



# Protein Structure

Andrés Becerra



# Theodosius Dobzhansky

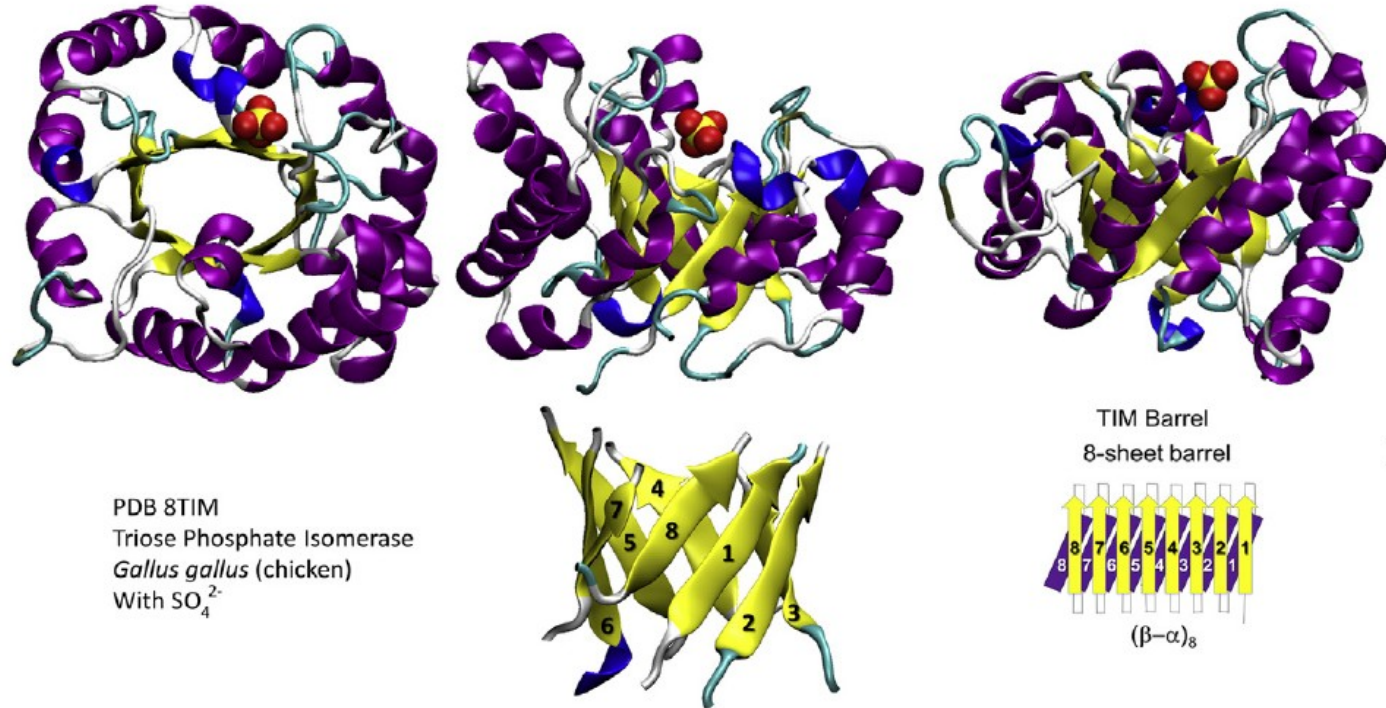
- ***"Nothing in Biology Makes Sense Except in the Light of Evolution"***
- is a 1973 essay published in American Biology Teacher



## Main source

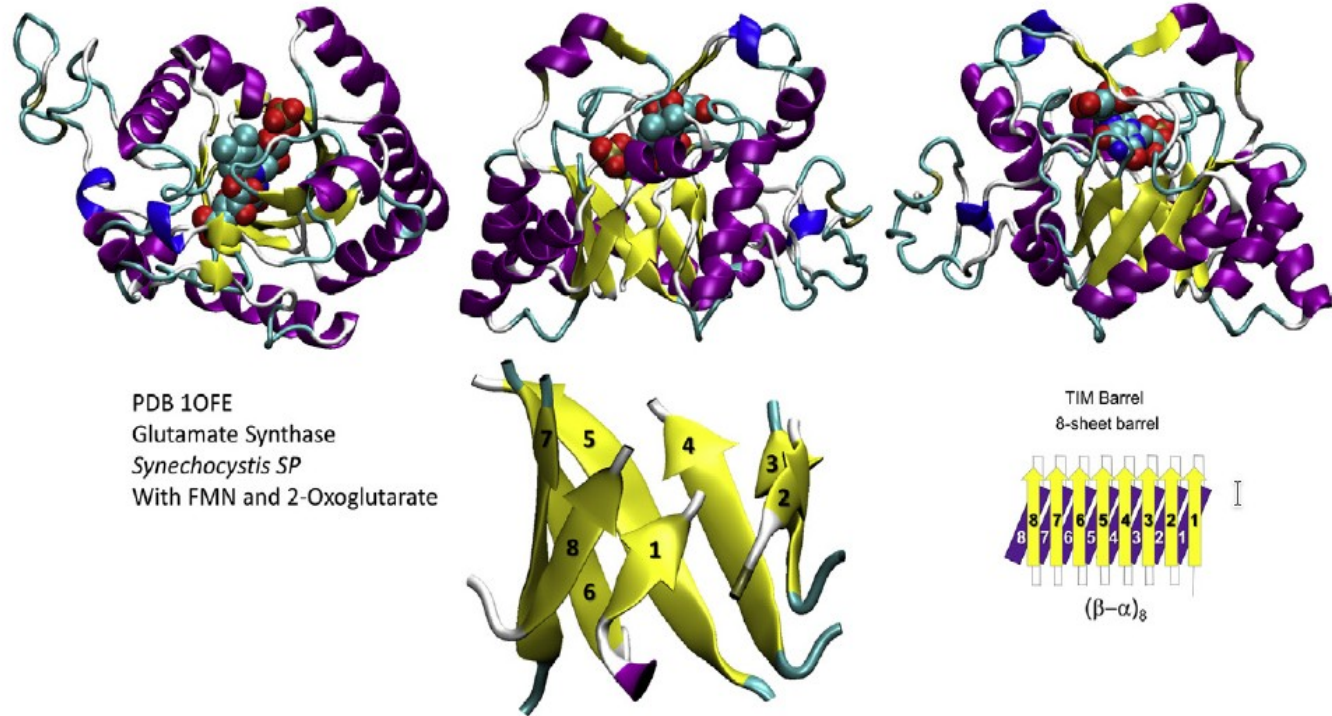
- Evolution since Coding. <http://dx.doi.org/10.1016/B978-0-12-813033-9.00013-5>
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# TIM Barrels



**FIGURE 11.2** A TIM barrel protein (PDB 8TIM): *Gallus gallus* (chicken) triose phosphate isomerase. Two views.  $\text{SO}_4^{2-}$  is a phosphate ( $\text{PO}_4^{2-}$ ) mimic to indicate the enzyme active site. So far as I know, active sites of TIM barrel enzymes always locate to the C-terminal end of the  $\beta$ -sheets.  $\beta$ -sheets (yellow arrows) and  $\alpha$ -helices (purple rectangles) are indicated.

# TIM Barrels



**FIGURE 11.3** A TIM barrel protein (PDB 1OFE): *Synechocystis* Sp. glutamate synthase, a cyanobacterial FMN-dependent oxidoreductase. Three views. FMN and 2-oxoglutarate are shown to indicate the enzyme active site.  $\beta$ -sheets (yellow arrows) and  $\alpha$ -helices (purple rectangles) are indicated.

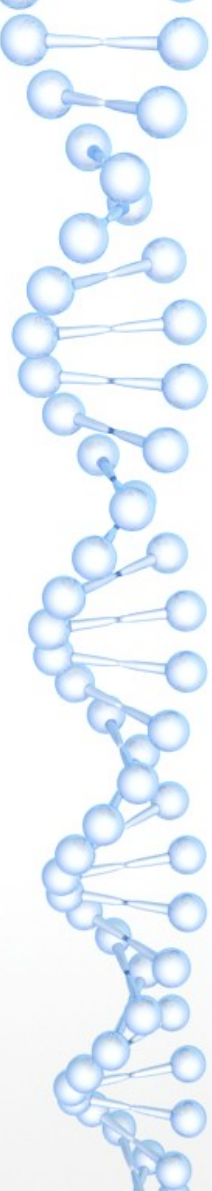


# TIM\_phosphate\_bind- ing\_superfamily

- NCBI Conserved Domain Database cl21457
- <https://www.ncbi.nlm.nih.gov/cdd/>



# Big Family



Genomic variance of the 2019-nCoV cor... CDD Conserved Protein Domain Family: TIM - Falkon

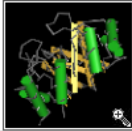
https://www.ncbi.nlm.nih.gov/cdd/ DuckDuckGo

## Conserved Protein Domain Family

### TIM

HOME SEARCH SITE MAP Entrez CDD Structure Protein Help

#### cl21457: TIM Superfamily ?

 **TIM-like beta/alpha barrel domains**  
A large family of domains similar to triose phosphate isomerase (TIM) which, in general, share an eight beta/alpha closed barrel structure.

**Links ?**

Taxonomy: [root](#)  
PubMed: [420 links](#)  
Book: [31 links](#)  
Protein: [Related Protein](#)  
[Related Structure](#)

**Statistics ?**

Accession: cl21457  
RSCMId: 389746

**Superfamily ?**

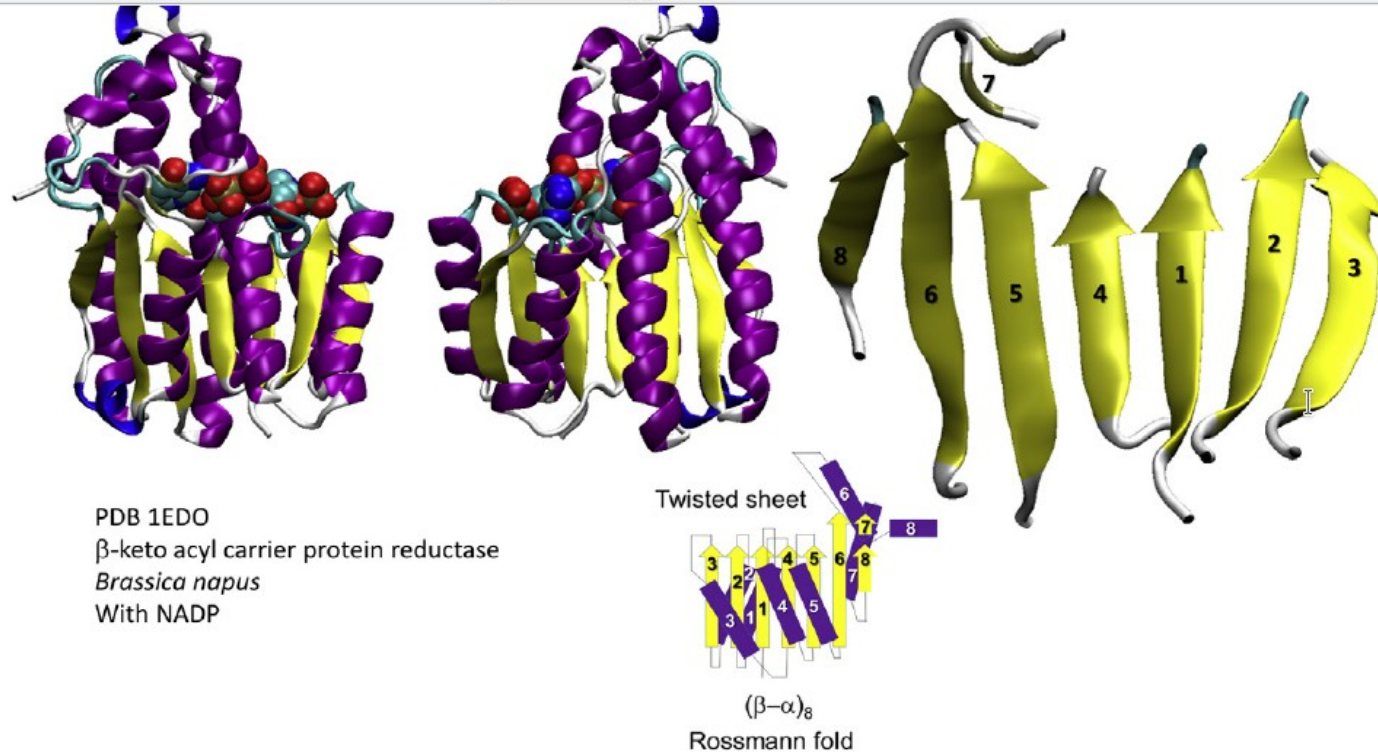
**Curated CD ?**

cd04722	cd03174	cd00945	cd00308
cd00453	cd00516		

**Imported CD ?**

pfam04481	TIGR00343	TIGR00419	TIGR00674
TIGR00736	TIGR00742	TIGR00875	TIGR00876
TIGR01232	TIGR01520	TIGR01521	TIGR01769
TIGR01858	TIGR01859	TIGR02134	TIGR02313
TIGR02317	TIGR02319	TIGR02321	TIGR02708

# Rossmann Folds



**FIGURE 11.5** A Rossmann-fold protein (PDB 1EDO):  $\beta$ -keto-acyl carrier protein reductase, a plant NADP-dependent oxidoreductase. NADP is located at the active site, at the C-terminal end of the  $\beta$ -sheets.

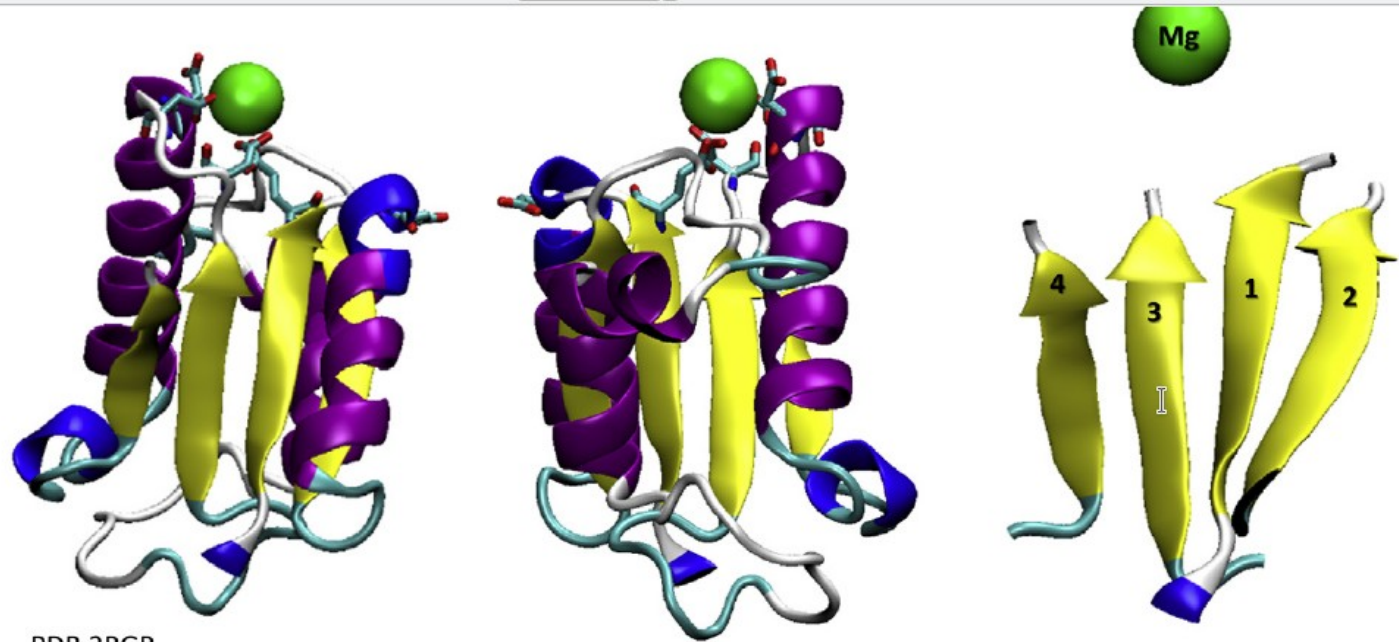




# SDR (short-chain dehydrogenases/reductases) Superfamily

- <https://www.ncbi.nlm.nih.gov/Structure/cdd/cddsrv.cgi?uid=389744>

# TOPRIM Folds

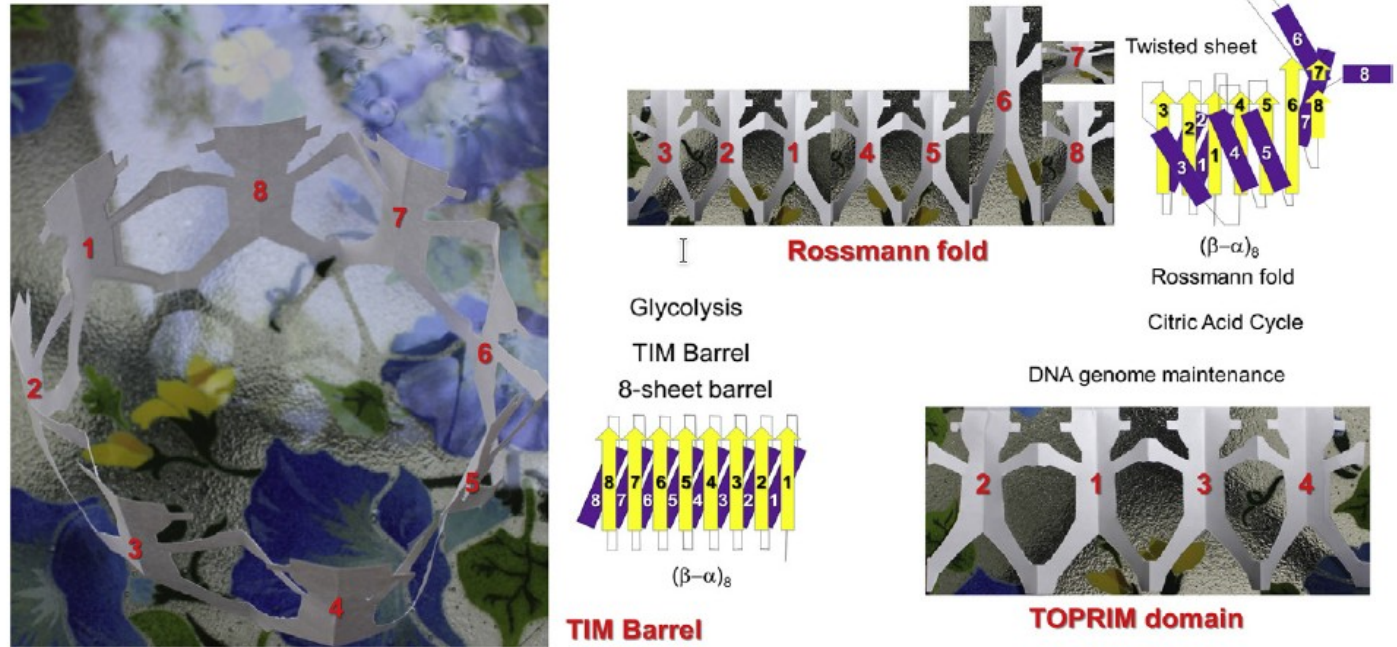


PDB 2RGR  
DNA topoisomerase IIA  
DNA gyrase type  
TOPRIM domain  
*Saccharomyces cerevisiae*

**FIGURE 11.6** A TOPRIM domain. PDB 2RGR is shown.  $\beta$ -sheets (yellow arrows) and  $\alpha$ -helices (purple rectangles) are indicated. The chelated  $Mg^{2+}$  forms part of the topoisomerase active site. The TOPRIM fold appears to be a simplified version of a Rossmann fold.

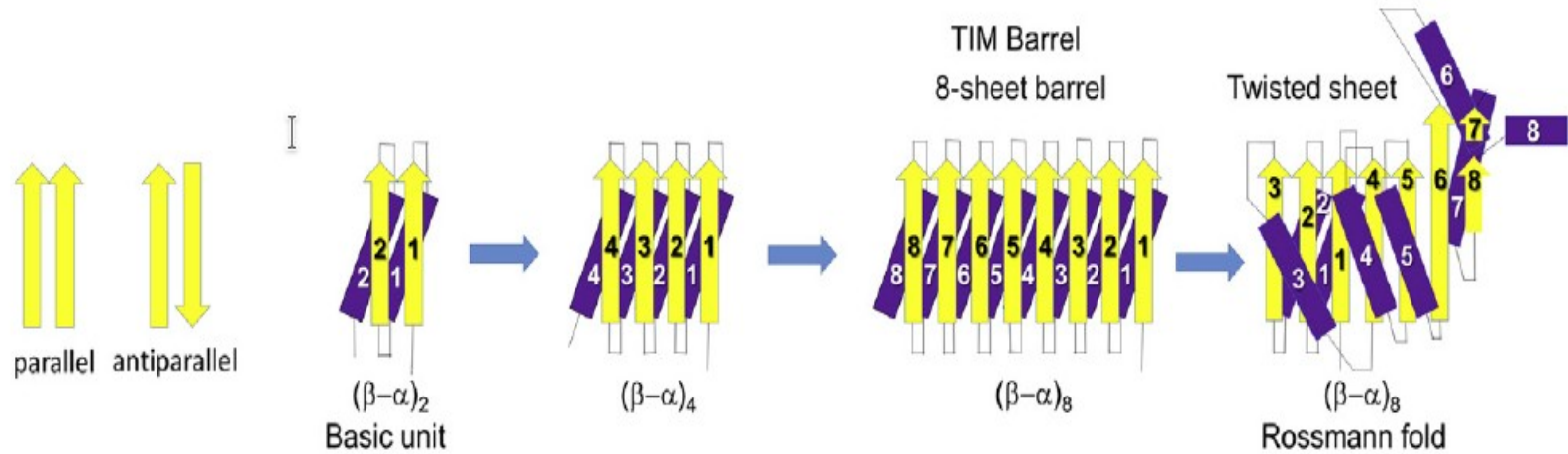
# Cutting Dolls

$\alpha/\beta$  Proteins Chapter | 11 43



**FIGURE 11.12** Ancient  $(\beta-\alpha)_n$  repeat proteins modeled as cutout dolls with  $\beta$ -sheets numbered according to their order in the polypeptide chain.

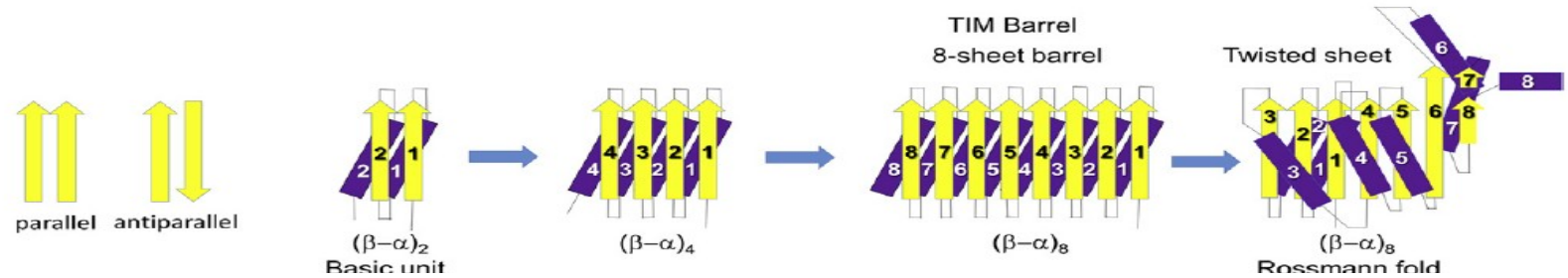
# Folds Structure



**FIGURE 11.1** TIM barrels and Rossmann folds comprise some of the oldest and most enduring enzymes. TIM barrels and Rossmann folds are generated from repetition of a  $\beta$ - $\alpha$ - $\beta$ - $\alpha$  unit.  $\beta$ -sheets (yellow arrows) and  $\alpha$ -helices (purple rectangles) are indicated.  $\beta$ -sheets can be either parallel or antiparallel. In  $(\beta-\alpha)_n$  repeat proteins, the primary fold includes only parallel  $\beta$ -sheets.

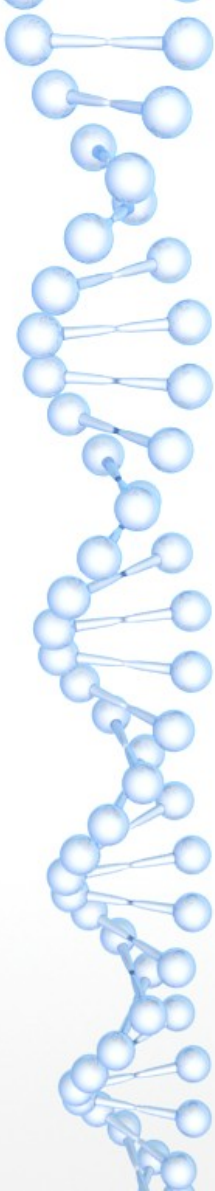


# Ancient Folds

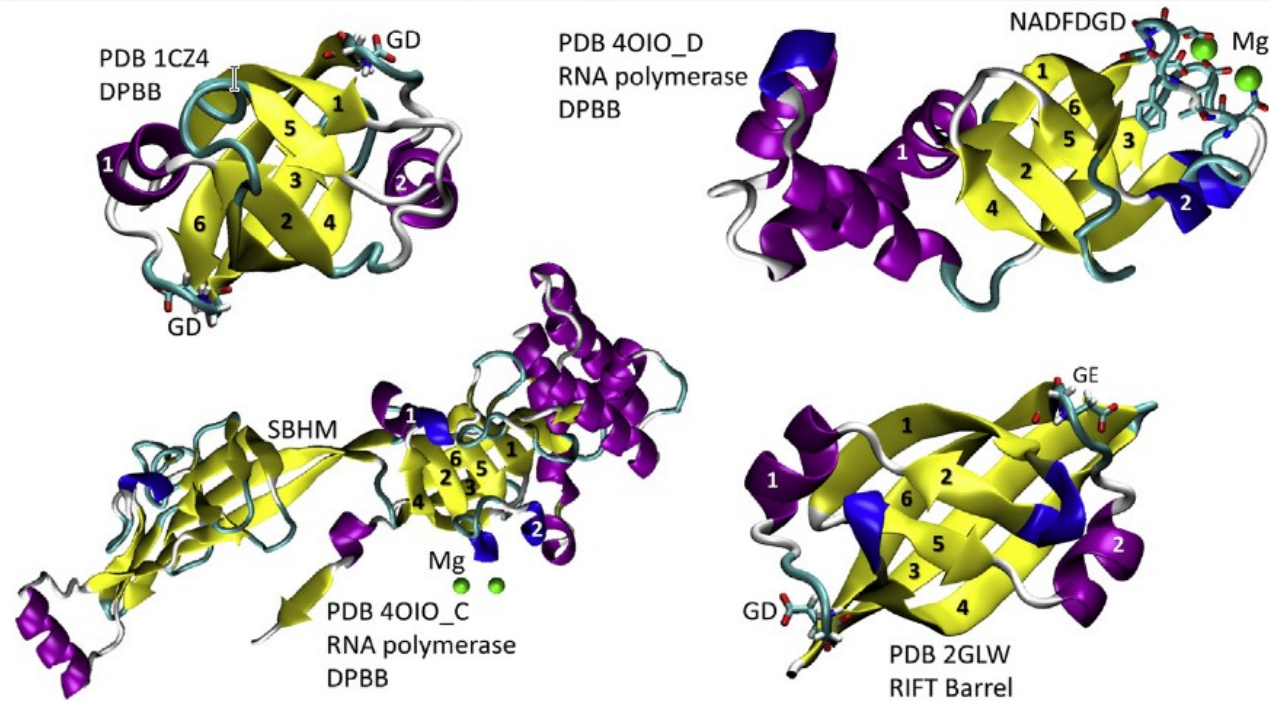


Remarkably,  $\alpha/\beta$  repeat folds comprise about 25% of extant proteins in all of life. These are among the most ancient protein folds and the folds with the most parallel  $\beta$ -sheets. FYI:  $\beta$ -sheets can be arranged relative to a neighboring  $\beta$ -sheet either in a parallel or an antiparallel orientation (Fig. 11.1). Because  $\beta$ -sheets form by interaction to another  $\beta$ -sheet, they must exist at least in pairs. So, by itself, a  $\beta$ -sheet is not a  $\beta$ -sheet. Without a partner, a  $\beta$ -sheet could fold into a  $\alpha$ -helix or something even worse. TOPRIM domains are  $\sim(\beta-\alpha)_{4-5}$  repeats [i.e.,  $(\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha)$ ], Rossmann folds are  $(\beta-\alpha)_8$  repeats (i.e.,  $\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha$ ), and TIM barrels are  $(\beta-\alpha)_8$  repeats ( $\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha-\beta-\alpha$ ). TOPRIM domains and Rossmann folds are twisted linear sheets. TIM barrels dance in a circle to close the barrel. It is likely that



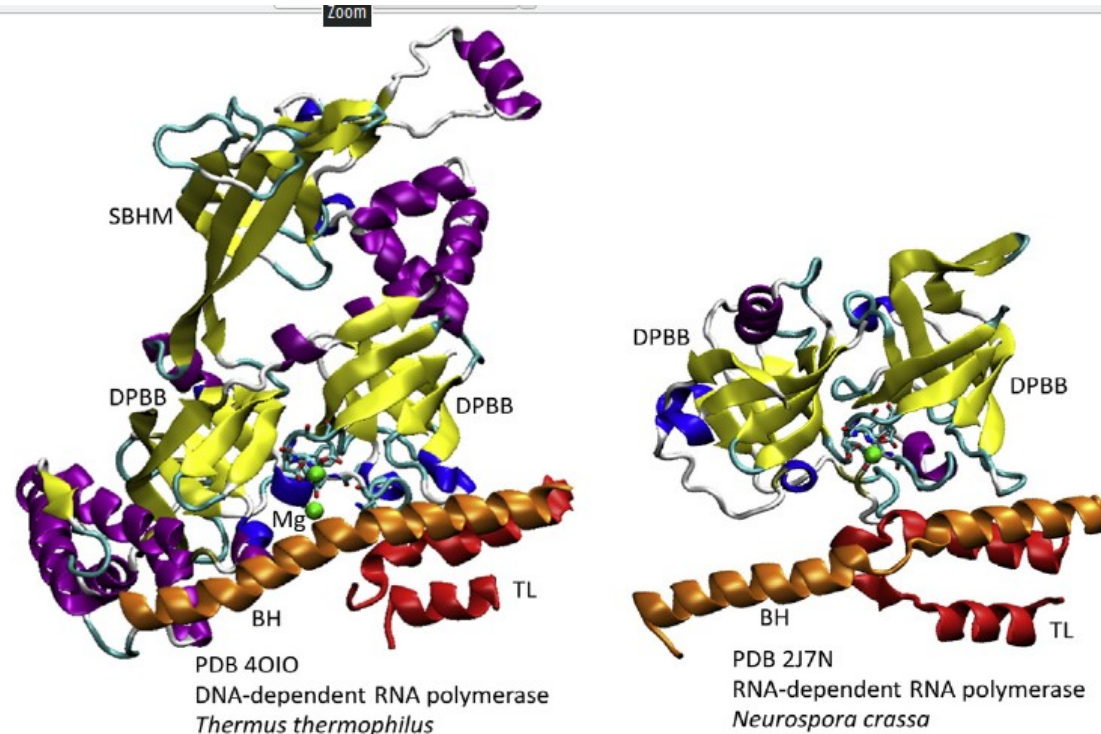


# Cradle Loop Barrels: RIFT, DPBB



**FIGURE 17.2** Monomeric double- $\Psi$ - $\beta$ -barrels (DPBB) and a monomeric RIFT barrel. The  $\Psi$  pattern of crossing chains is indicated for double- $\Psi$ - $\beta$ -barrels. The double- $\Psi$ - $\beta$ -barrels of RNA polymerases include insertions (i.e., SBHM for sandwich barrel hybrid motif). The monomeric RIFT barrel is the parent of the monomeric double- $\Psi$ - $\beta$ -barrel (Fig. 17.1). GD, related GE, and NADFDGD boxes are indicated.

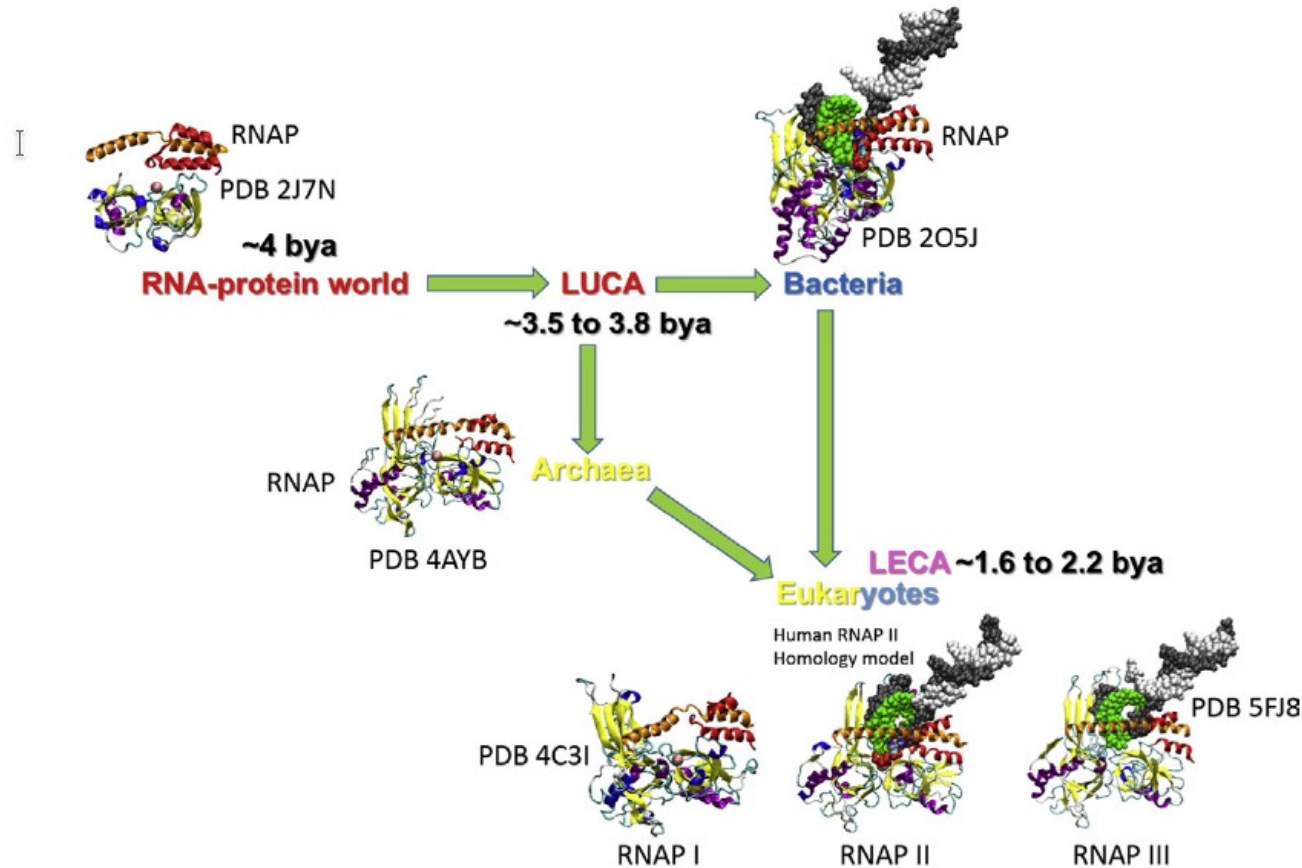
# DNA and RNA dependent Polymerases



**FIGURE 17.4** The catalytic cores of two double- $\Psi$ - $\beta$ -barrel-type DNA-template-dependent and RNA-template-dependent RNA polymerases. SBHM is for sandwich barrel hybrid motif. The bridge helix (BH) is orange. The trigger loop (TL) is red. Mg is green. Positively charged  $\text{Mg}^{2+}$  is held by acidic groups (i.e., aspartic acid; charge  $-1$ ).

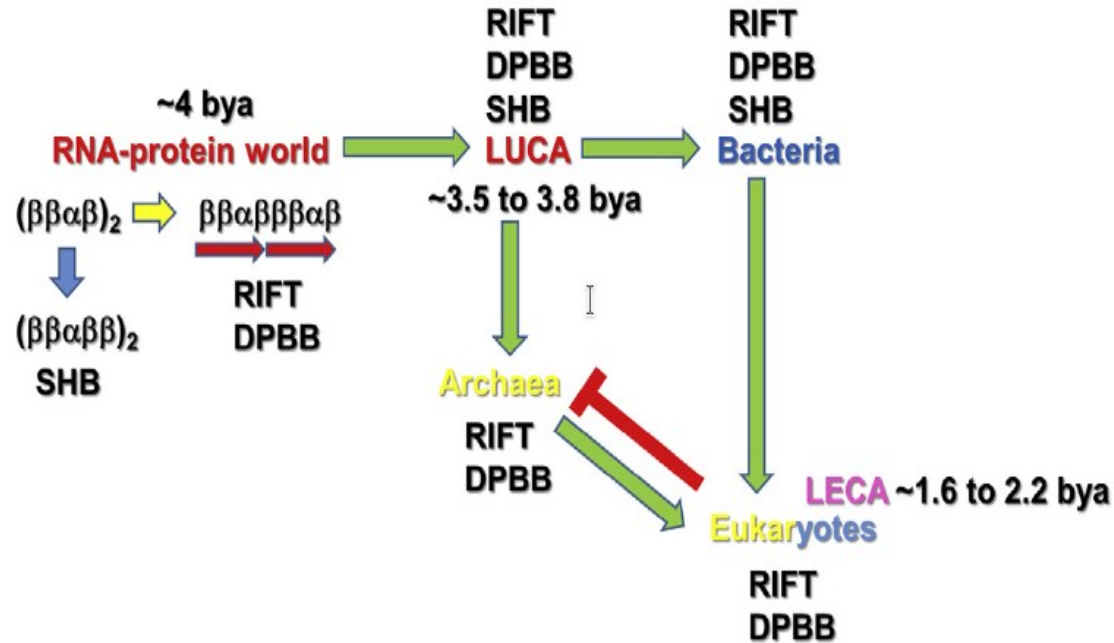


# DNA and RNA dependent Polymerases



**FIGURE 19.3** Evolution of RNA polymerases. Three RNA polymerases in eukaryotes. One in bacteria. One in archaea. Only the catalytic core of the RNA polymerase (RNAP) is shown.

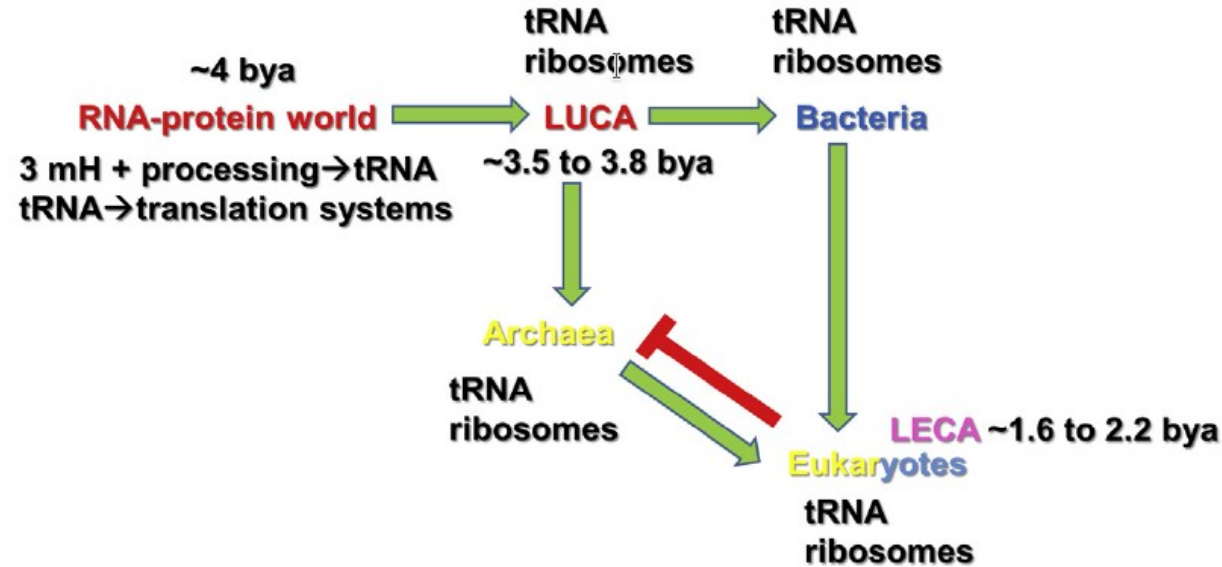
# Informed speculation: barrels evolution



**FIGURE 10.1** A simple model for generation of cradle-loop barrels, which arose in the RNA-protein world. *Small yellow arrows* indicate ligations. *Small red arrows* indicate repeats. DPBB for double-Ψ-β-barrels. SHB for swapped-hairpin barrels. Eukaryotes are posited to have competed with their parent archaea (red symbol).

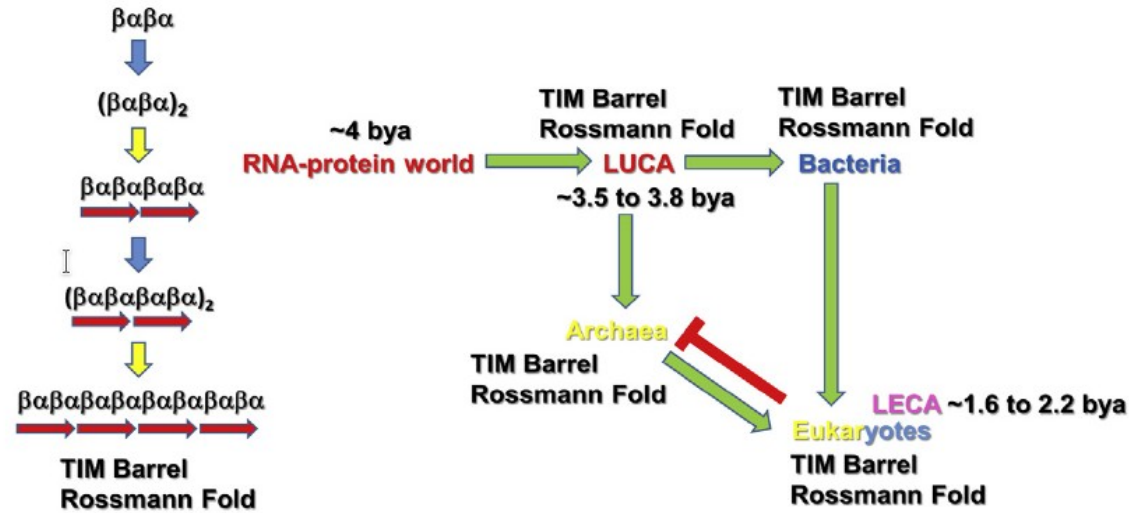


# Informed speculation: translation



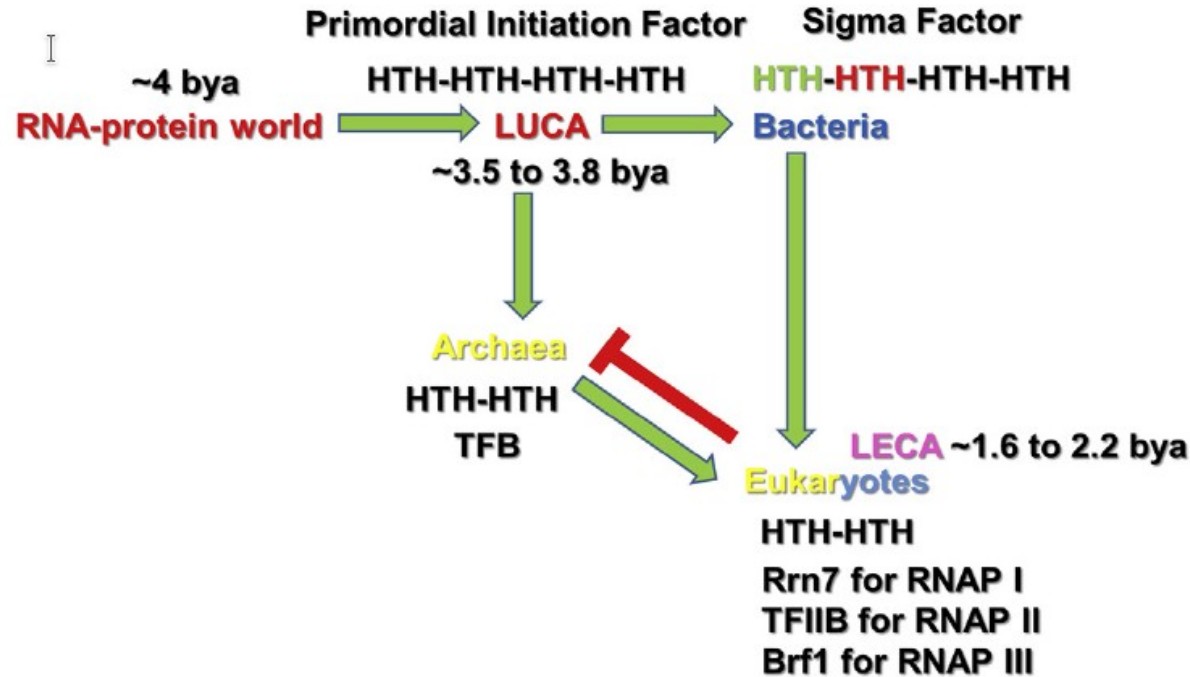
**FIGURE 10.2** Evolution of translation systems. Cloverleaf tRNA was an early and radical innovation. Translation systems evolved around tRNA.

# Informed speculation: metabolism



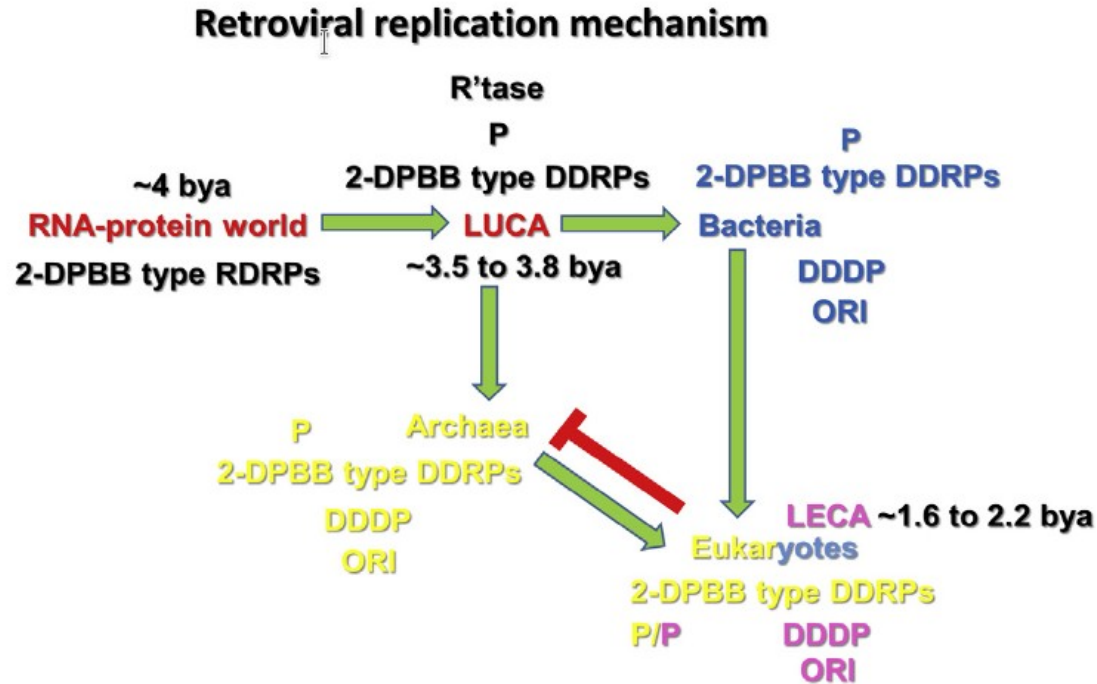
**FIGURE 10.3** A simple model for evolution of metabolism. TIM barrels and Rossmann folds (posited to be a rearranged TIM barrel) are posited to have arisen in the RNA-protein world and to have radiated to all subsequent life on earth.

# Informed speculation: Transcription Factors



**FIGURE 10.4** A simple model for evolution of a core general transcription factor. A four HTH primordial initiation factor is posited to have been present at LUCA and radiated to form sigma factors in bacteria (four HTH), TFB in archaea (two HTH) and Rrn7, TFIIB and Brf1 in eukaryotes (two HTH).

# Informed speculation: template based copying



**FIGURE 10.5** Evolution and utilization of RNA and DNA templates. *DDDP*, DNA-template-dependent DNA polymerase; *DDRP*, DNA-template-dependent RNA polymerase; *DPBB*, double-Ψ-β-barrel; *ORI*, origin of replication; *P*, promoter; *RDRP*, RNA-template-dependent RNA polymerase; *R'tase*, reverse transcriptase. Colors represent bacterial (blue), archaeal (yellow), and eukaryotic (pink) innovations.