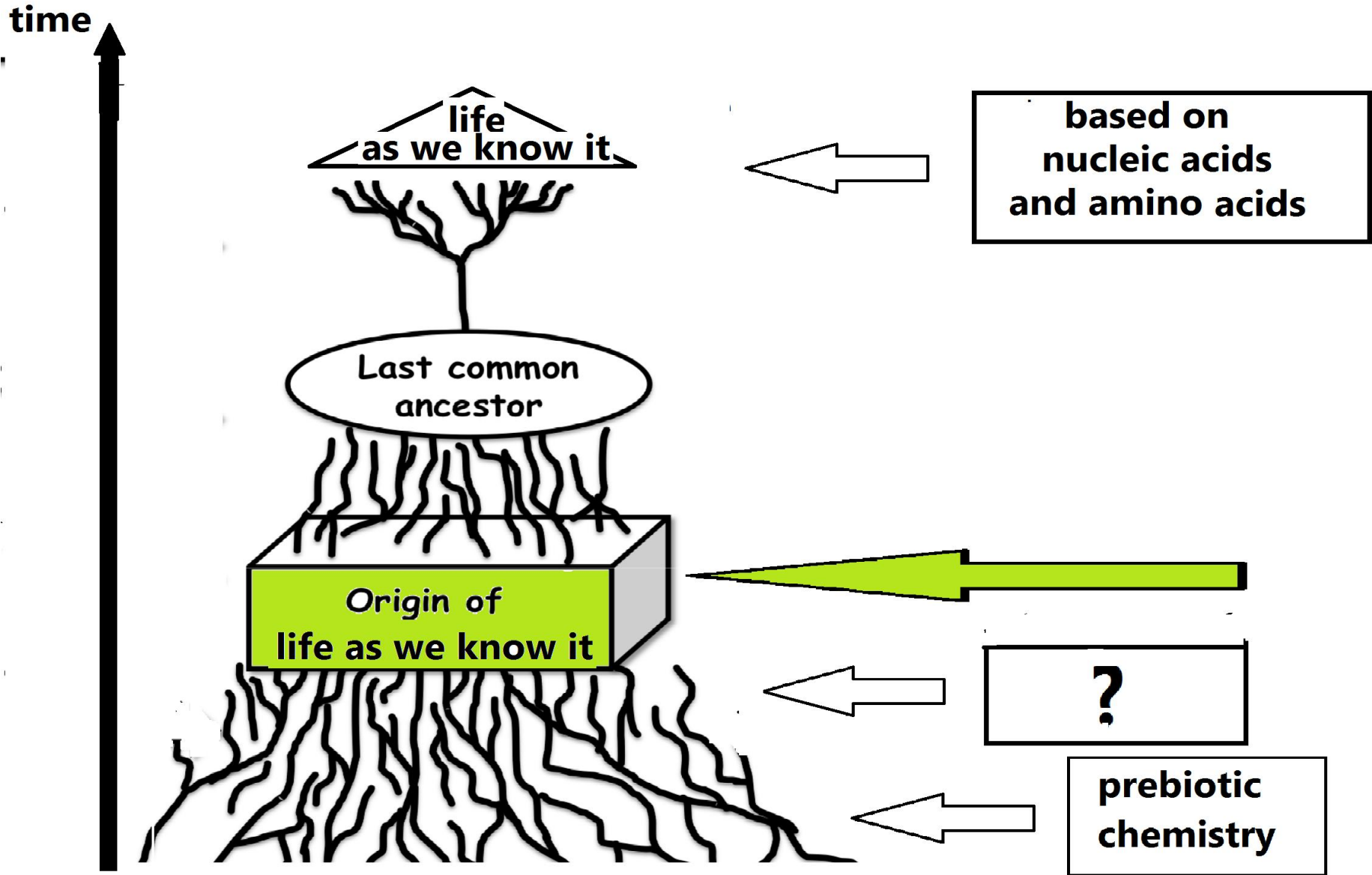
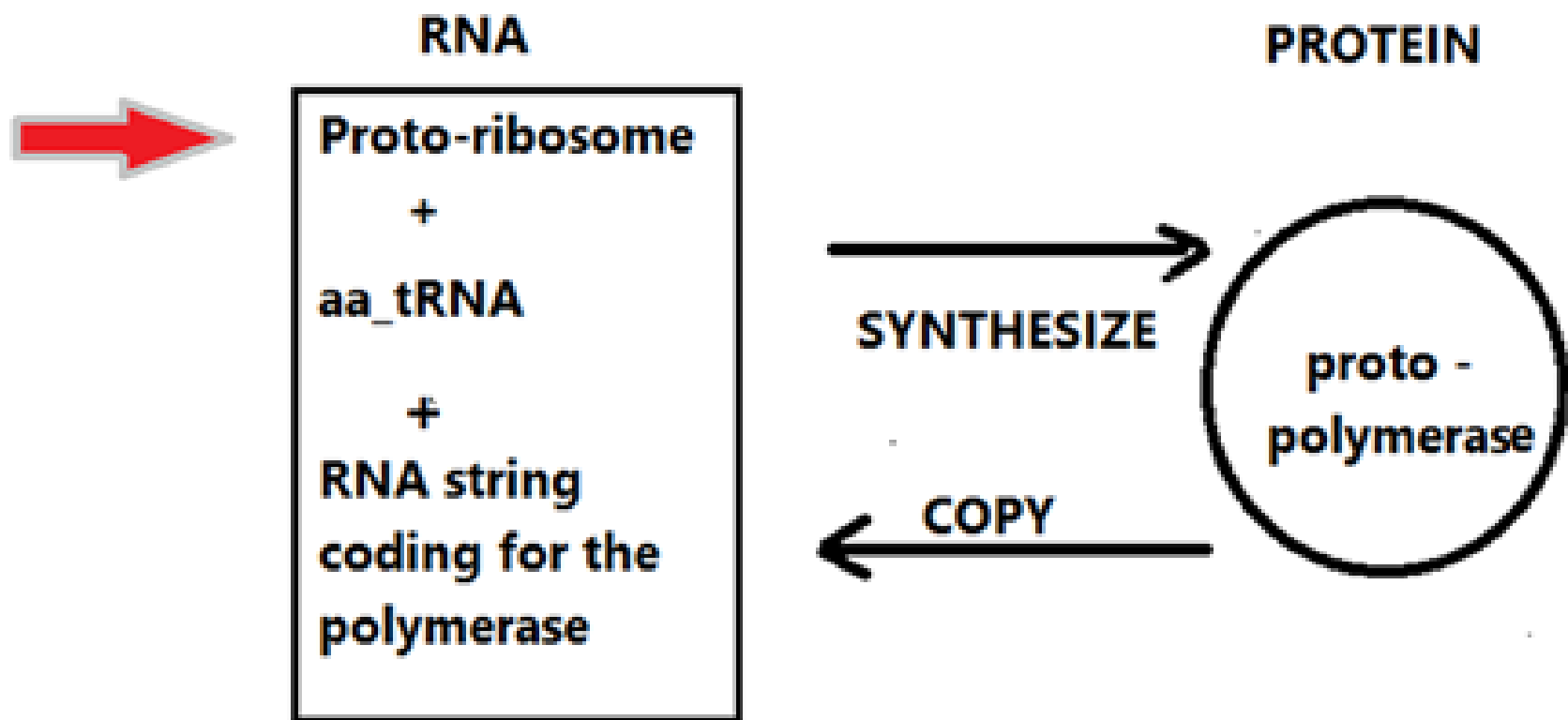


# **From the contemporary ribosome towards the origin of life**

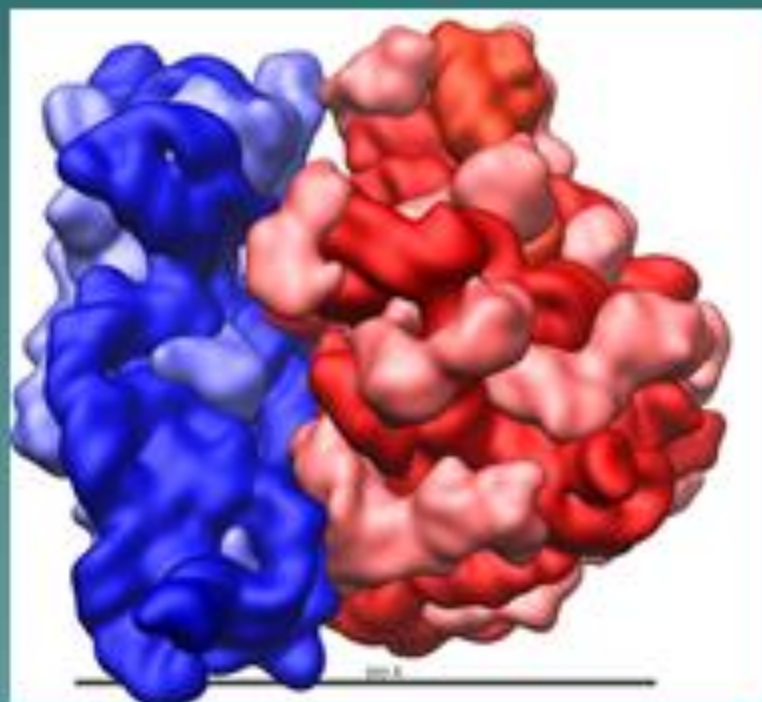
**Ilana Agmon, Technion**



# The minimal ACS (autocatalytic set) leading to life as we know it



## 70S ribosome from *E.coli*

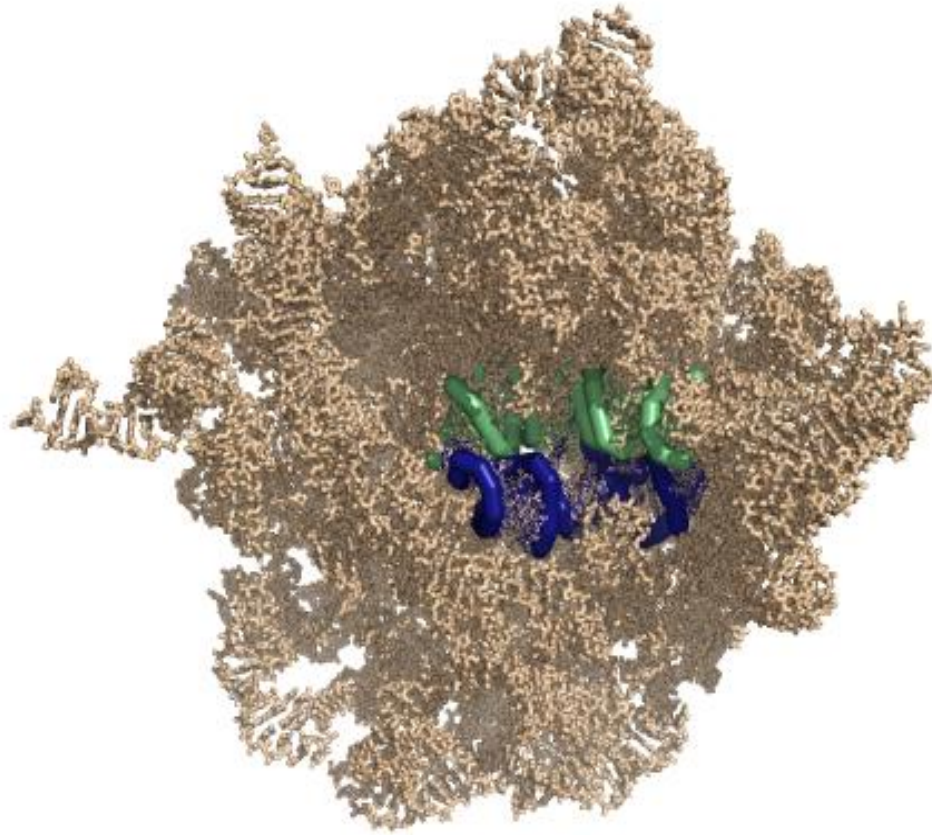


**Molecular Weight: 2.5 MD**

**LSU (50S): 2 RNA chains  
(~3000 nt), 34 proteins**

**SSU (30S): 1 RNA chain  
(~1500 nt), 21 proteins**

**65% RNA, 35% proteins**



Peptide bond formation takes place at the PTC, the active site of the large subunit, which is composed solely of RNA. It contains a 2-fold symmetry axis\*

\*Agmon I. et al, *biol. Chem* 2005

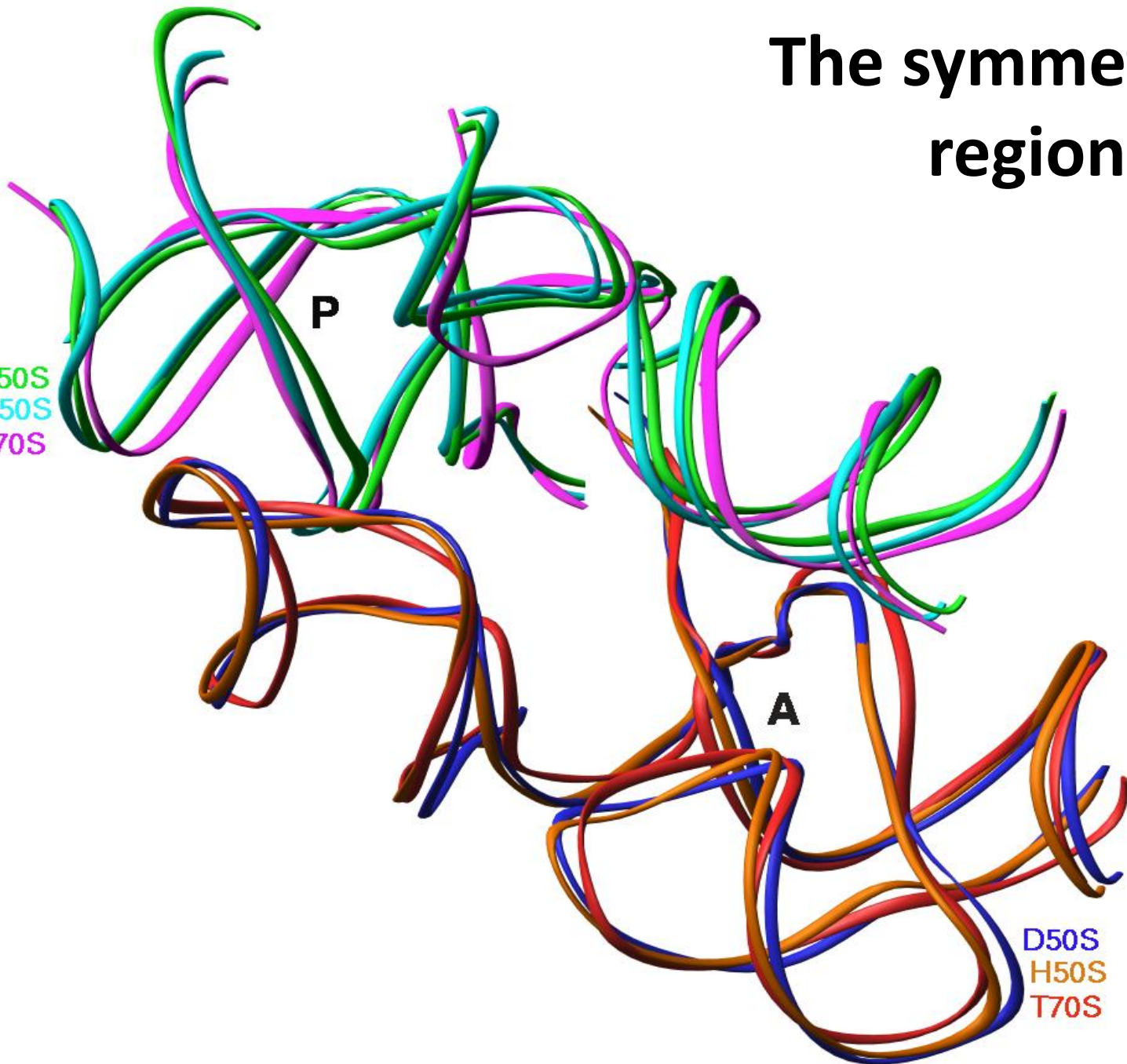
# The symmetrical region

D50S  
H50S  
T70S

P

A

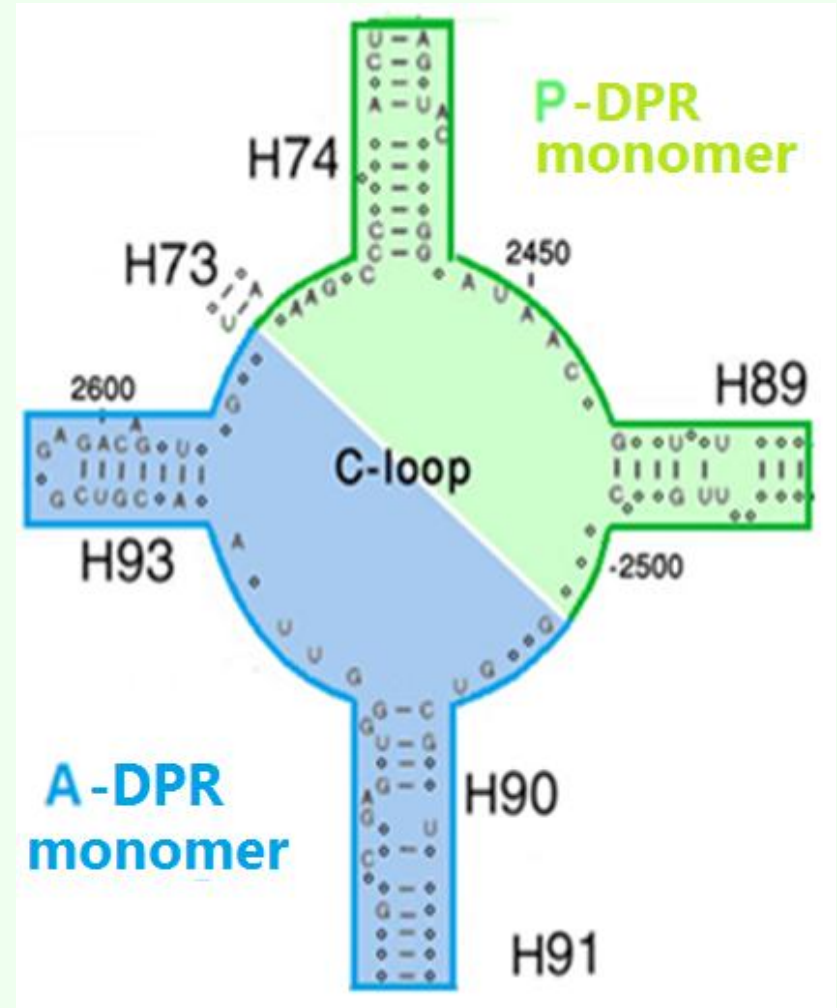
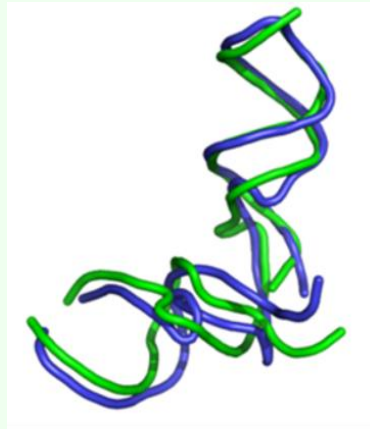
D50S  
H50S  
T70S



# The dimeric proto-ribosome



Catalyzes peptide bond formation between 2 random amino acids



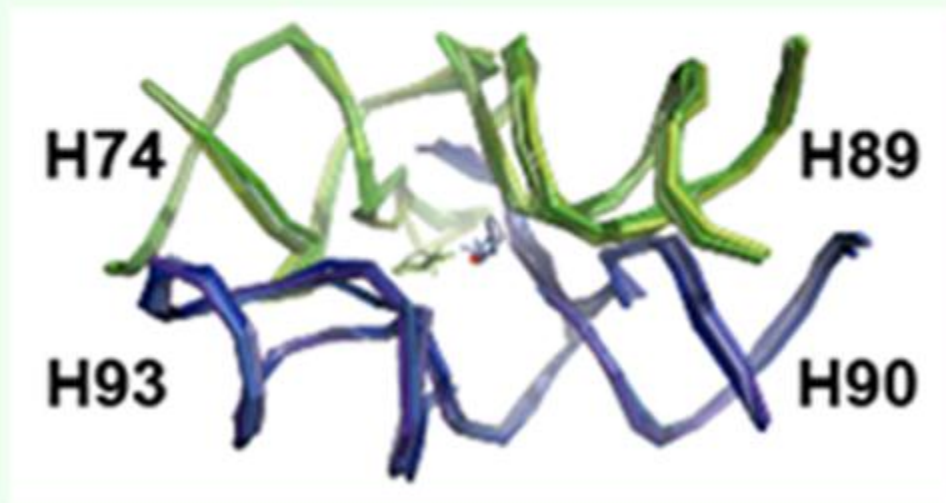
# The proto-ribosome

- It includes the site of peptide-bond formation.
- Its 3D structure is identical in the 3 life domains.
- The sequence of each monomer can fold spontaneously into an L-shaped monomer\* (Mfold\*\*).
- Its type of dimerization is energetically favorable\*\*\*.

\*Agmon I. IJMS 2009

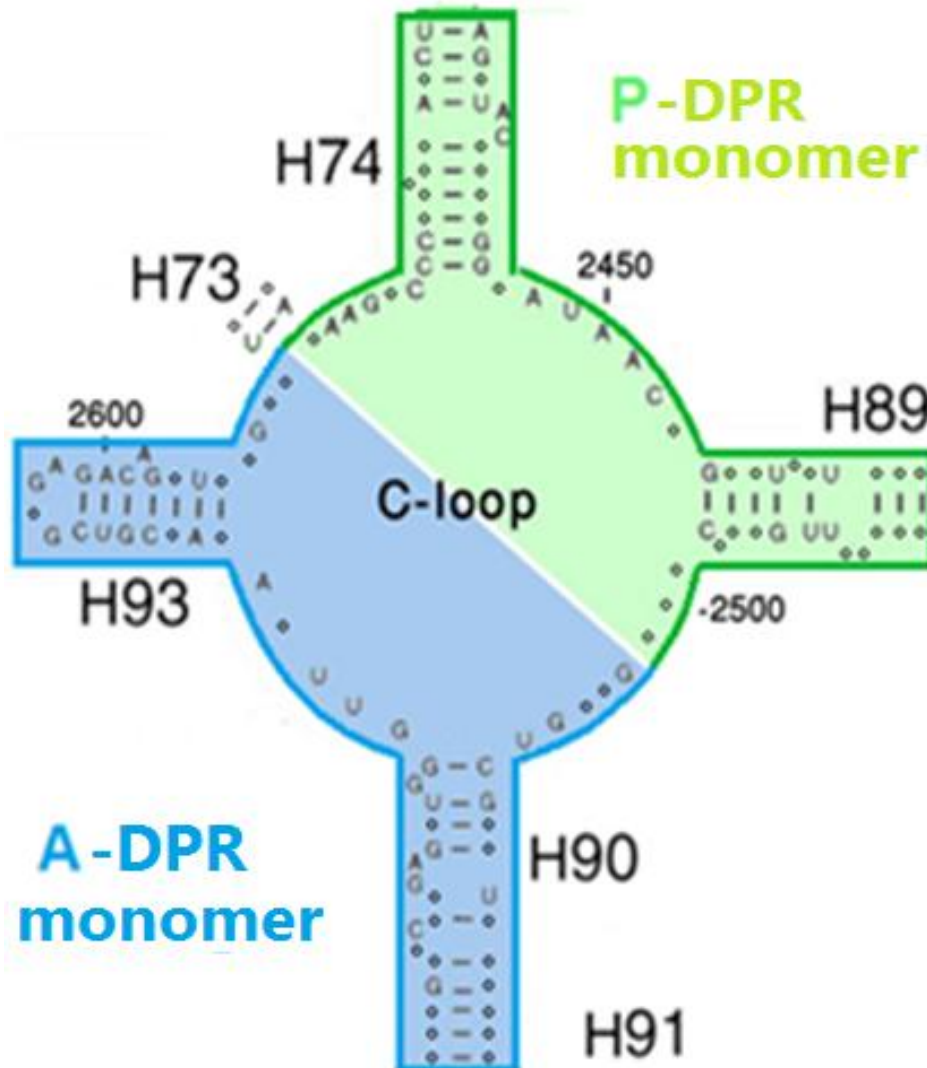
\*\*Zuker, M. NAR 2003

\*\*\*Davis, J.H. et al. J. Mol. Biol. 2005



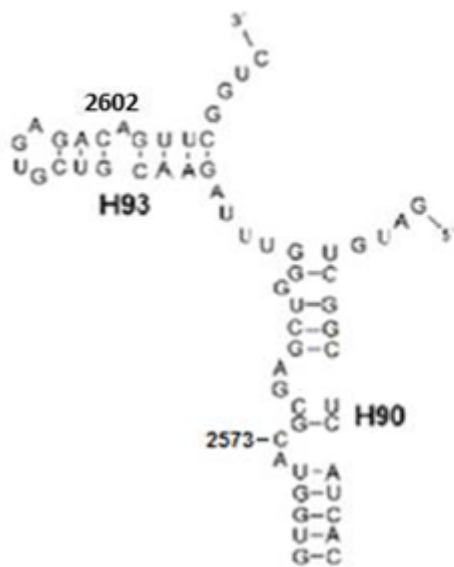


# Can a proper string occur randomly?

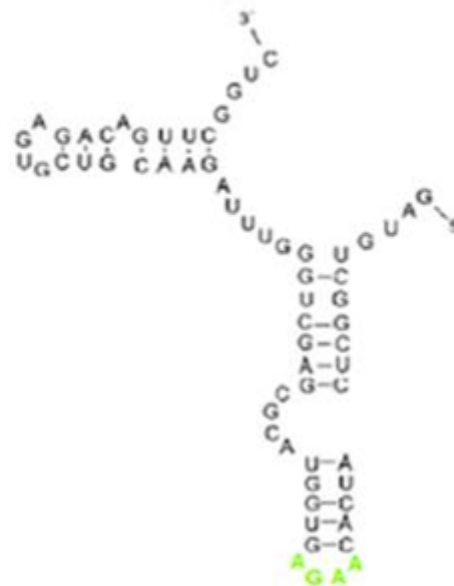


- Sequence requirements:
1. Fully conserved nucleotides should retain their type.
  2. Base-pairs should be retained

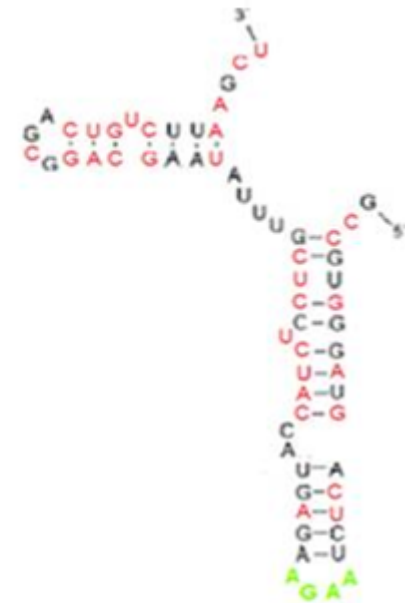
1 L of 1mM solution ~ 500 RNA oligonucleotides having sequences predisposed to form L-shaped monomers with dimerization affinity and conserved reactant accommodation position.



(a) A-DPR monomer as found in the modern ribosome of

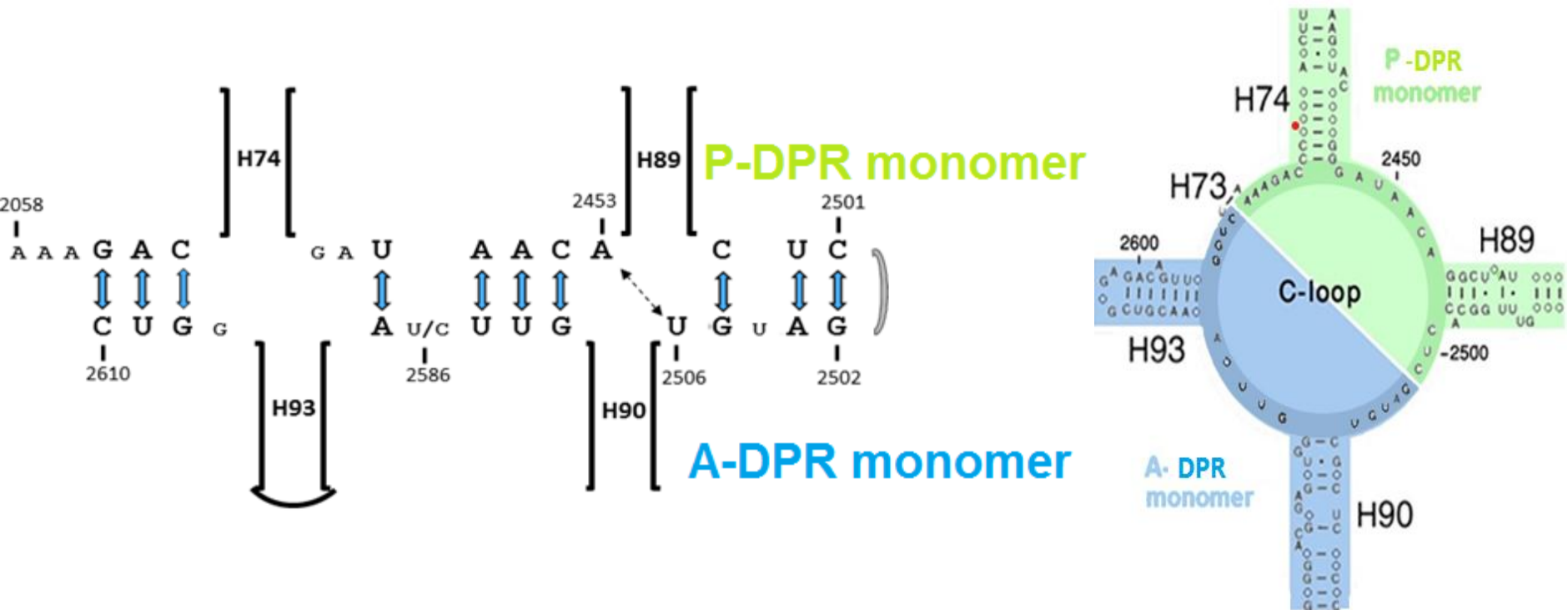


(b) A-DPR monomer as obtained from folding the sequence in (a) with mfold

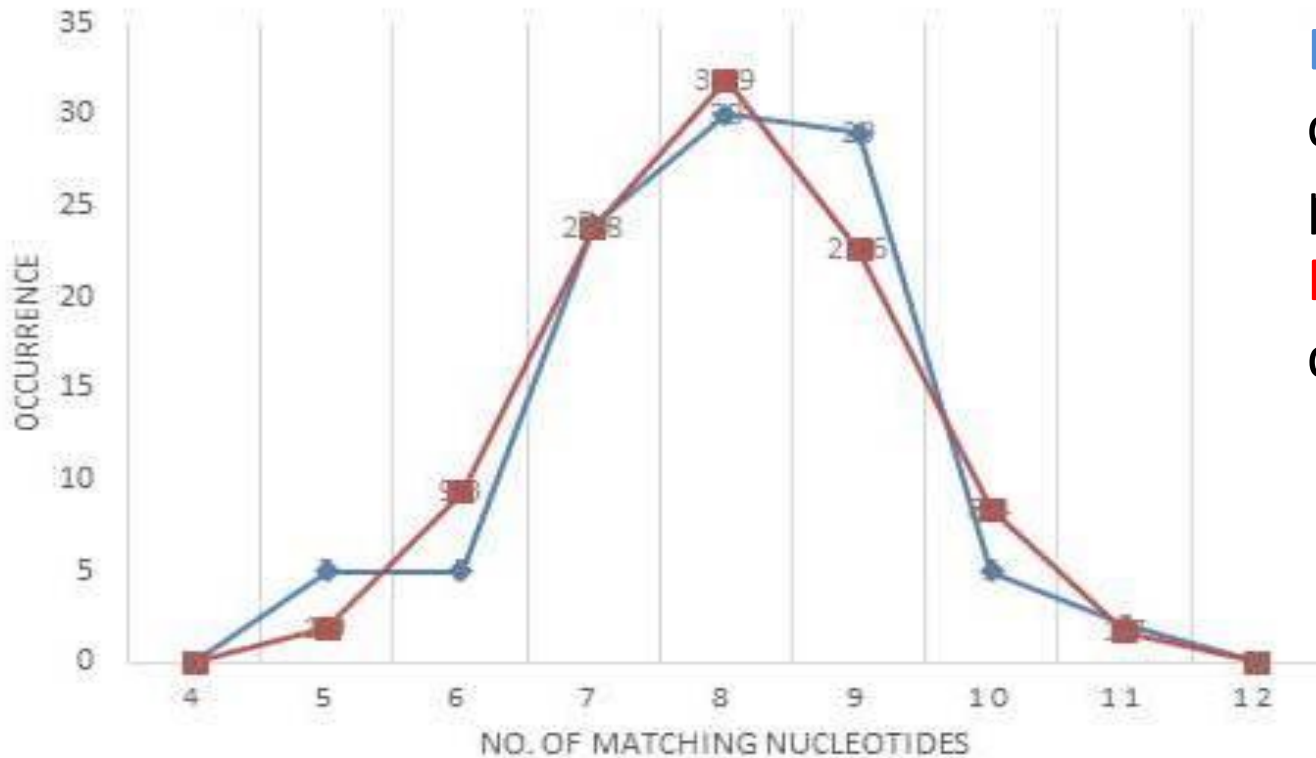


(c) Exchange of over 50% of the original sequence, while preserving the fully conserved nucleotides and base-pairing, results in an L-shaped molecule

# Plausible replication?



## COMPLEMENTARITY BENCHMARK



Blue- observed complementary pairs

Red-normal distribution

Sequence complementarity would have allowed the strand of each monomer to act as a template for the synthesis of its counterpart, forming a self-replicating ribozyme.

# The **dimeric proto-ribosome**:



- Highly conserved ✓
- Can catalyze peptide bond ✓
- Can materialize spontaneously from random RNA chains ✓
- Can be relatively easily replicated ✓



**The dimeric proto-ribosome offers a feasible starting point for the evolution of translation**

**Technion -**

Tal Mor

Yuval Elias

Itay Fayerverker

**WIS -**

Ada Yonath

Anat Bashan