2000

An overview of protein synthesis

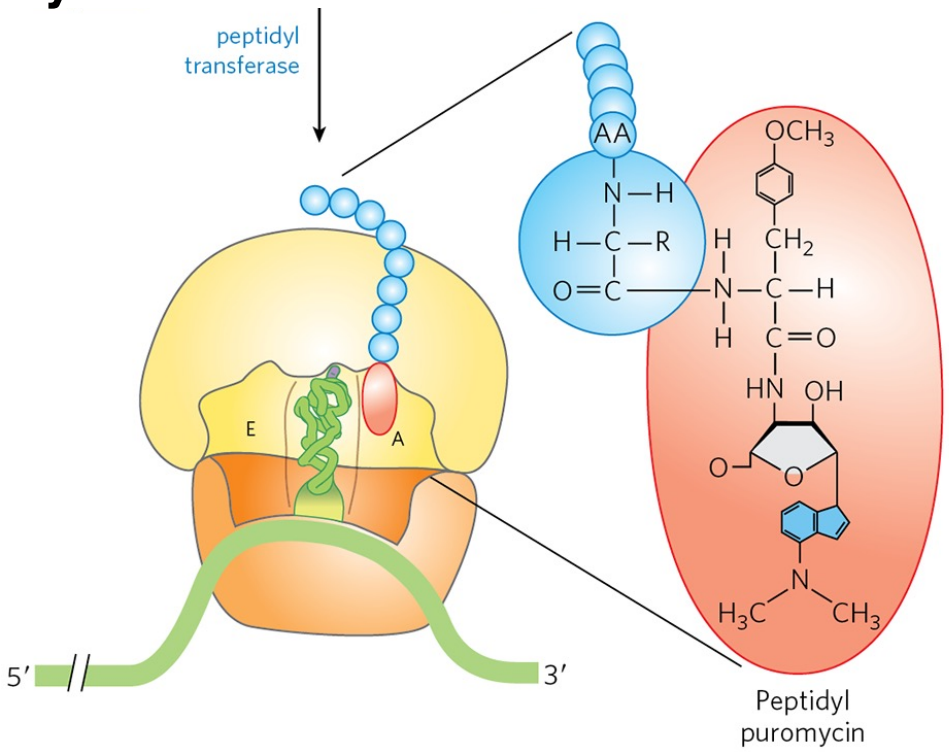


Many antibiotics inhibit bacterial translation

Puromycin is one of the best understood examples



- **Puromycin structure is very similar to the end of an aminoacyl-tRNA**
- **Puromycin binds in the A site & participates in peptide bond formation → peptidyl-tRNA**
- **Prematurely terminates polypeptide synthesis**



Mutation terminology

- **Missense mutation: mutation in the DNA that results in a change in the amino acid sequence of the protein**
- **Nonsense mutation: converts a codon into a stop codon**
- **Silent mutation: mutation in the DNA that does not alter the amino acid sequence of the protein**
- **Frameshift mutation: insertion or deletion that is not a multiple of 3 and thereby changes the reading frame**

Quality Control of Translation:

Quality control pathways prevent the accumulation of truncated or deficient proteins due to defects in mRNAs:

- truncated mRNAs (because of random breaks in RNAs)

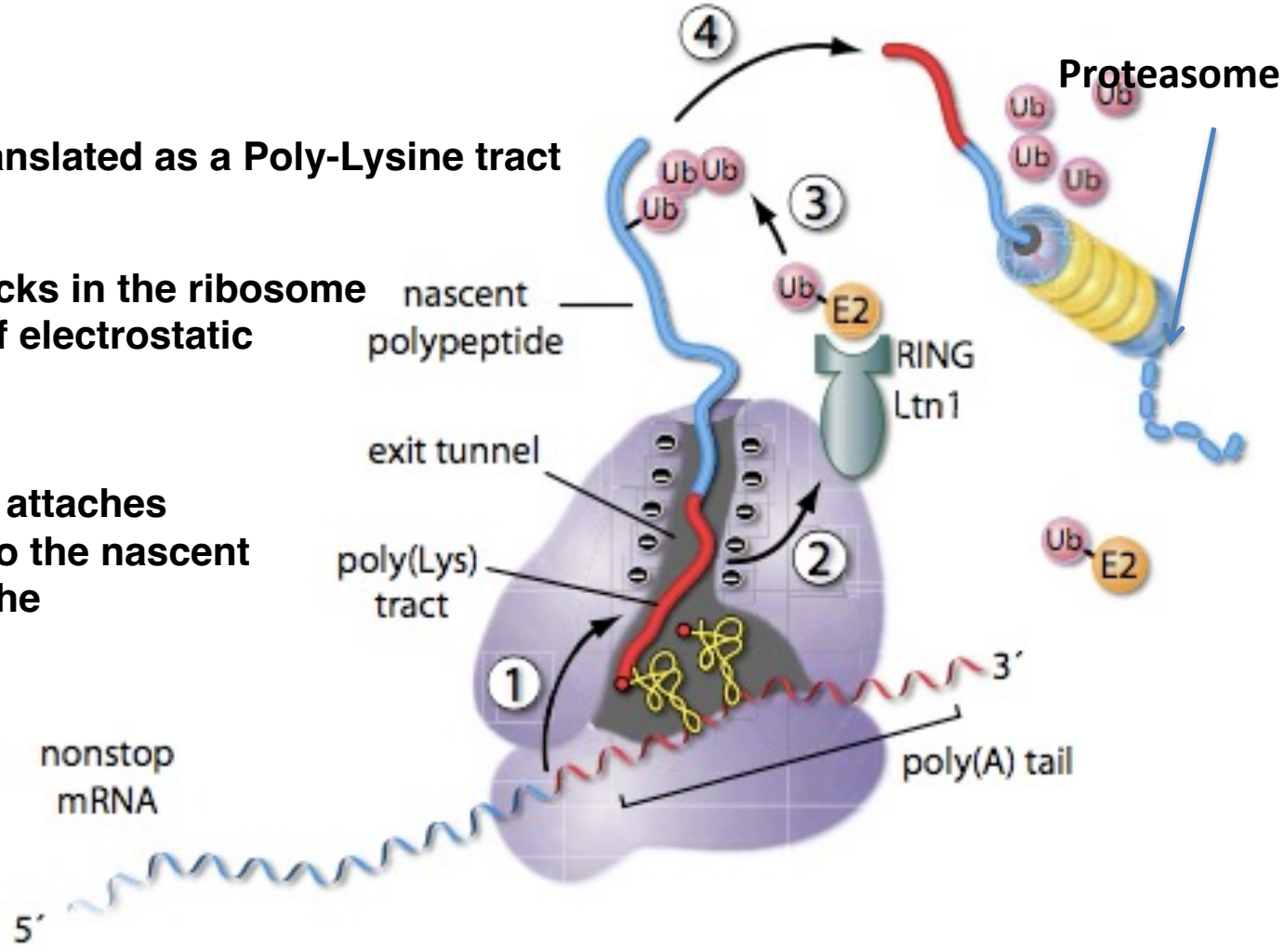
- mRNAs that do not contain stop codons (because of mistakes in the 3´-end processing reactions)

- mRNAs containing premature termination codons (gene mutations, errors made by RNA polymerase, or mistakes in splicing)

An example of translation QC in eukaryotes: "Nonstop" protein degradation in eukaryotes

Quality control of translation for “non-stop” mRNAs

- **Non-stop mRNAs can be generated if the poly(A) tail is added before the stop codons**
- **The Poly(A) tail is translated as a Poly-Lysine tract**
- **Poly-Lysine tract sticks in the ribosome exit tunnel because of electrostatic interactions**
- **Ltn1 ubiquitin ligase attaches polyubiquitin chains to the nascent polypeptide stuck to the ribosome**
- **This marks the aberrant protein for degradation by the proteasome**



Bengston & Joazeiro – Nature 2010 - doi: 10.1038/nature09371