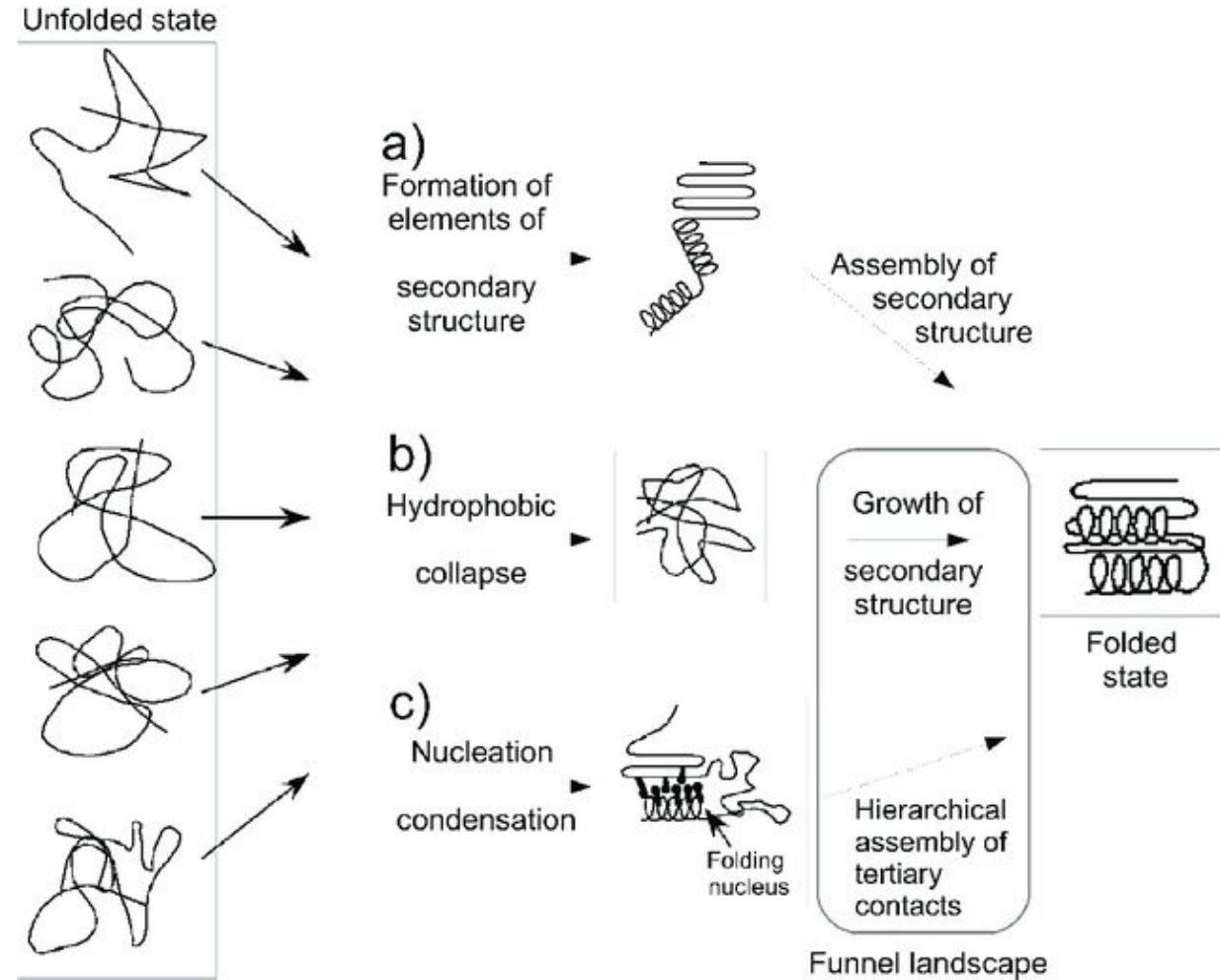
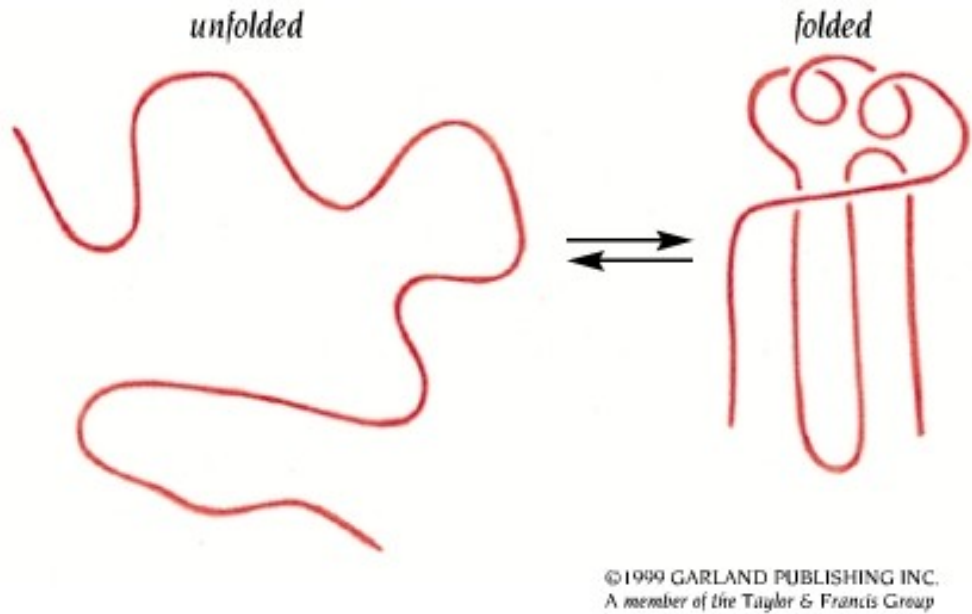


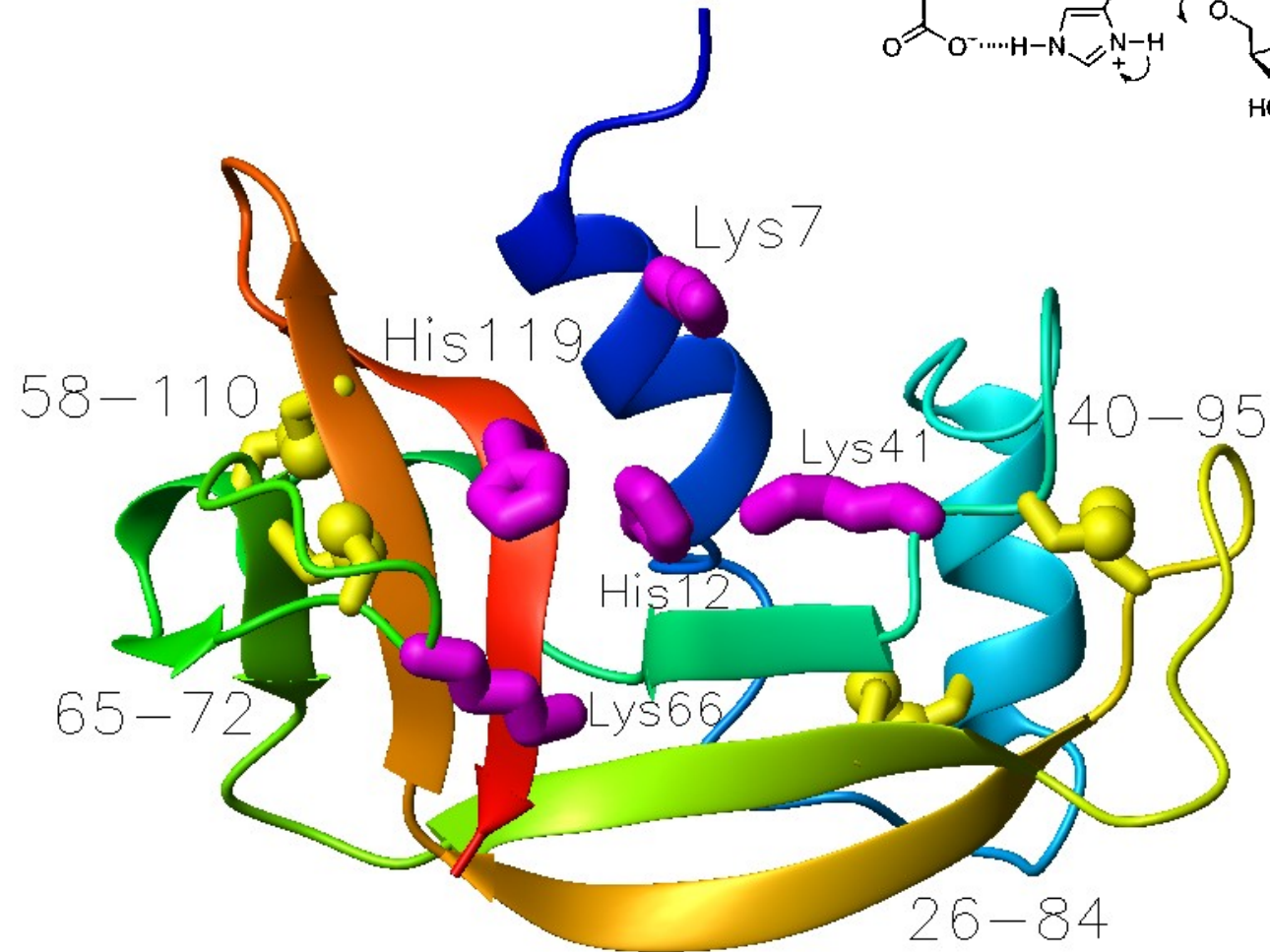
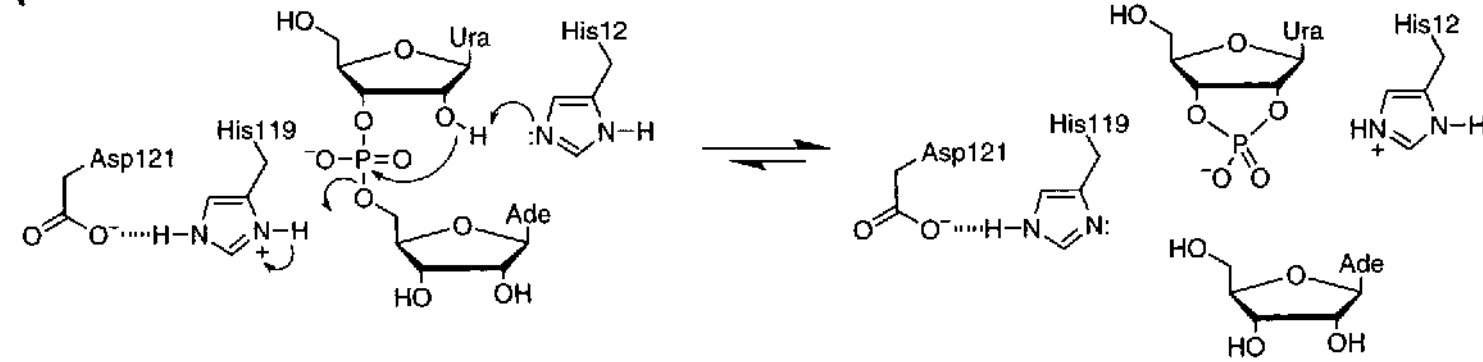
Protein folding



Protein folding

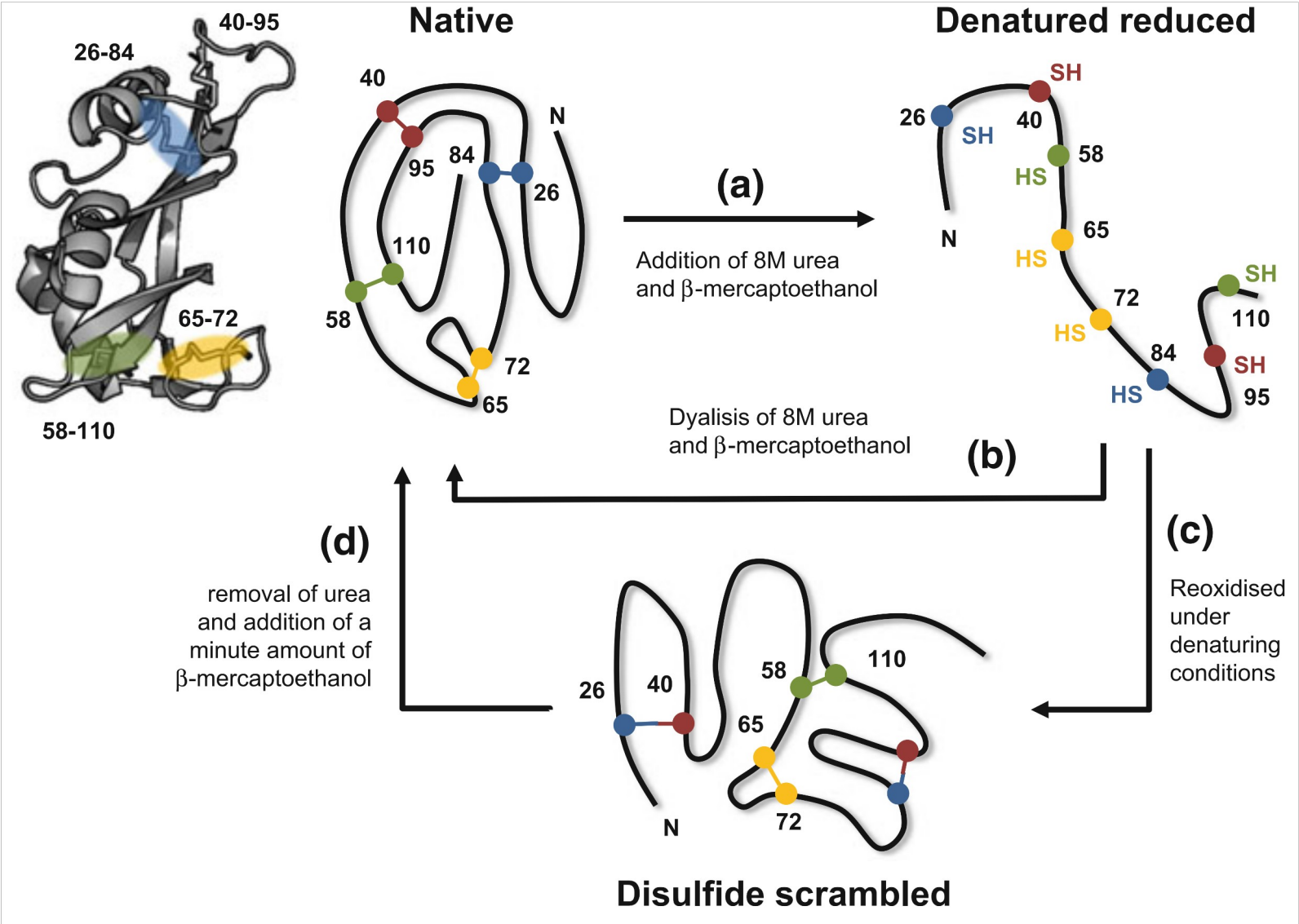
ribonuclease A

A



Protein folding

Anfinsen experiment

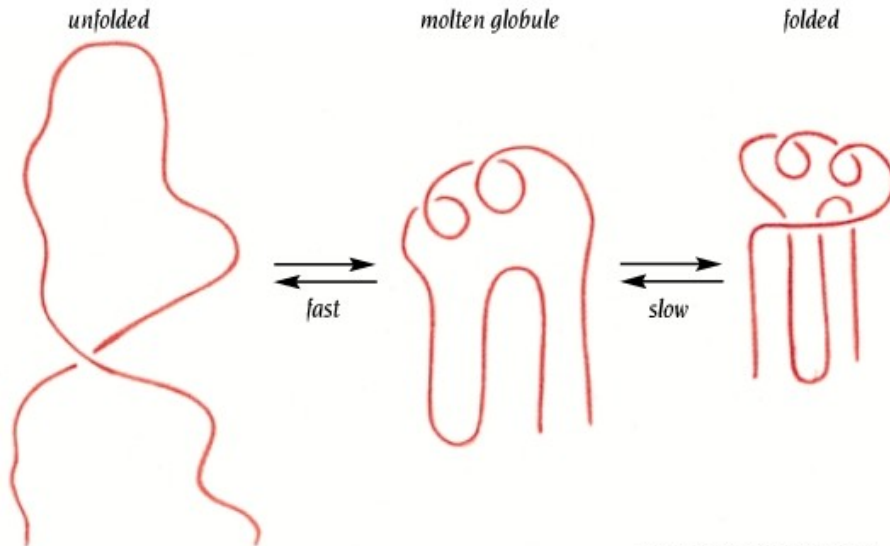


The thermodynamic hypothesis

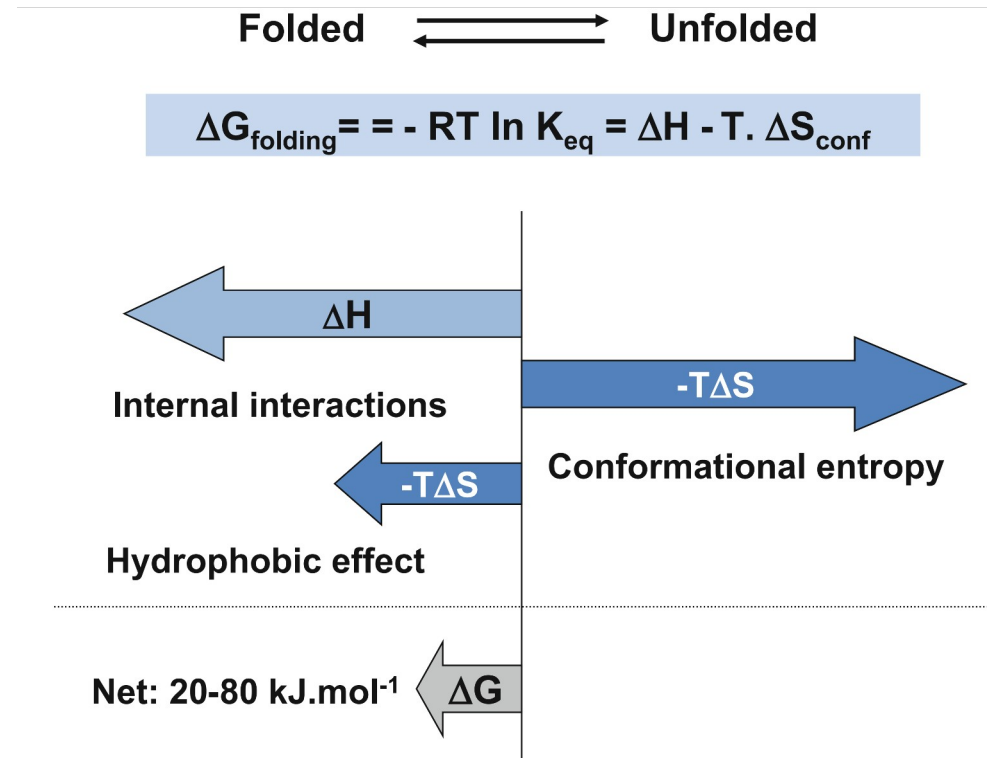
Για κάθε ένωση σε ένα χημικό σύστημα ισχύει η **$G = H - TS$**

Οι μεταβολές της ενέργειας Gibbs μπορούν να υπολογισθούν από τις μεταβολές της ενθαλπίας και της εντροπίας – οι πρότυπες τιμές των μεγεθών

$$\Delta_r G^0 = \Delta_r H^0 - T \Delta_r S^0$$



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The thermodynamic hypothesis

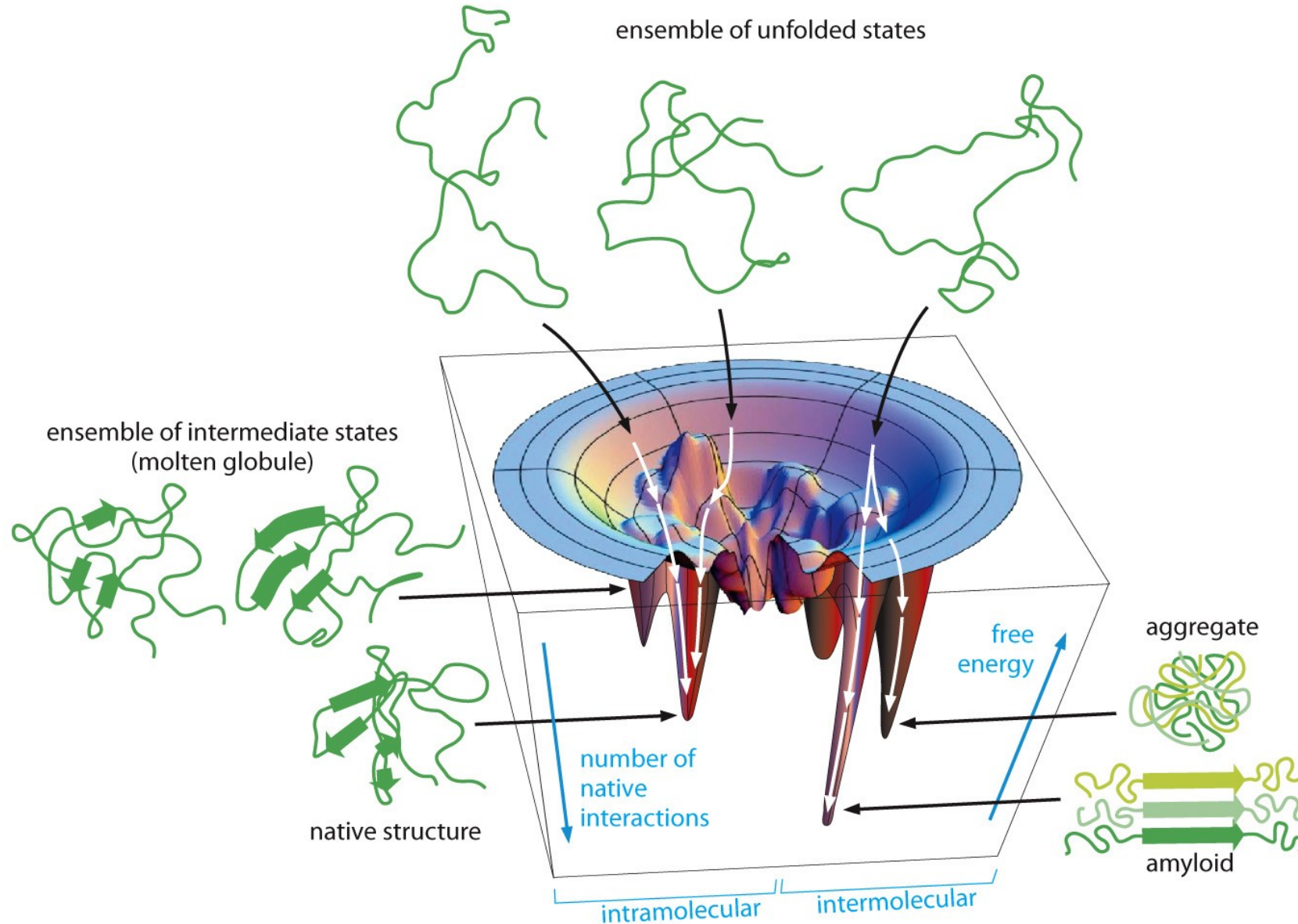


Figure 1.12 Molecular Biology of Assemblies and Machines (© Garland Science 2016)

Energy landscapes

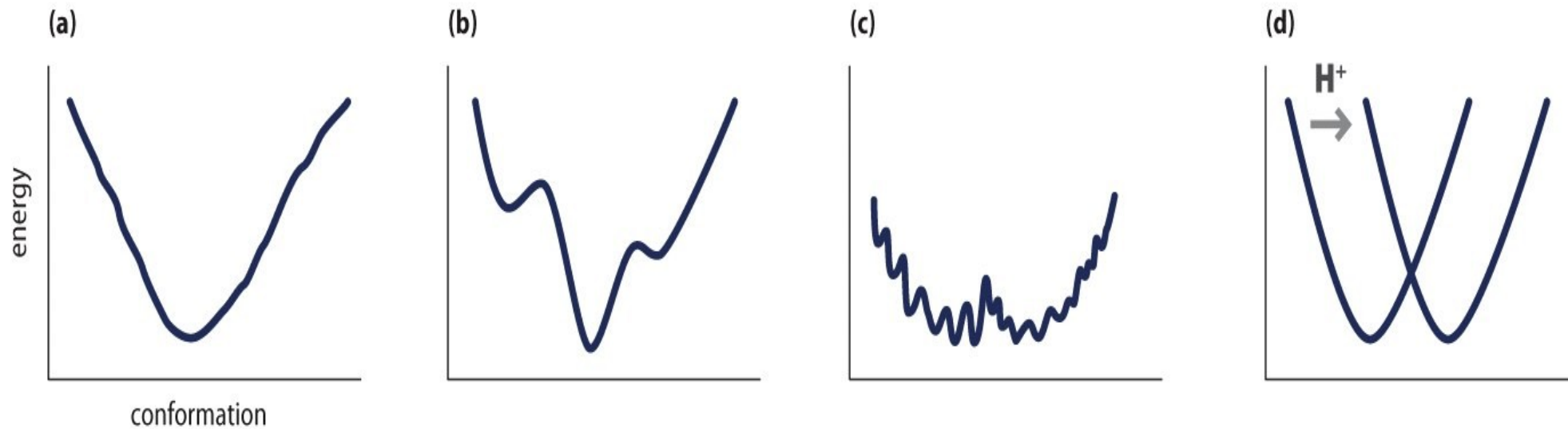


Figure 1.45 How Proteins Work (©2012 Garland Science)

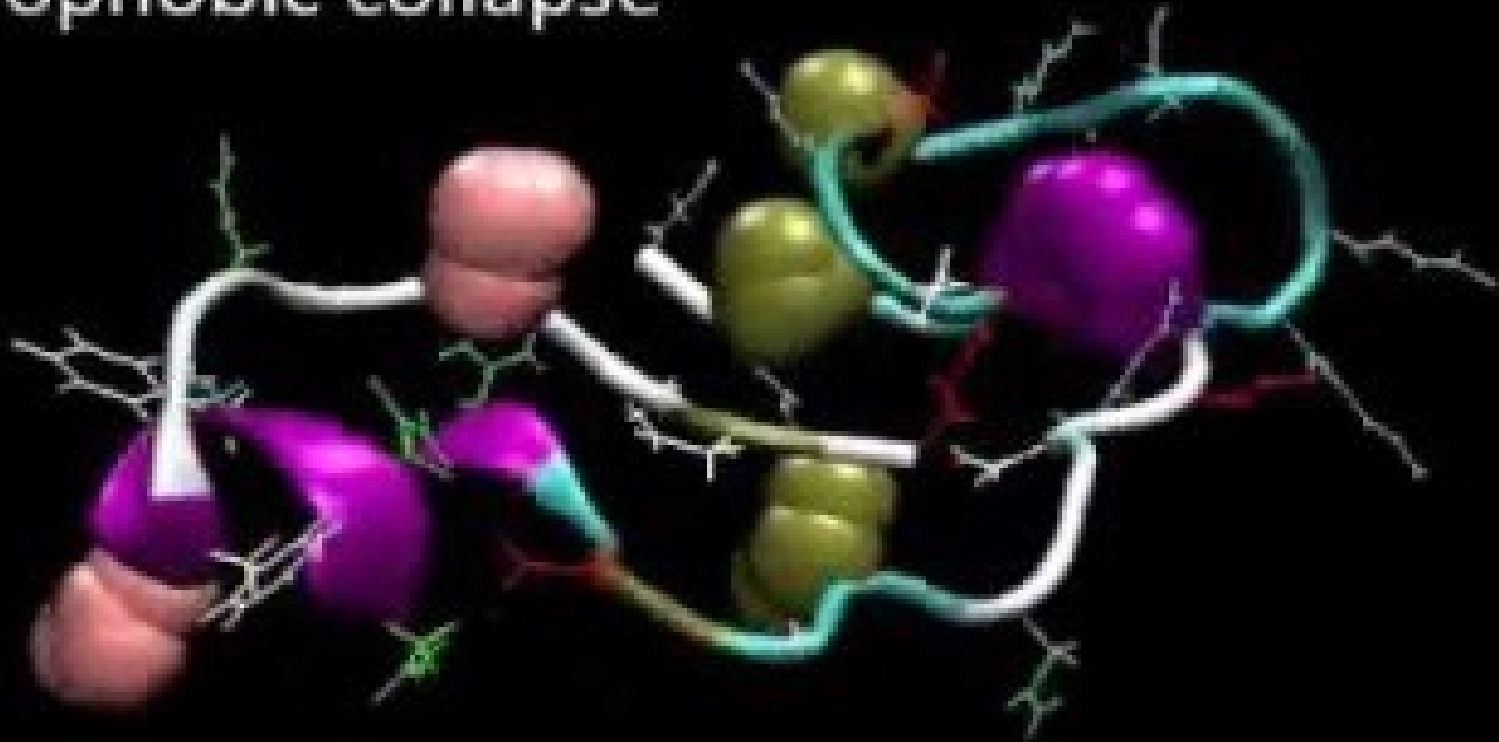
Single well defined
energy minimum

Higher energy
metastable states

Locally

Change in conditions

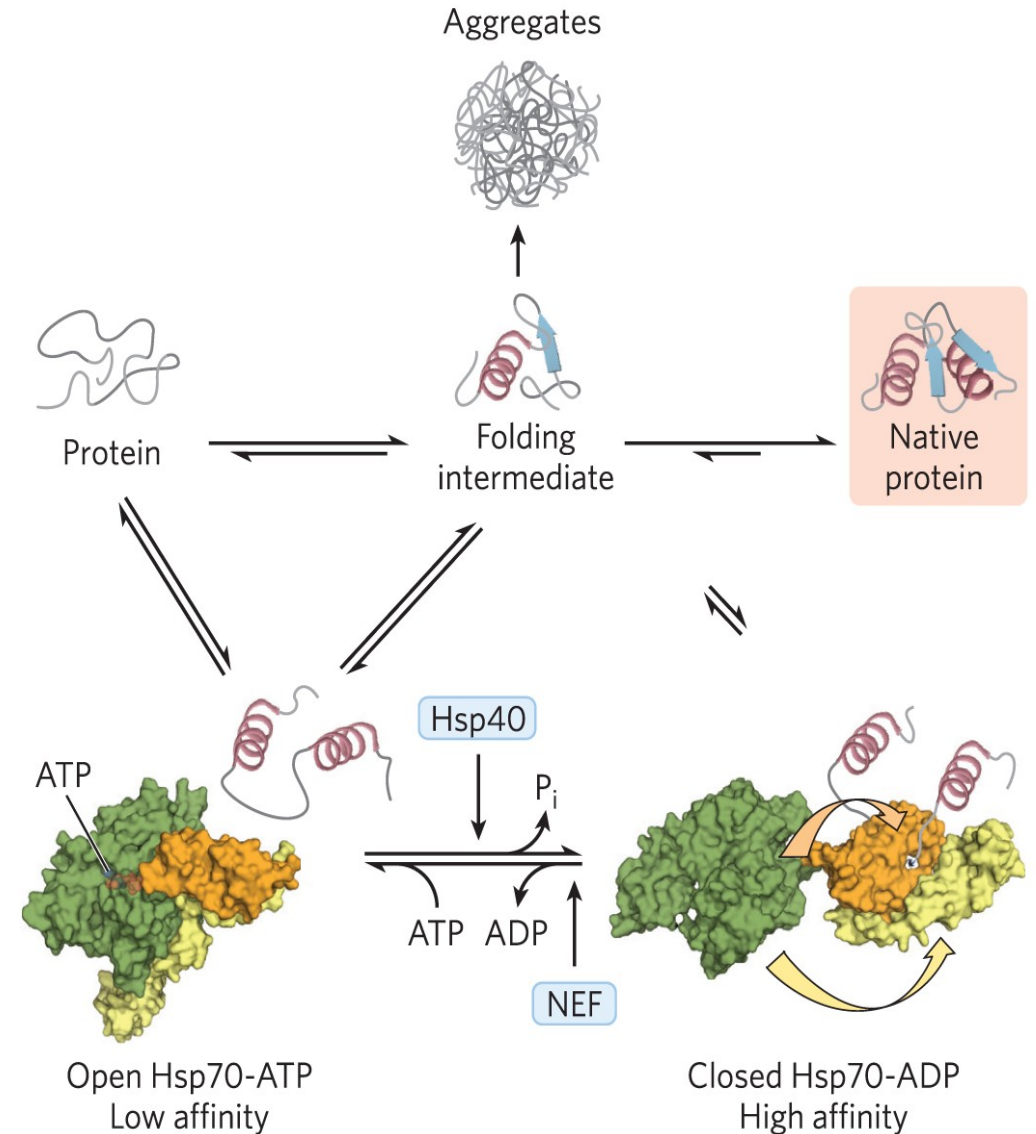
hydrophobic collapse



<https://www.youtube.com/watch?v=gFcp2Xpd29I>

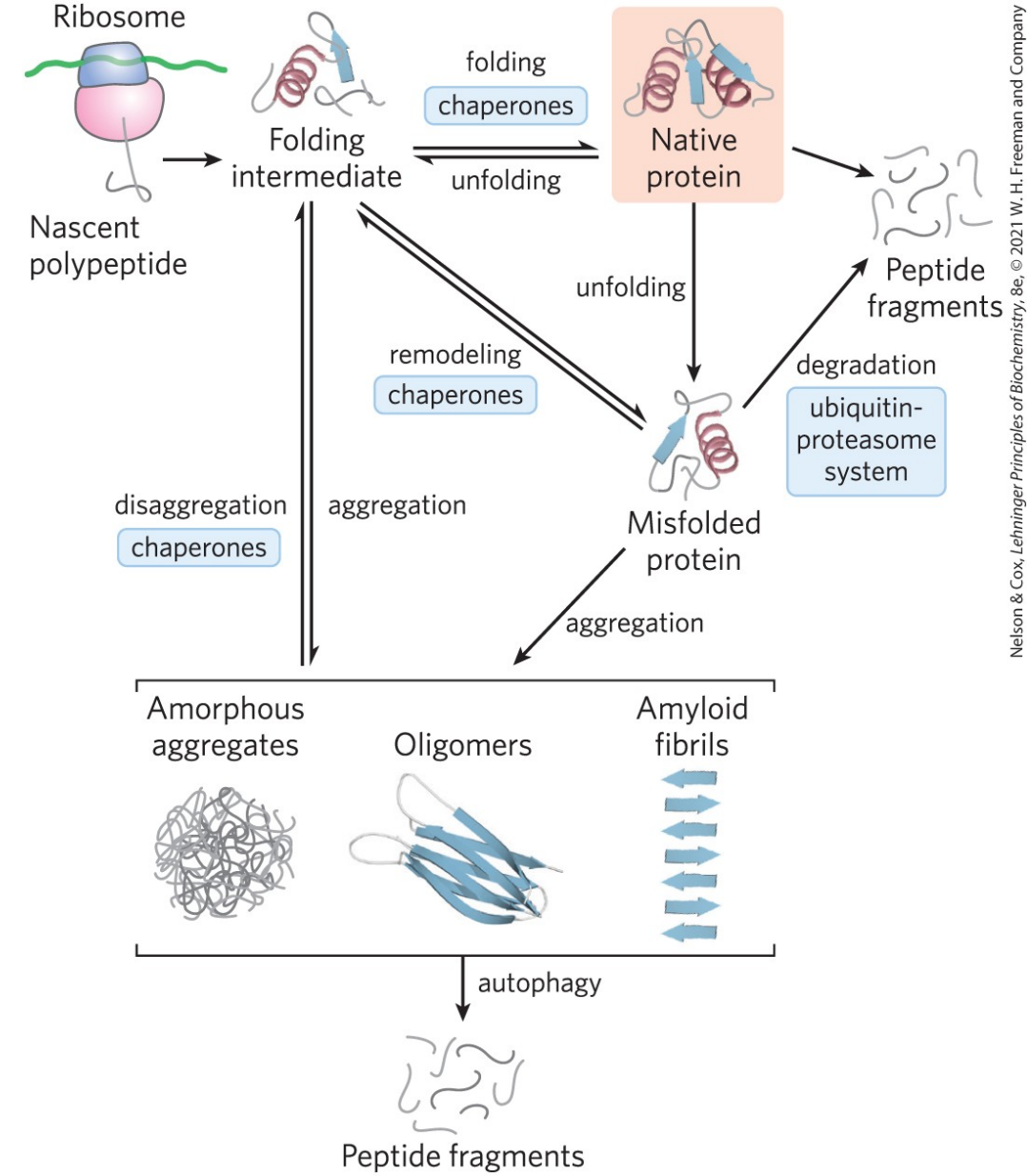
Some Proteins Undergo Assisted Folding

- **chaperone** proteins = facilitate correct folding pathways or ideal microenvironments
 - **Hsp70** = bind to hydrophobic regions
 - **chaperonins** = required for the folding of proteins that do not fold spontaneously



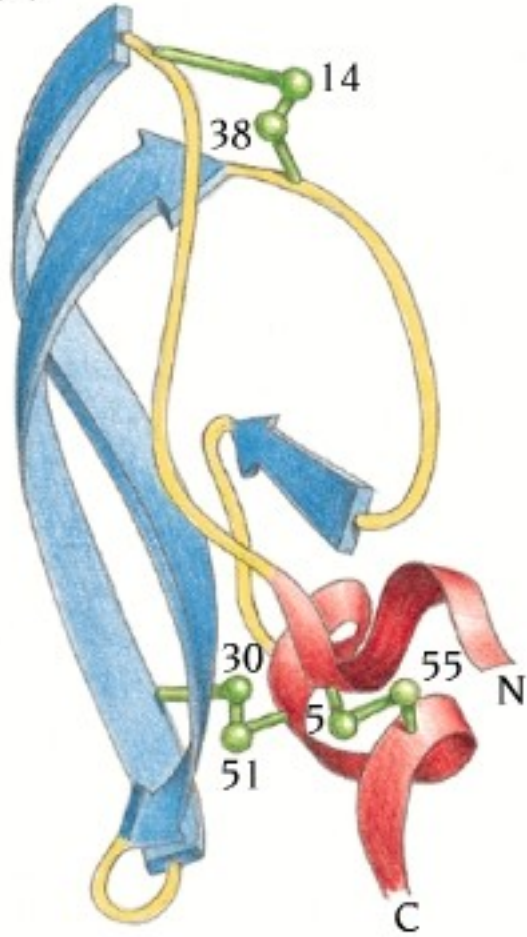
Pathways Involved in Proteostasis

- **proteostasis** = continual maintenance of the active set of cellular proteins required under a given set of conditions

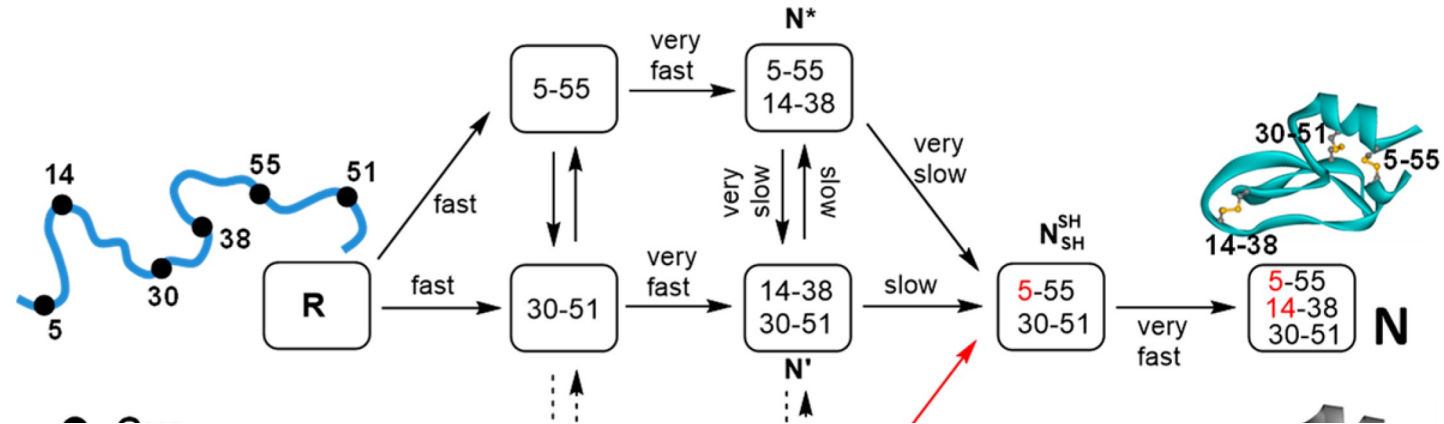


Bovine pancreatic trypsin inhibitor, BPTI.

(a)

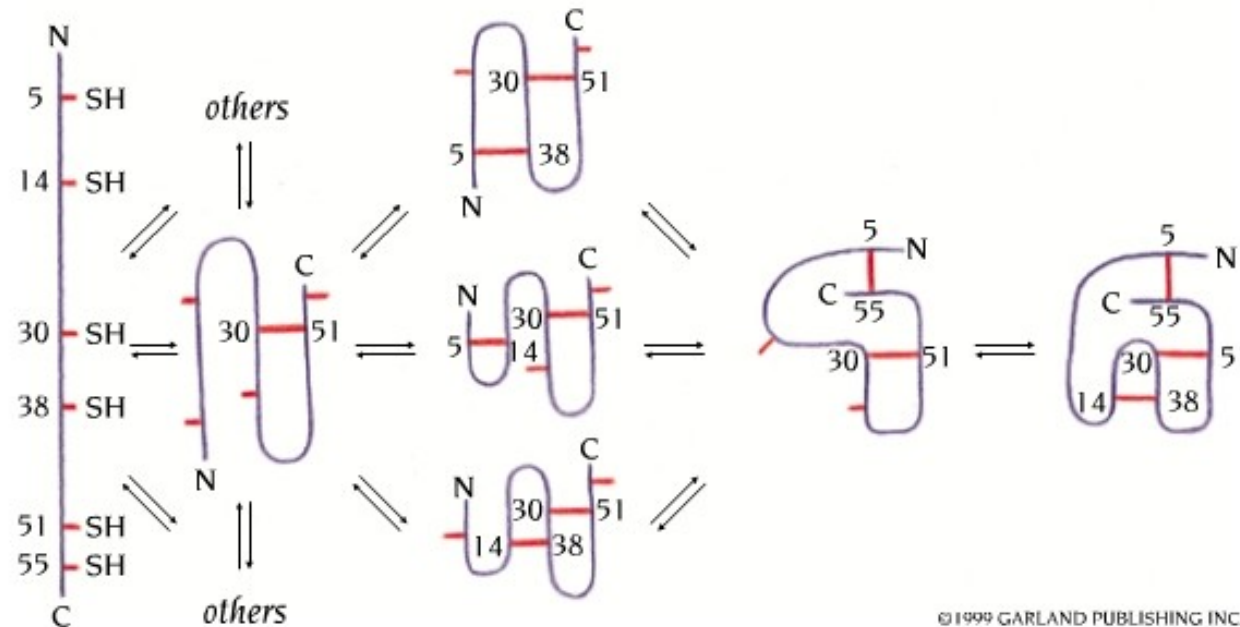


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Pathways for wild-type BPTI

(b)



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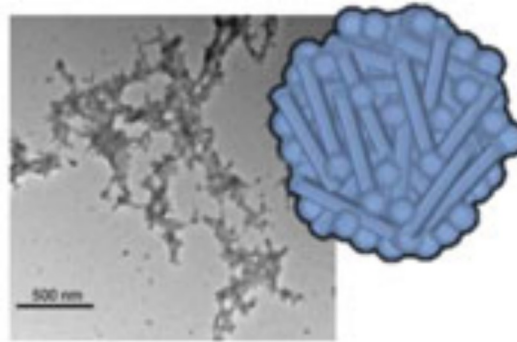
Physical and structural characteristics of misfolded proteins

Destabilized protein



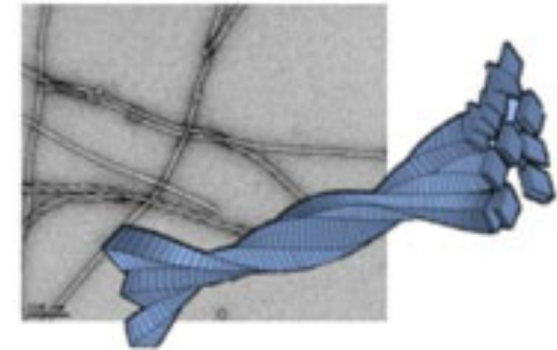
- Low stability conformational state
- May have locally altered secondary structure or poor tertiary interactions.
- It usually retains some biological function
- More susceptible to proteolysis than native

Protein Aggregate



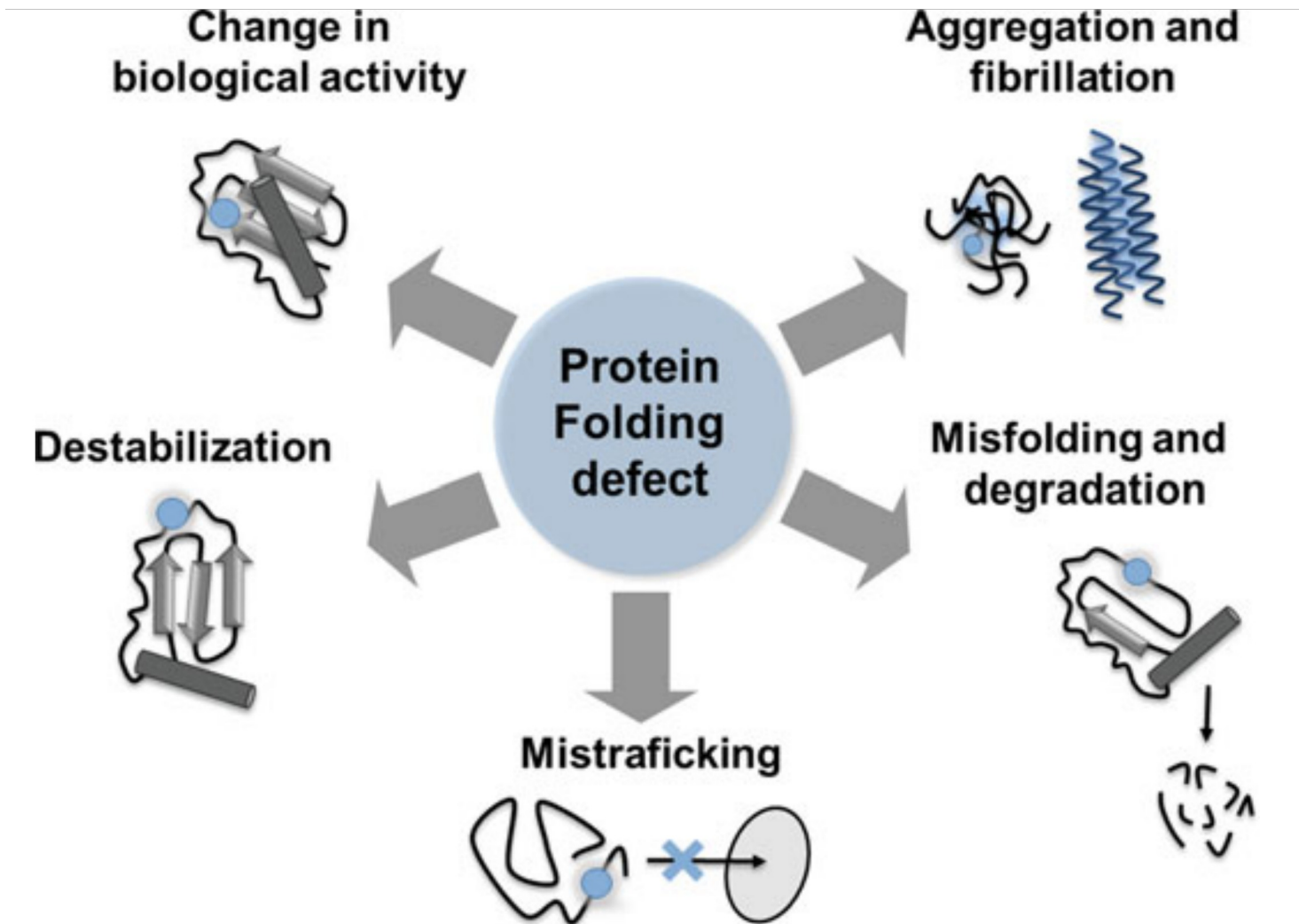
- Amorphous
- insoluble protein conglomerate
- Results from intermolecular hydrophobic interactions between misfolded proteins
- Readily resolubilized in buffer in native like conditions

Amyloid fibril

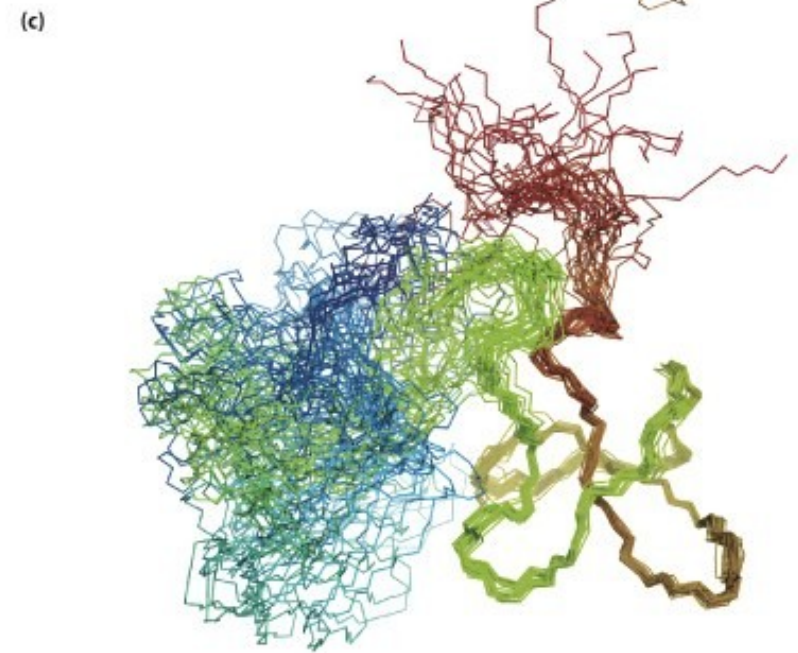
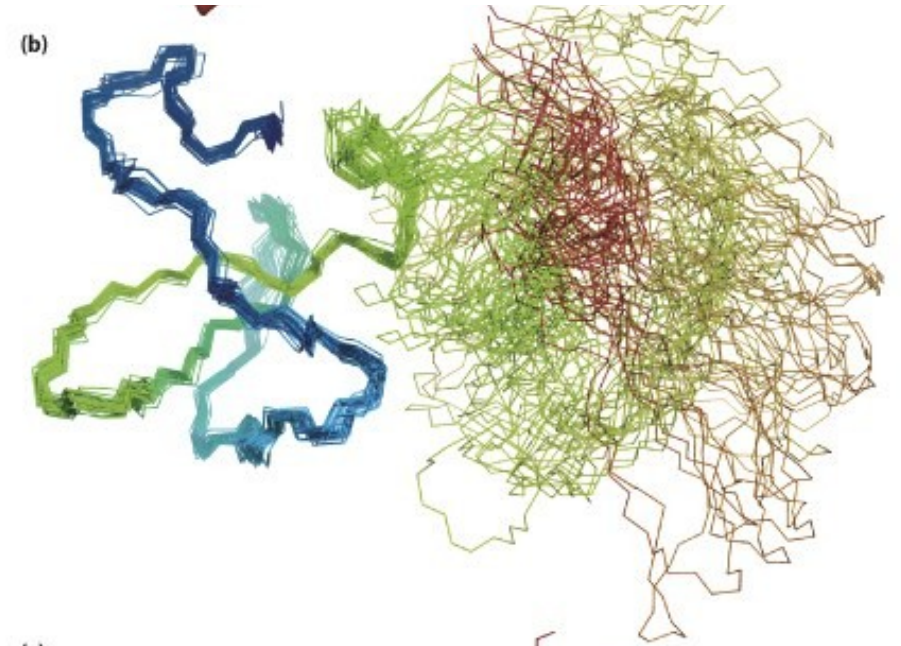
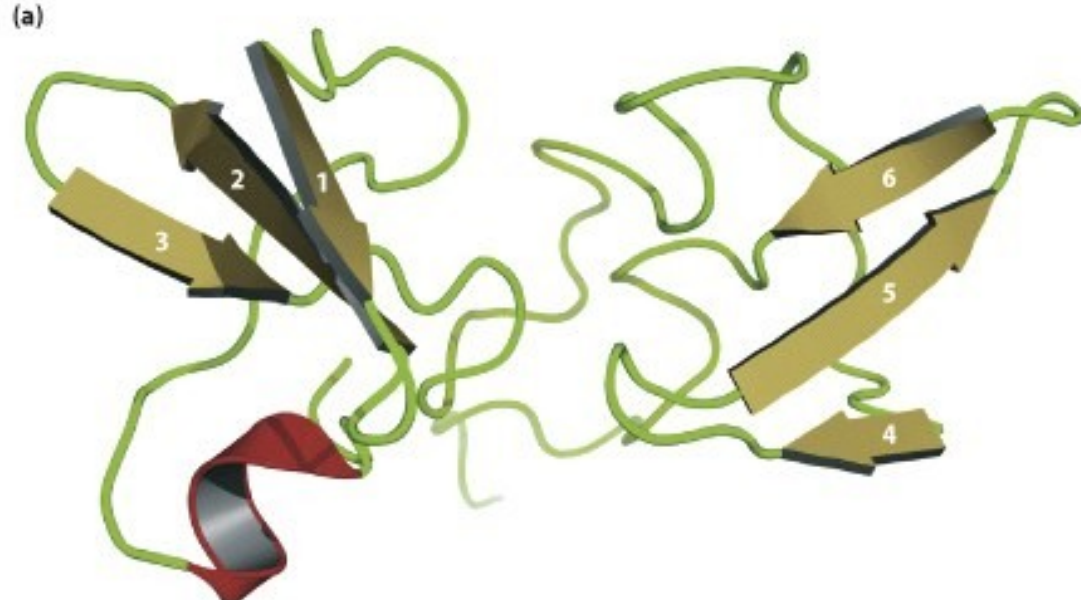


- Highly ordered
- Insoluble fibril-shaped protein aggregates
- formed from β -sheet stacking in a cross- β motif
- Highly resistant to proteolysis
- Requires high concentrations of denaturant or detergent to resolubilize

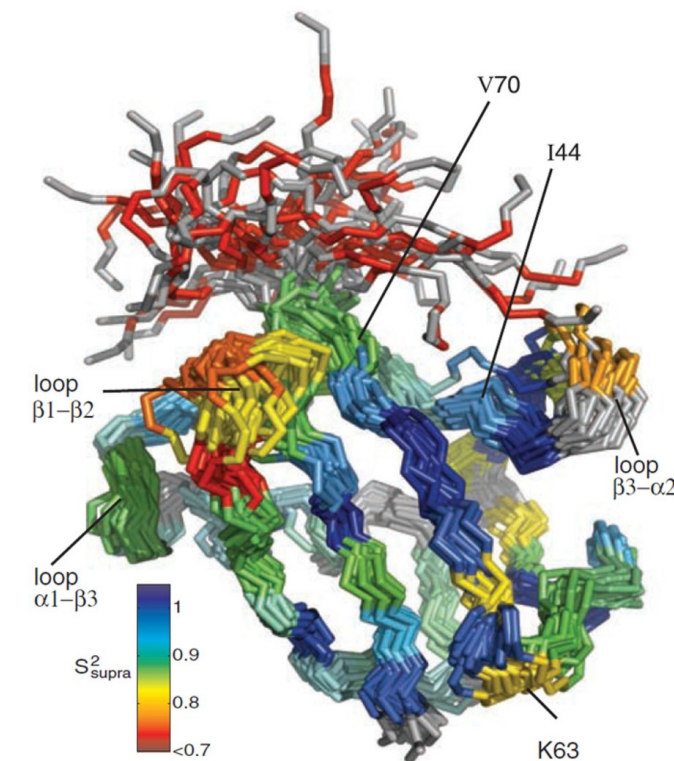
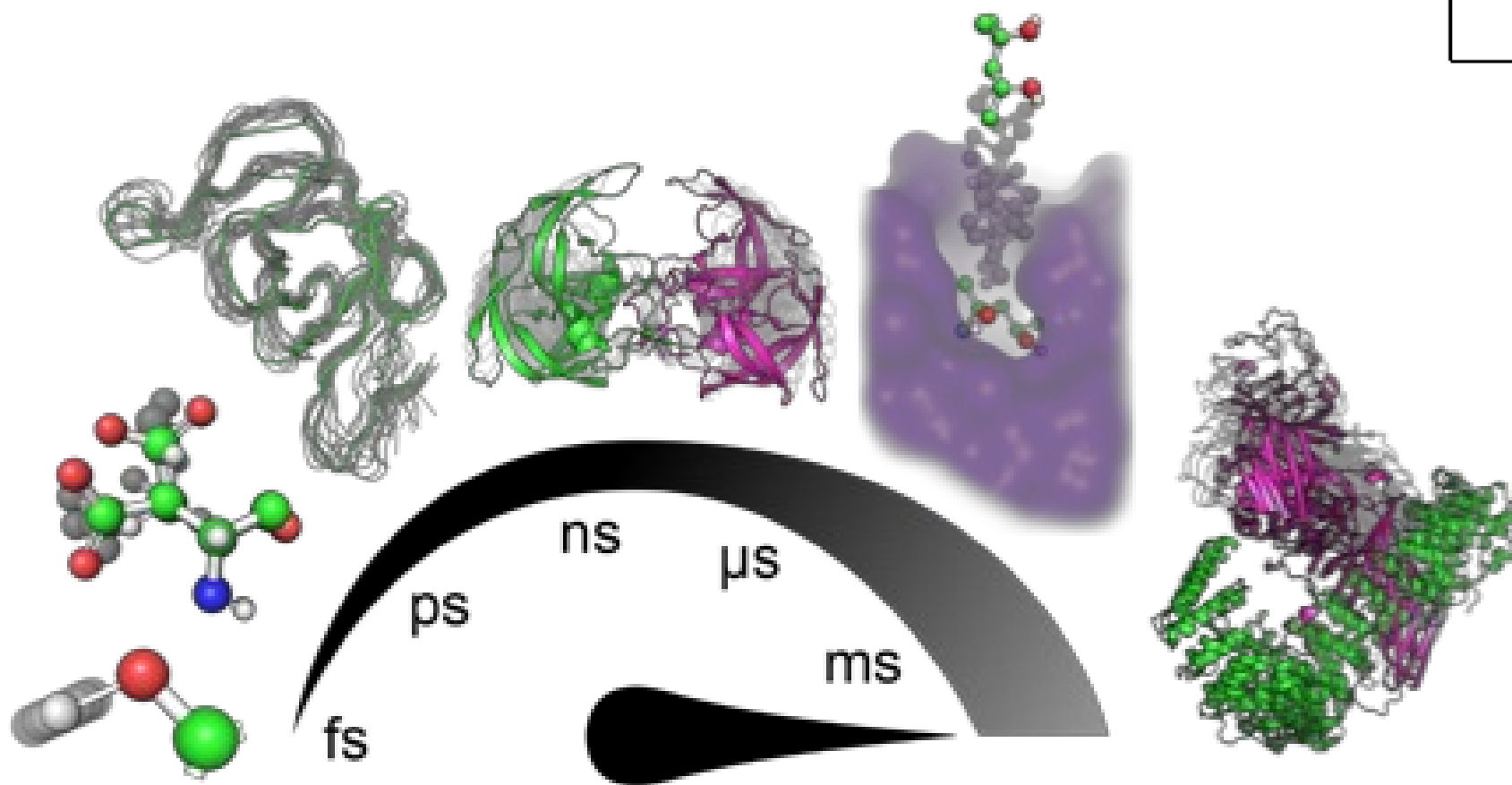
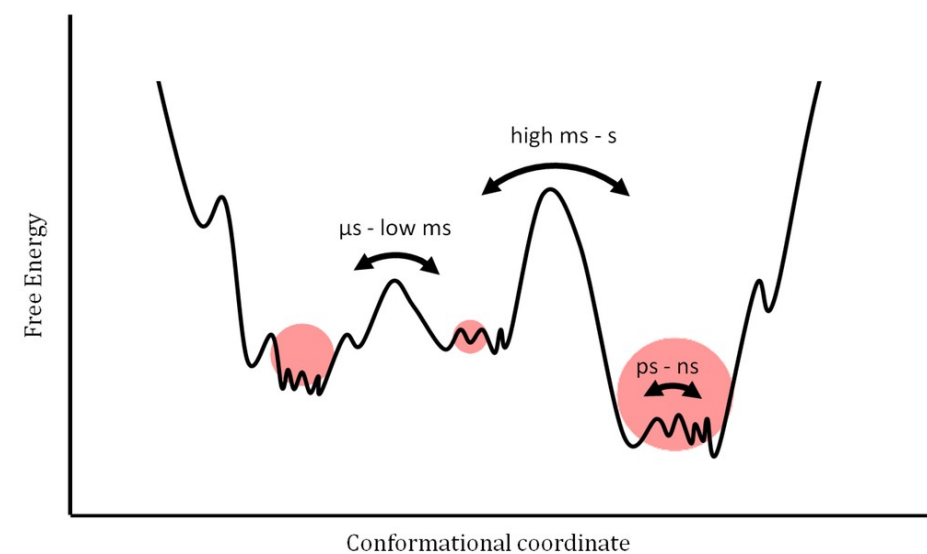
Misfolded proteins: multiple pathways to disease



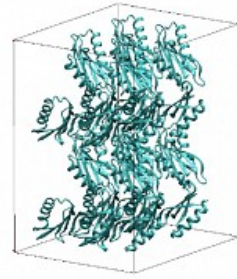
dynamics of a protein



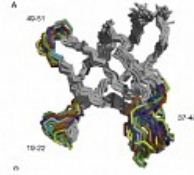
Motion in protein dynamics



Exploring the role of dynamics in protein function using NMR



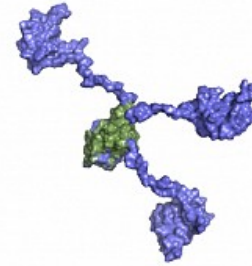
Dynamics in
microcrystalline
proteins



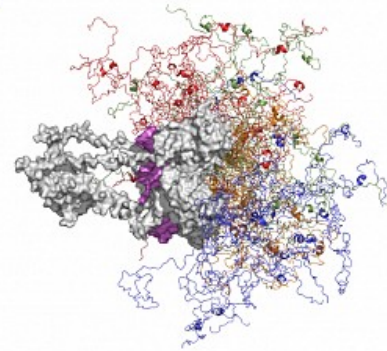
Local dynamic
modes on multiple
timescales....



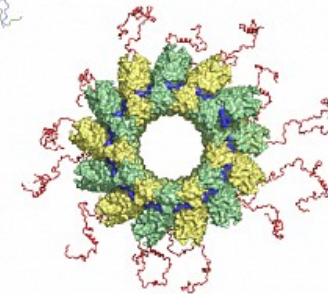
...and their role
in functional complexes



Multidomain proteins
with flexible linkers



Multidomain proteins
with highly disordered
functional domains



Flexible domains
in highly ordered
assemblies



Intrinsically
disordered
proteins

The order parameter

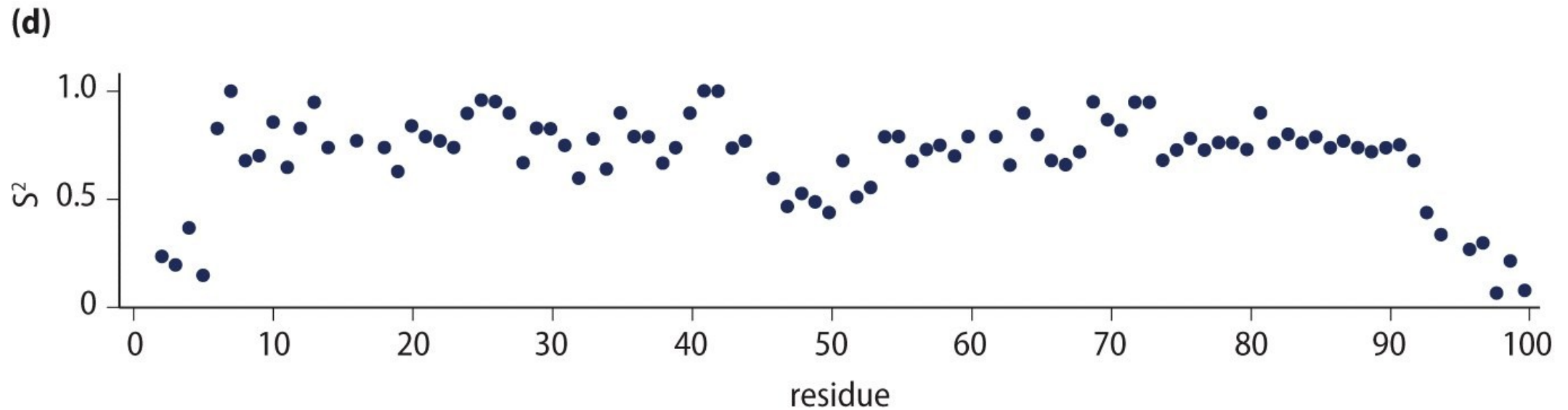
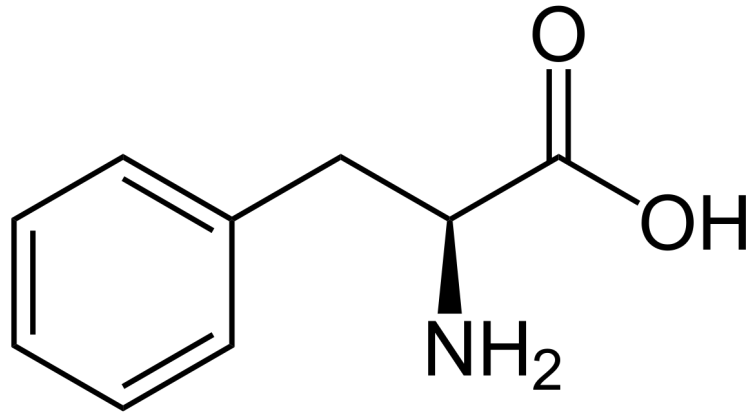


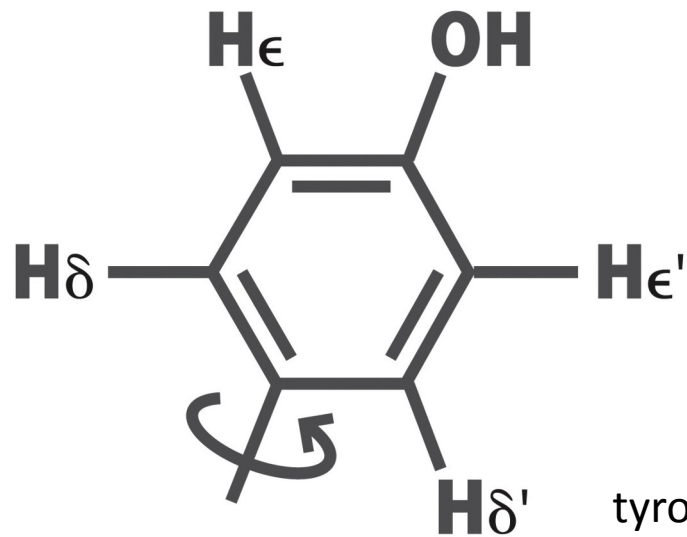
Figure 6.3 part 2 of 2 How Proteins Work (©2012 Garland Science)

The order parameter S^2 is obtained from ^{15}N relaxation data
It ranges from 0 (rapid unconstrained motion) to 1 (complete rigid body motion)

protein dynamics



phenylalanine



tyrosine

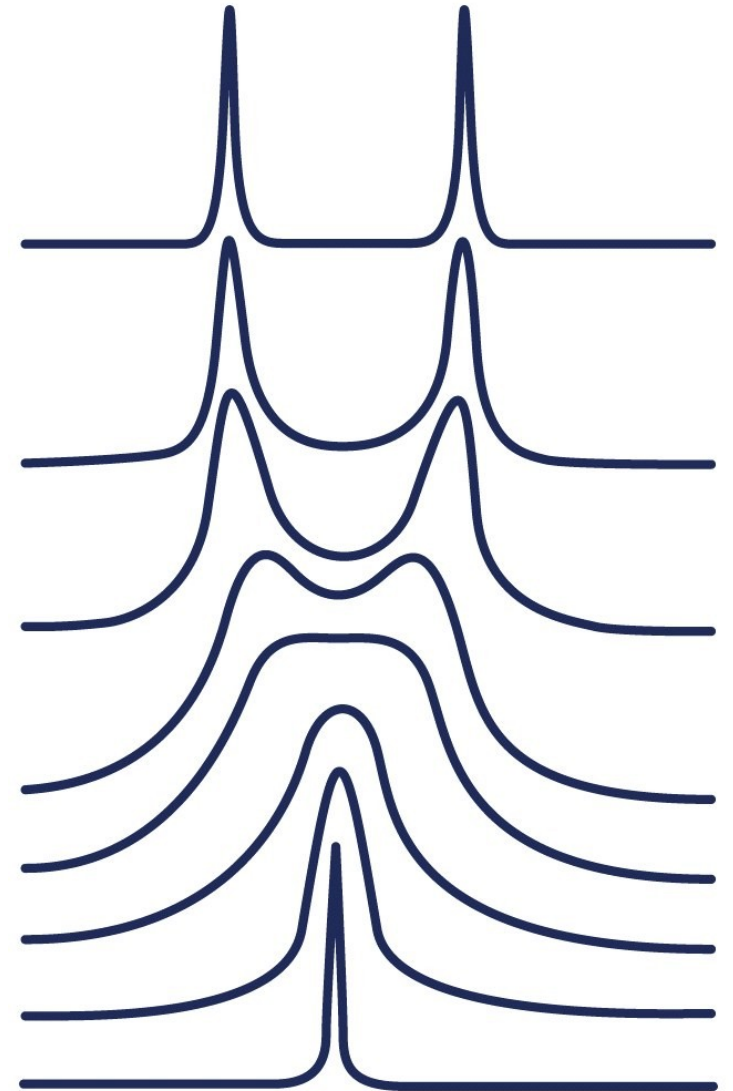
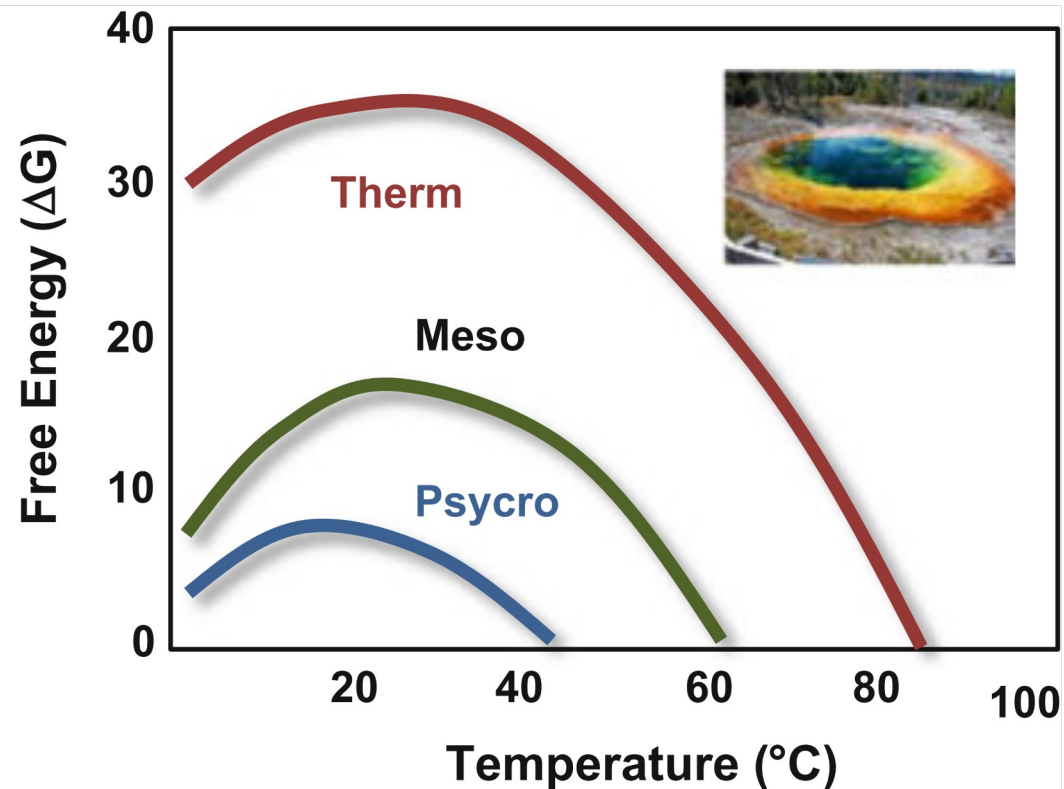


Figure 6.7 How Proteins Work (©2012 Garland Science)

Thermostable Proteins

thermophile is an organism that thrives at relatively high temperatures, between **41 and 122 °C**

DNA polymerase from the thermophilic bacterium *Thermus aquaticus* 80 °C PCR



Structural adaptations

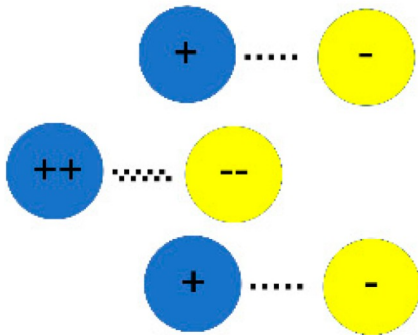
Sequence adaptations

Thermostable Proteins-Structural adaptations

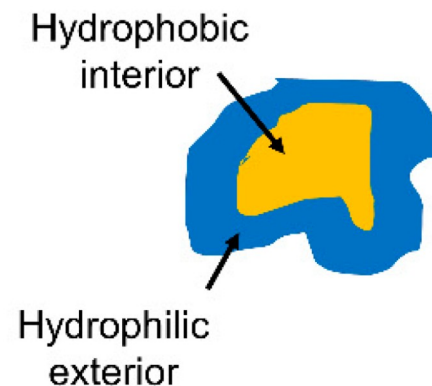
η προσαρμογή γενικά έχει ως αποτέλεσμα την αύξηση της δομικής ακαμψίας των πρωτεϊνών, διατηρώντας παράλληλα την τοπική ευκαμψία των λειτουργικά σημαντικών περιοχών

Characteristics of thermophilic proteins compared to mesophilic proteins

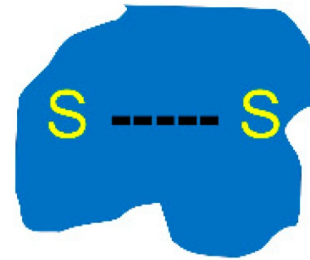
More ion pairs



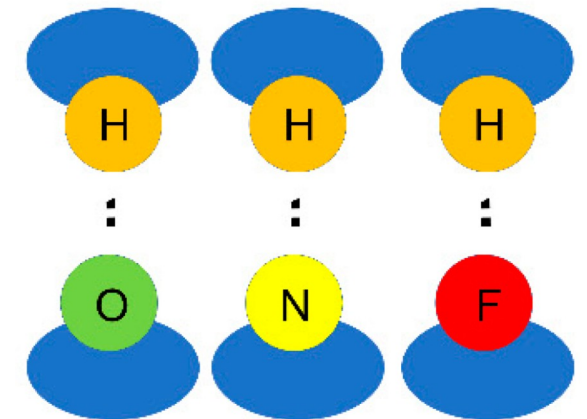
Greater average hydrophobicity of interior residues



More compact core containing disulfide bonds



More hydrogen bonds



Thermostable Proteins-Sequence adaptations

αύξηση των μη πολικών αμινοξέων, ειδικά των υδρόφοβων και των υπολειμμάτων Pro που συμβάλλουν στις υδρόφοβες αλληλεπιδράσεις.

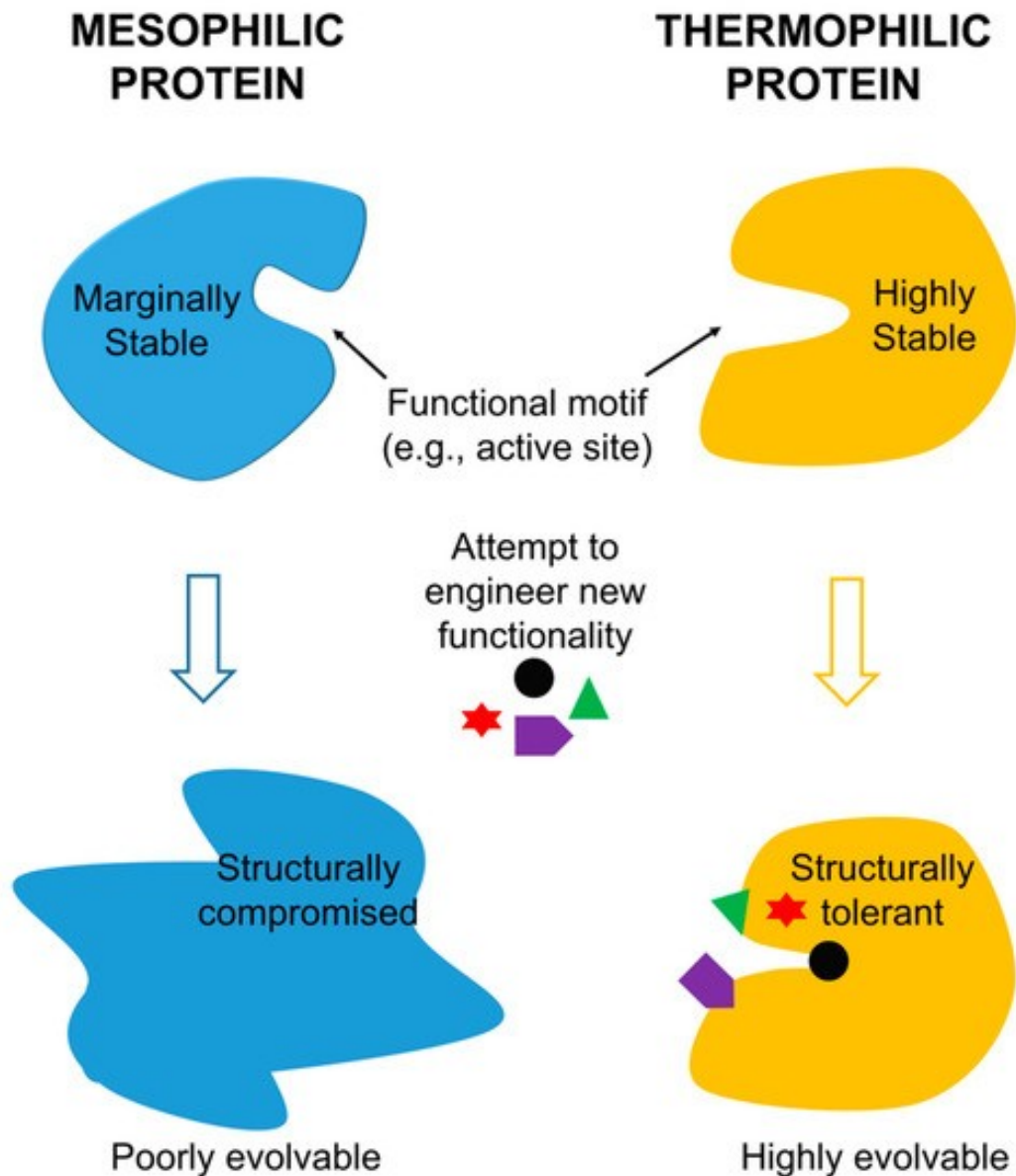
αύξηση των φορτισμένων αμινοξέων, ειδικά των υπολειμμάτων Arg και Glu που συμβάλλουν στις ιοντικές αλληλεπιδράσεις.

αύξηση των αρωματικών αμινοξέων, ειδικά των υπολειμμάτων Tyr που συμβάλλουν στις αλληλεπιδράσεις κατιόντων-π

μείωση των υπολειμμάτων Met και των μη φορτισμένων πολικών υπολειμμάτων, τα οποία είναι θερμοσταθερά αμινοξέα.

Στο άλλο άκρο, τα ψυχρόφιλα (δηλαδή οι οργανισμοί που ζουν σε θερμοκρασίες κάτω των 20 °C) πρέπει να περιέχουν πρωτεΐνες και ένζυμα προσαρμοσμένα στο κρύο, τα οποία απαιτούν ένα σύνολο χαρακτηριστικών που είναι κατά κάποιον τρόπο αντίθετα με αυτά που παρατηρούνται στις θερμόφιλες πρωτεΐνες.

functional evolution



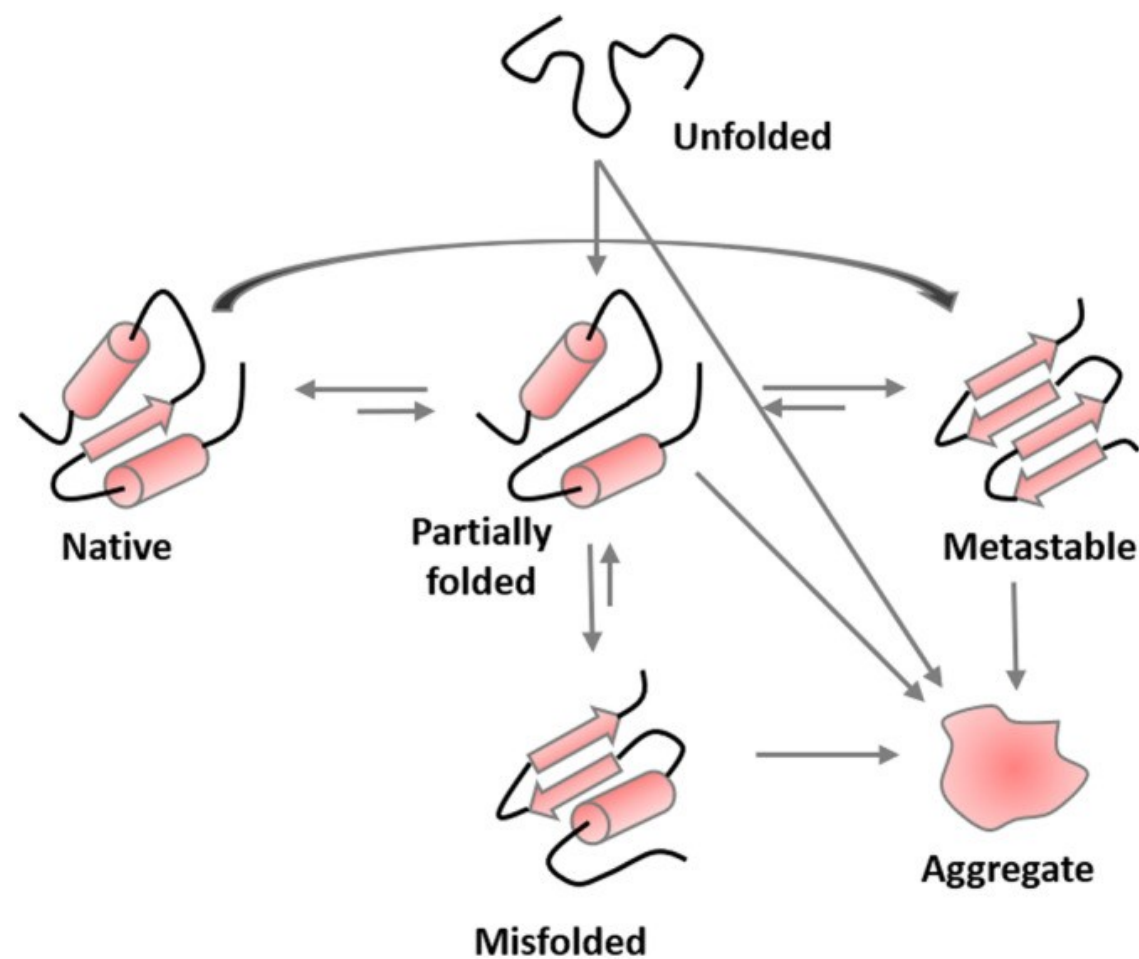
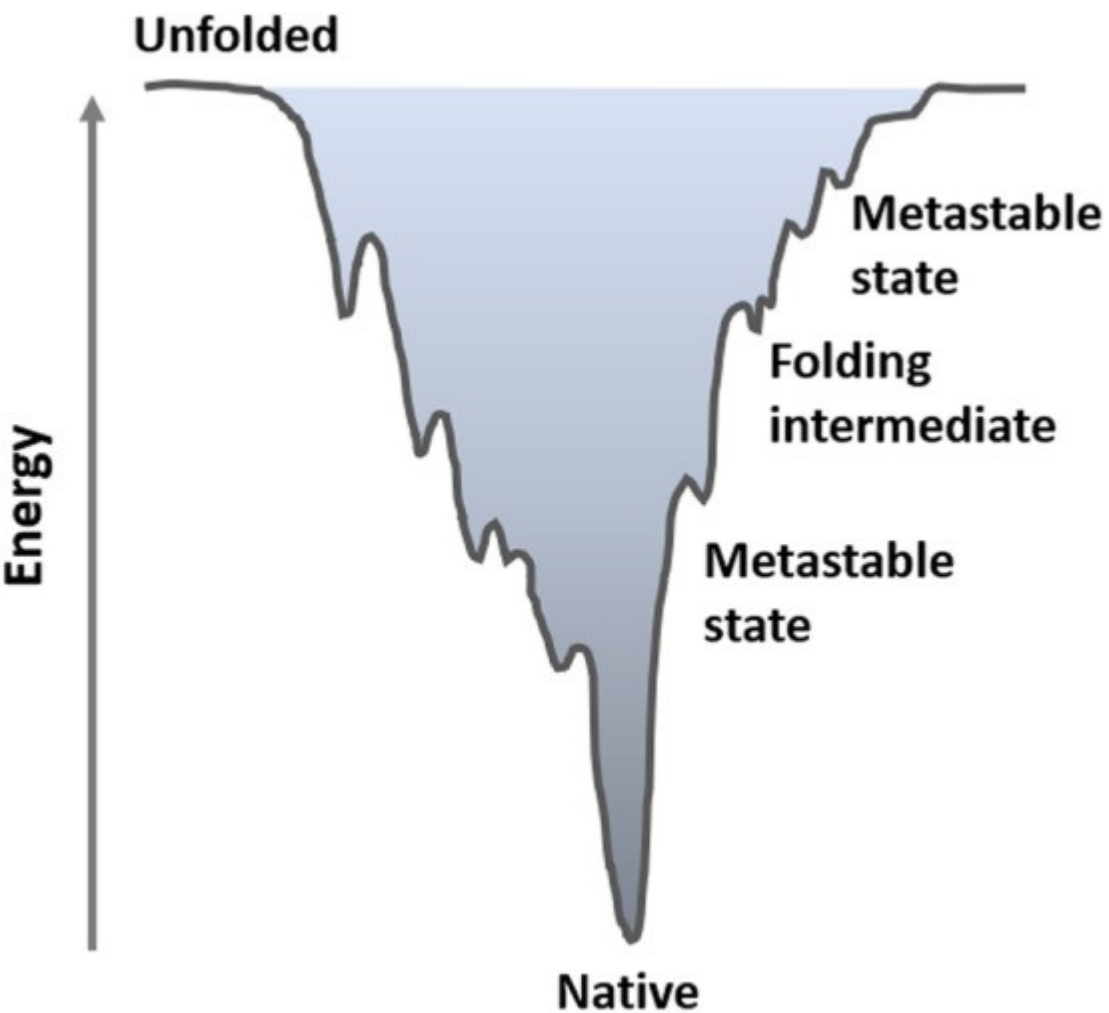
Οι θερμοφιλικές πρωτεΐνες αποτελούν μια αποτελεσματική και αποδοτική λύση στο πρόβλημα που θέτει η ταυτόχρονη διαχείριση της λειτουργίας των πρωτεϊνών και η διατήρηση της σταθερότητάς τους.

Η λειτουργικότητα και η σταθερότητα είναι πράγματι αλληλένδετες, η σταθερότητα προάγει την εξελικτικότητα

η αυξημένη σταθερότητα των θερμοφιλικών πρωτεϊνών καθιστά πράγματι αυτό το είδος πρωτεϊνών ένα μοναδικά αποτελεσματικό σκελετό για την εξέλιξη της λειτουργίας των πρωτεϊνών.

Οι θερμοφιλικές πρωτεΐνες θα είναι πιθανώς ο σκελετός επιλογής για τους μηχανικούς πρωτεϊνών του μέλλοντος.

Energy landscape of different folded structures of protein.



metastable structure

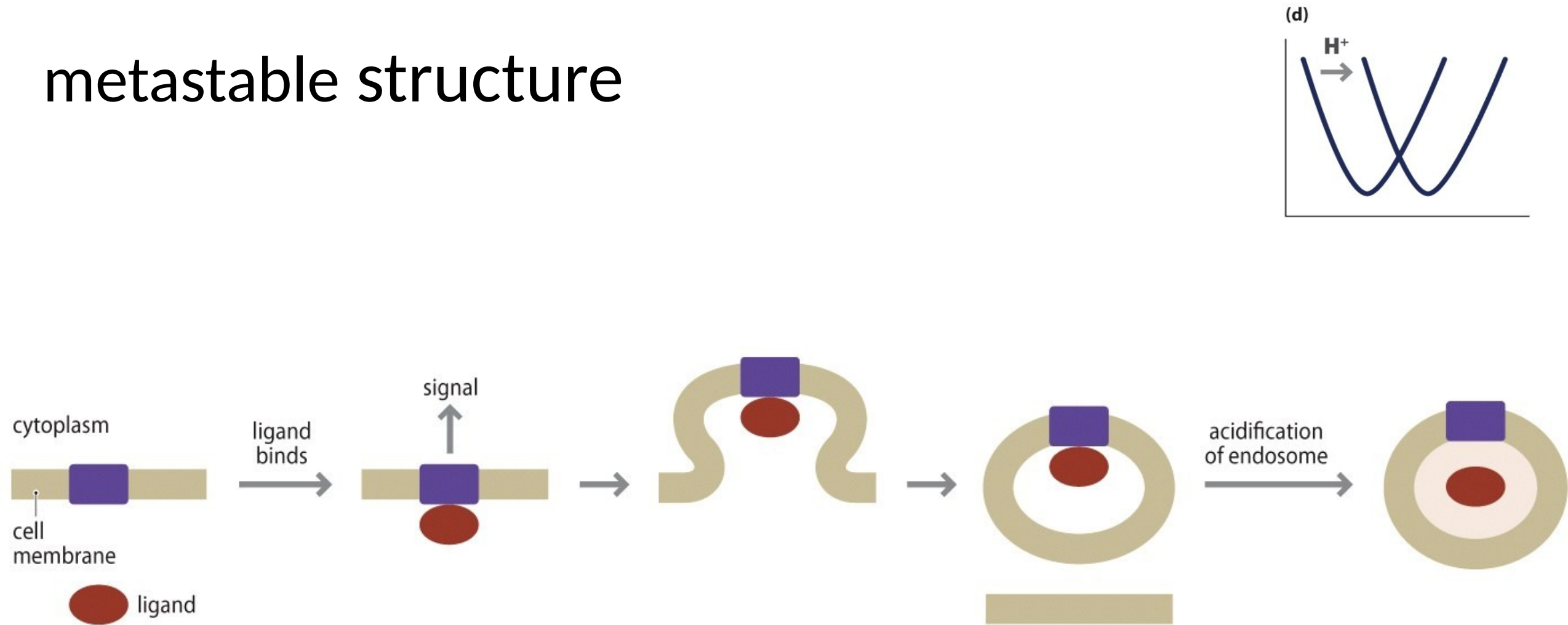


Figure 1.46 How Proteins Work (©2012 Garland Science)

metastable structure

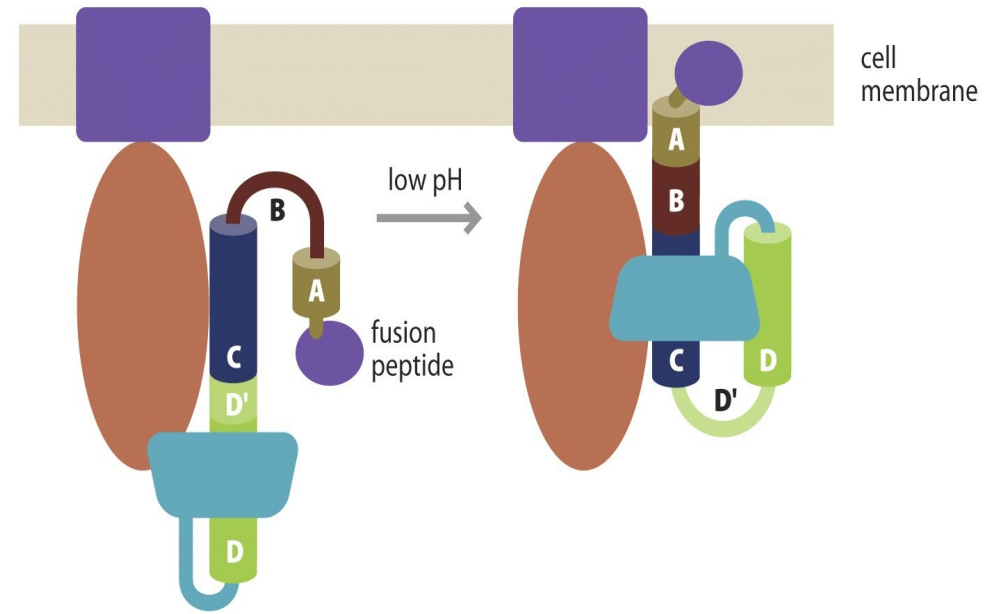
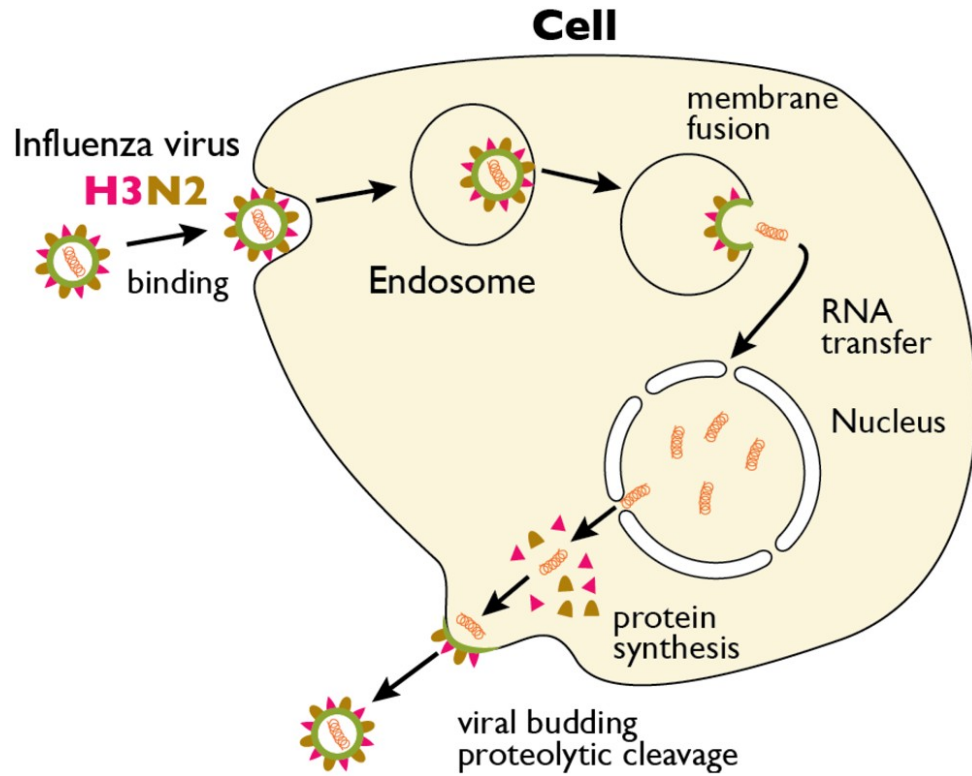
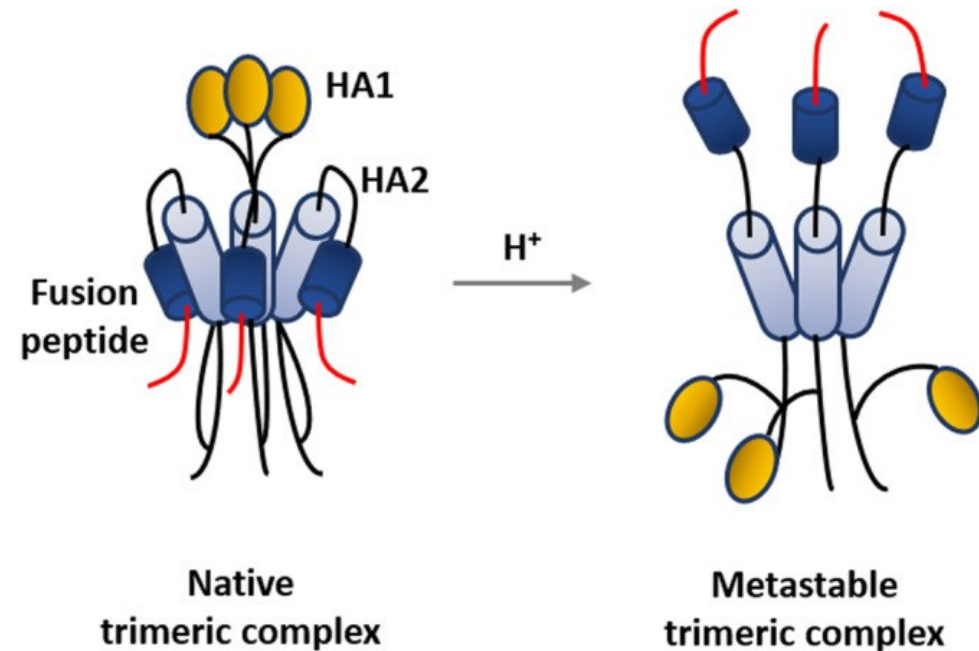


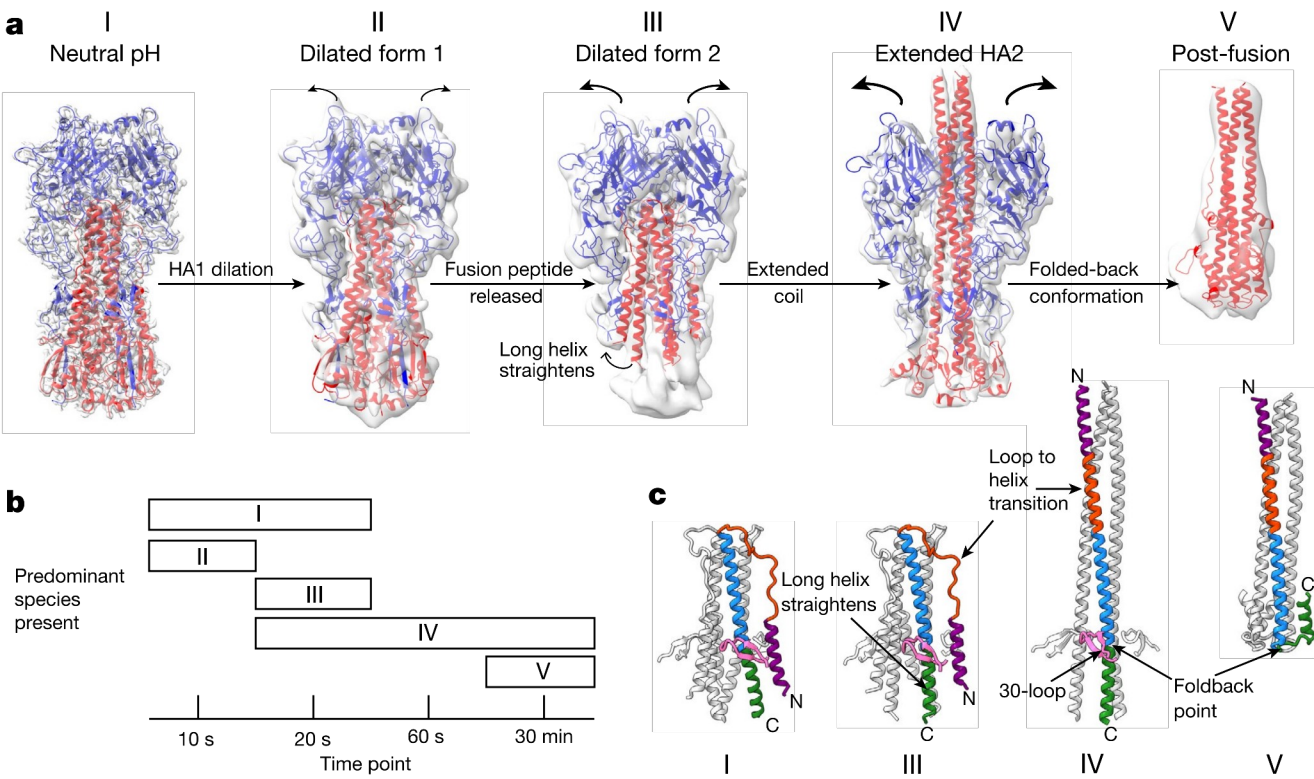
Figure 1.47 How Proteins Work (©2012 Garland Science)

Hemagglutinin, part of viral coat

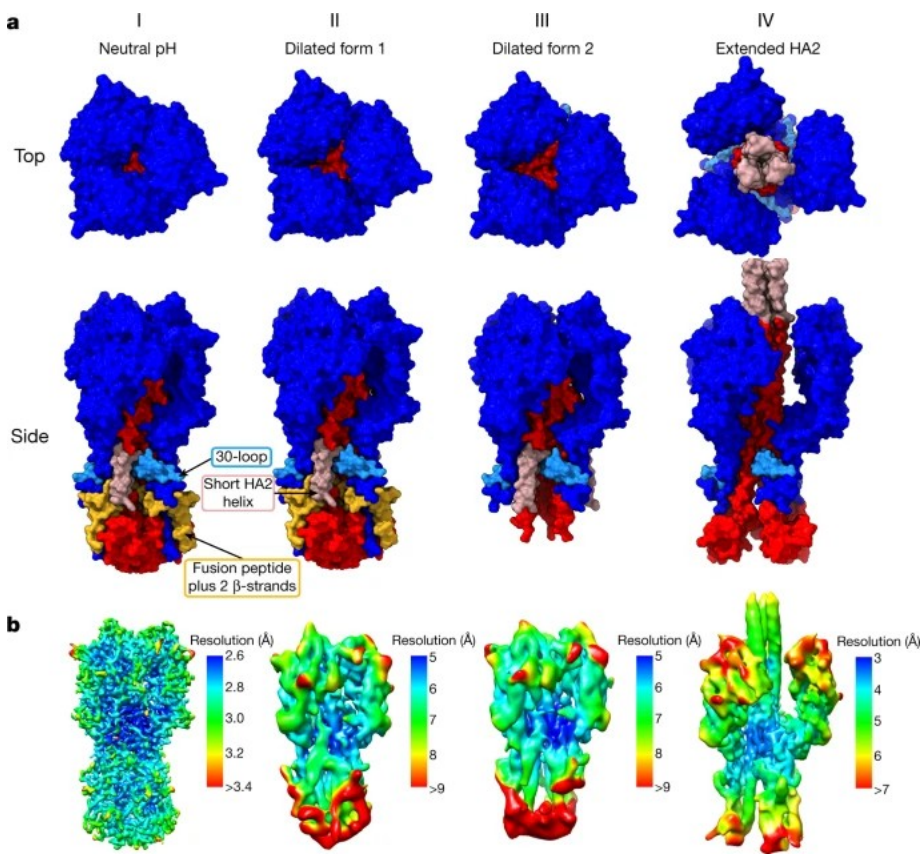


Structural transitions in influenza haemagglutinin at membrane fusion pH

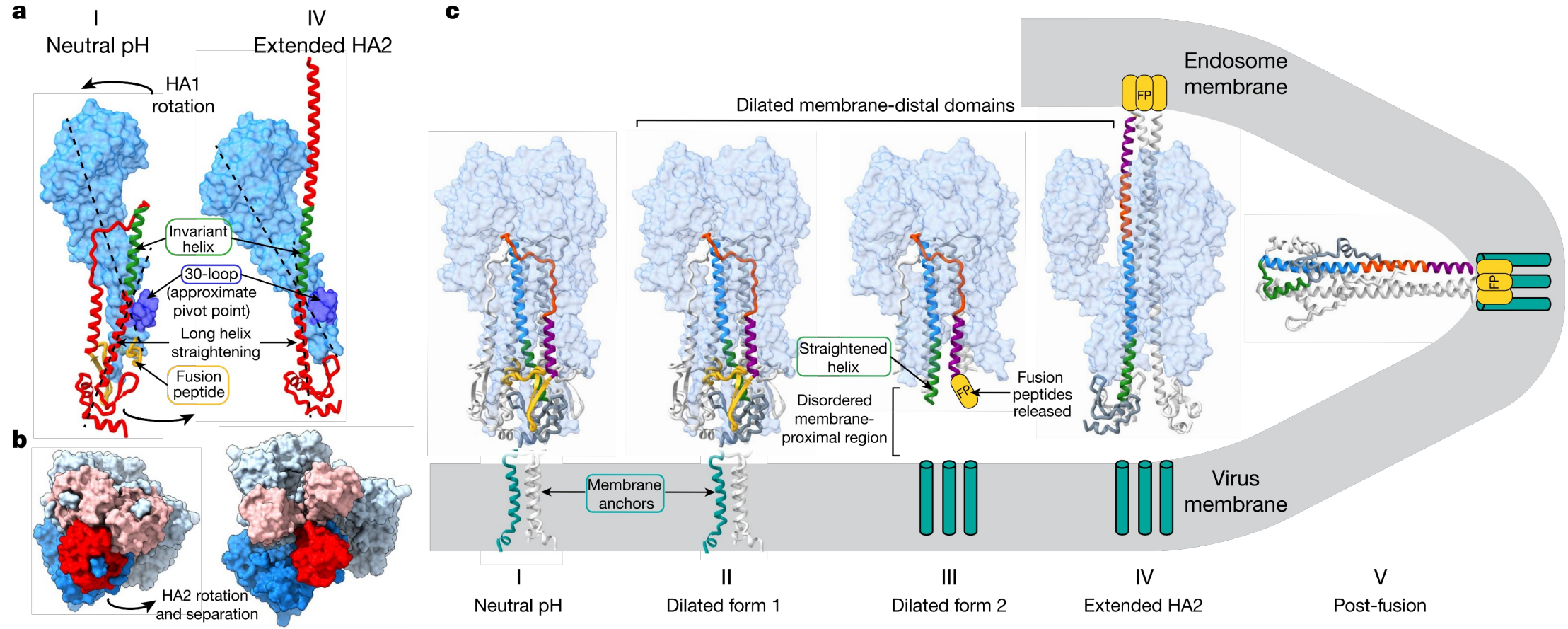
HA fusion intermediates.



Surface representations of HA fusion intermediates

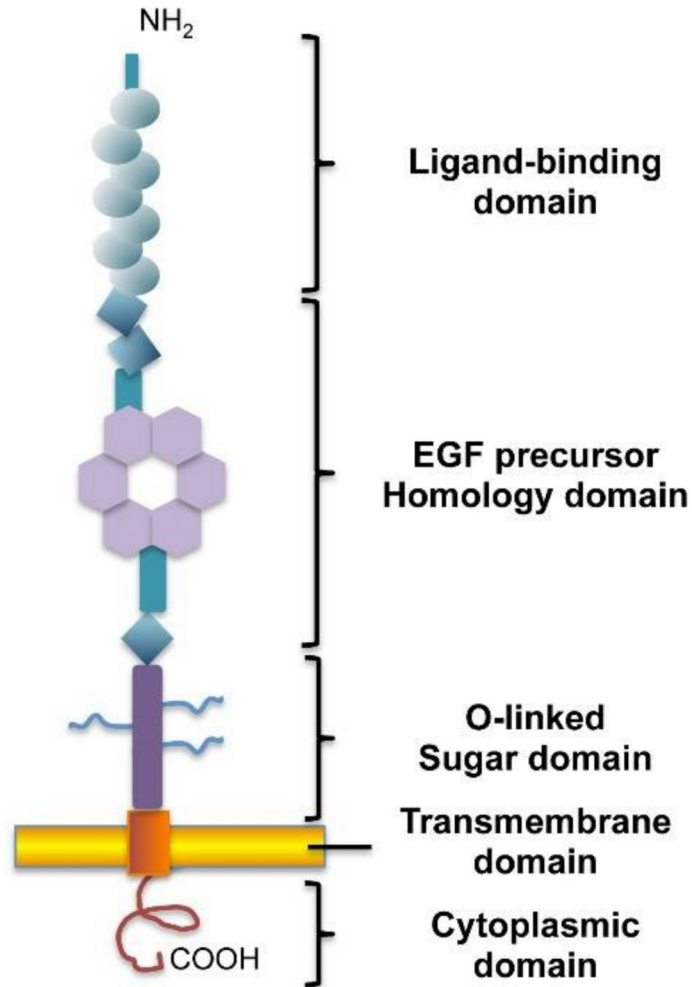


Structural rearrangements of HA fusion intermediates

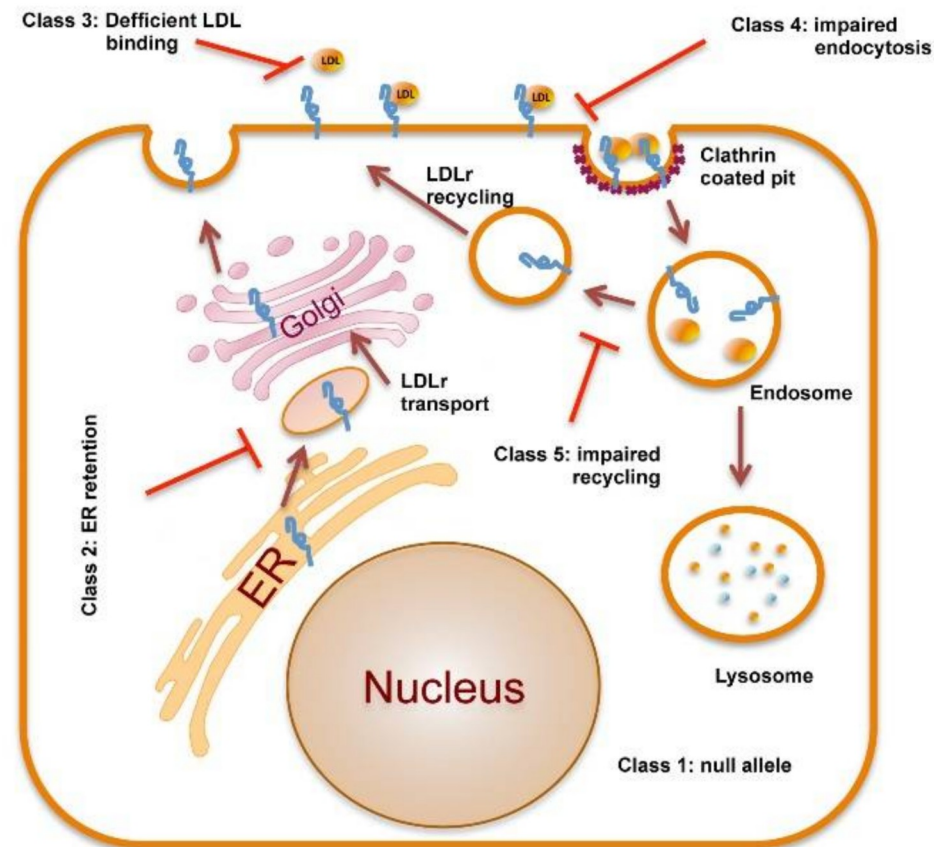


metastable structure

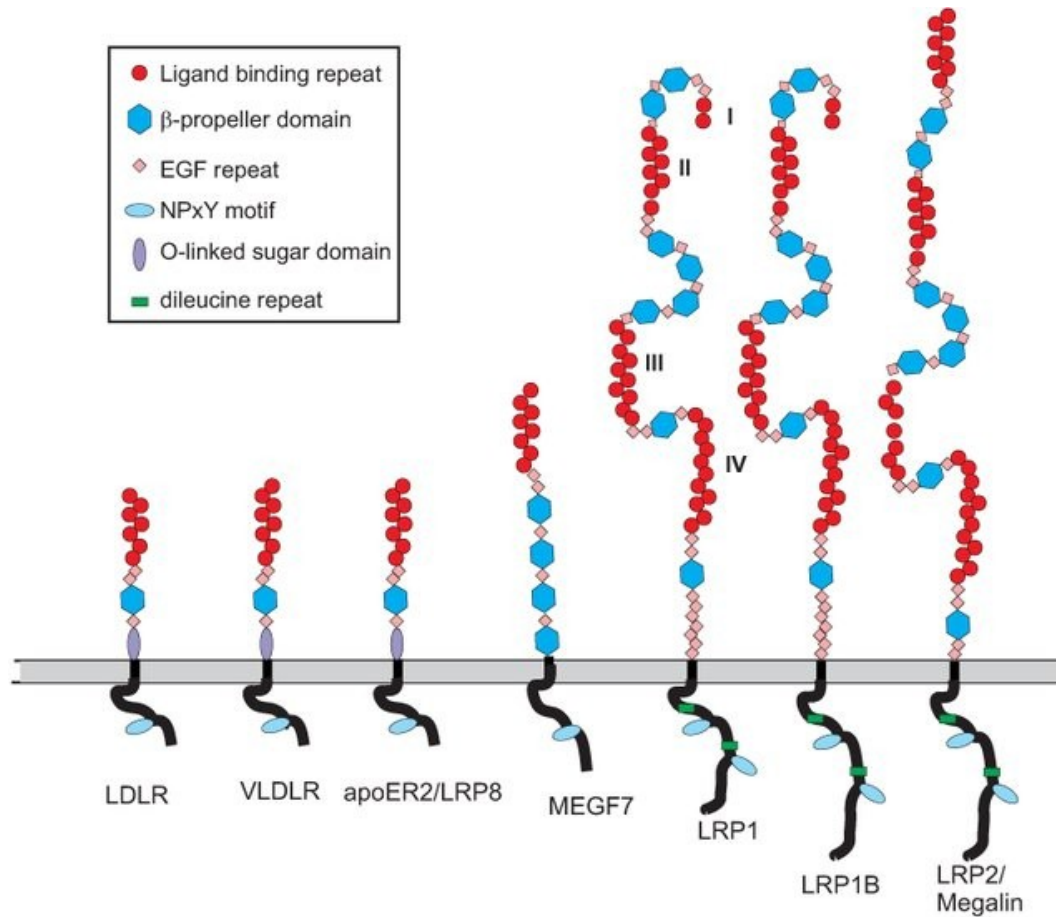
A) LDL receptor



B) LDLr pathway and its dysregulation



metastable structure



Modular domain organization of LDL receptor family members In LRP1, the four clusters of complement-type repeats are numbered I – IV.

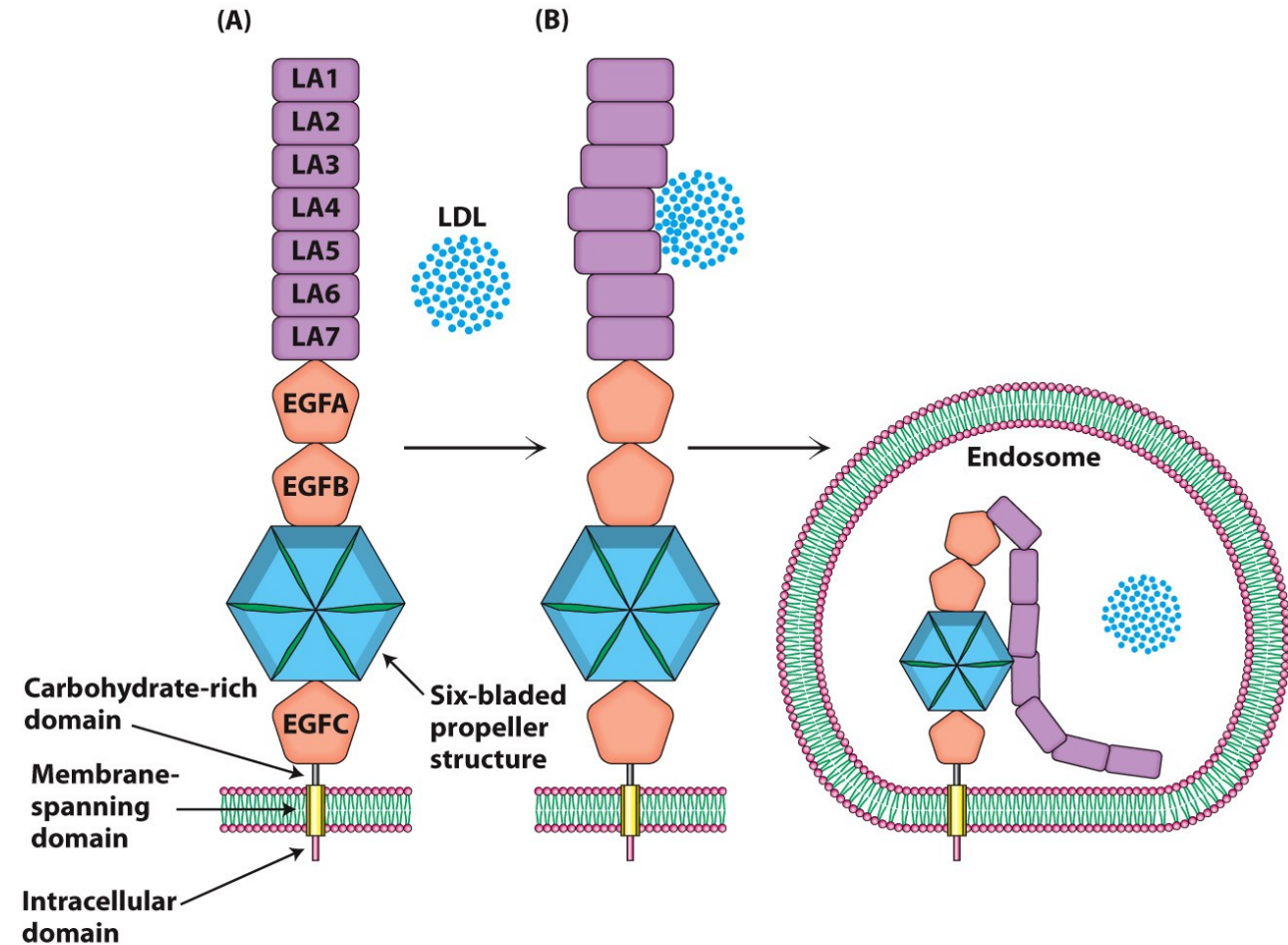
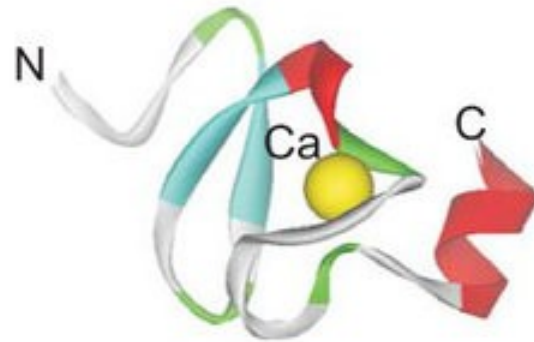


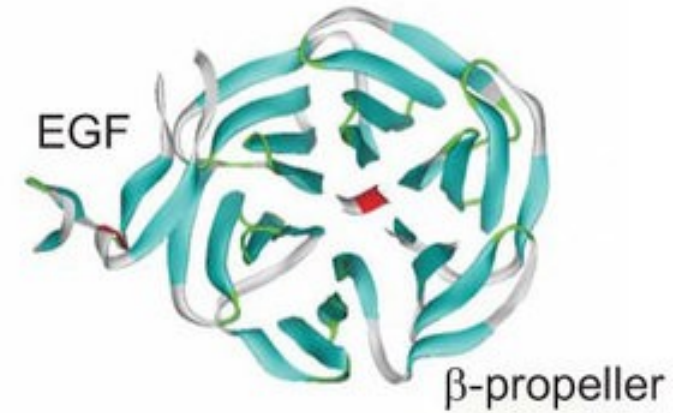
Figure 26.22
Biochemistry, Eighth Edition
© 2015 Macmillan Education

metastable structure

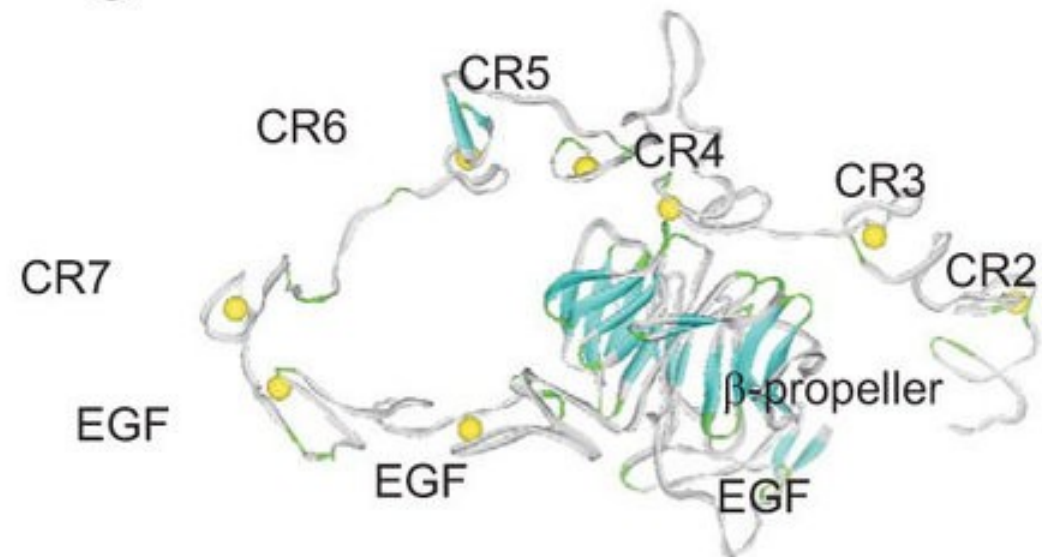
A



B



C



structure conservation

TABLE 1.3 Evolutionary rates of proteins

Protein	Rate ^a
Histone H4	0.0025
Histone H1	0.13
Cytochrome c	0.07
Insulin	0.07
Triosephosphate isomerase	0.05
Hemoglobin β	0.3
Snake short neurotoxin	1.3
Immunoglobulin IgG (V)	1.4

^aThe rate is quoted as amino acids per 100 residues altered per million years. (Data taken from A.C. Wilson, S.C. Carlson and T.J. White, *Annu. Rev. Biochem.* 44:573–639, 1977.)

sequence alignment

Chymotrypsin

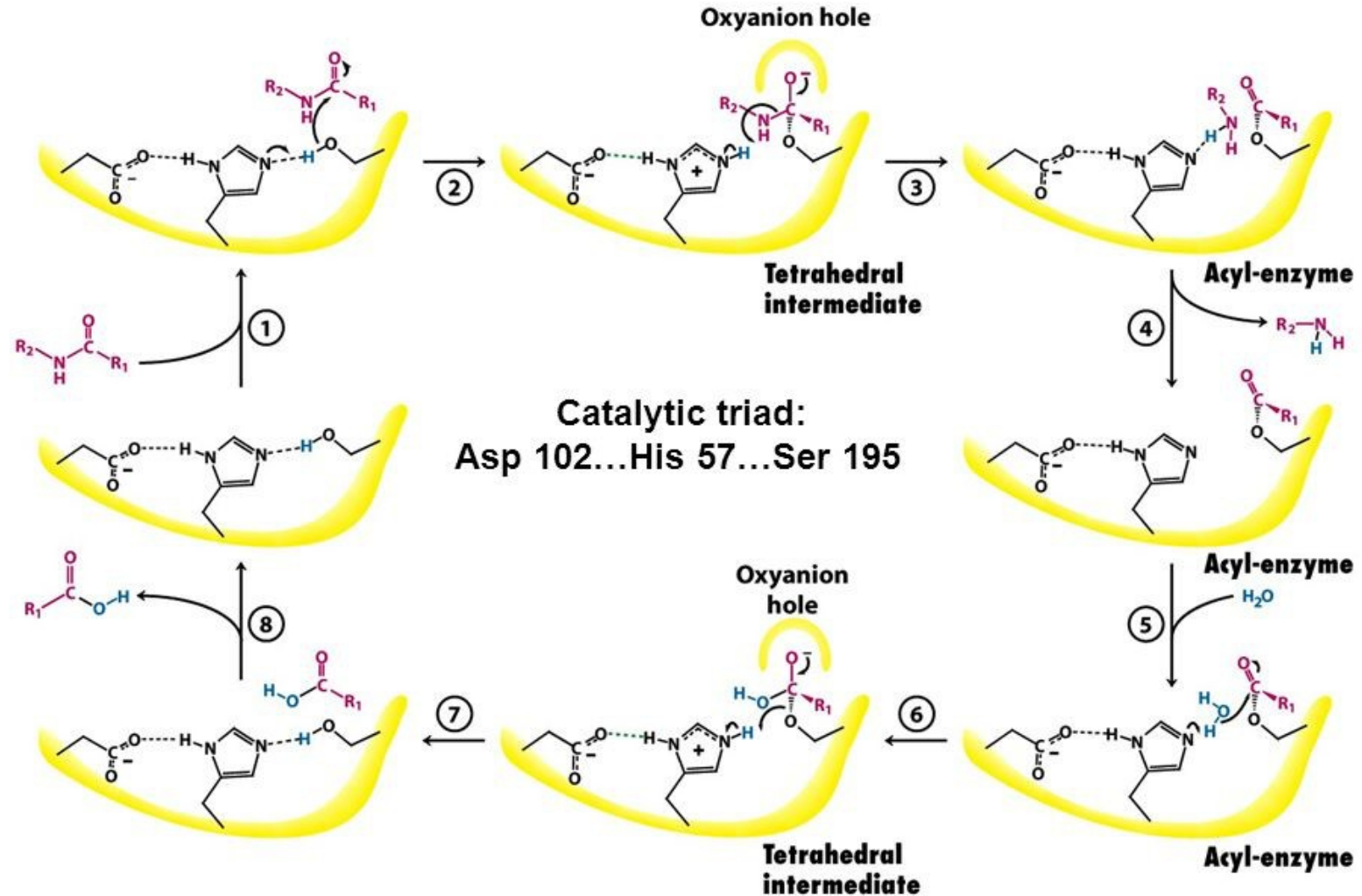
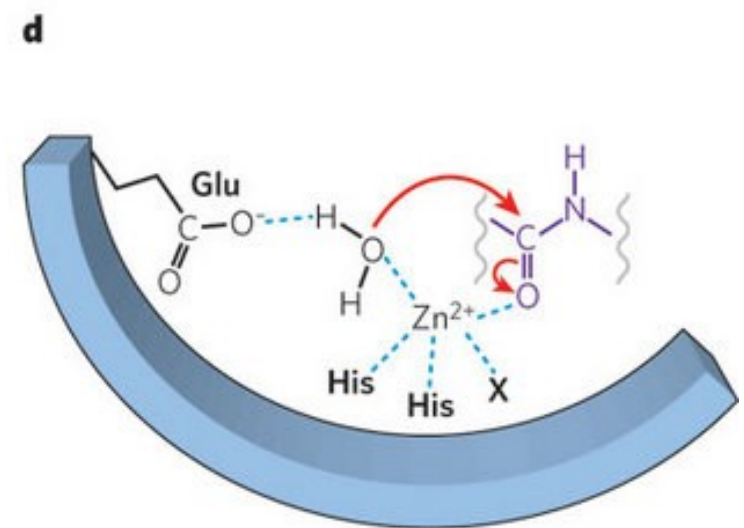
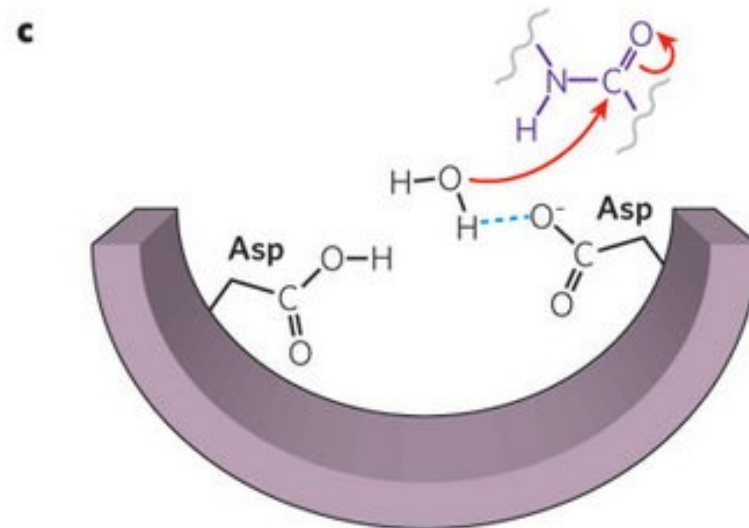
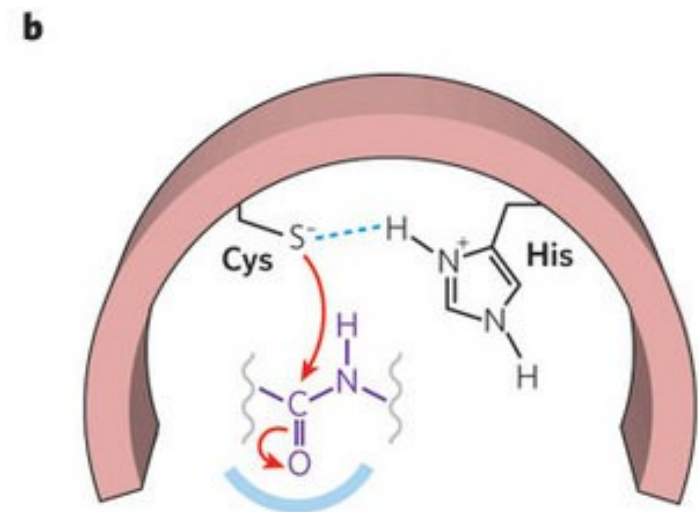
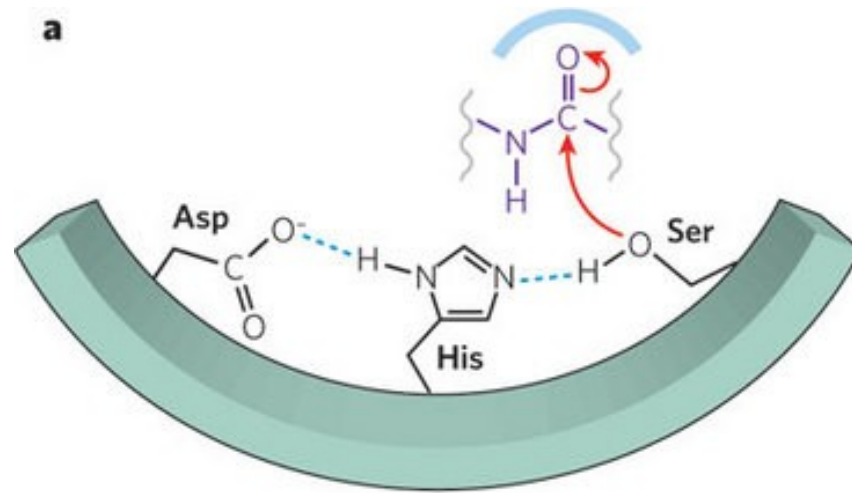


Figure 9-8
Biochemistry, Sixth Edition
© 2007 W. H. Freeman and Company

Protease



sequence alignment

score = 108 bits (271), expect = 8e-29, method: compositional matrix adjust
identities = 84/239 (35%), positives = 120/239 (50%), gaps = 24/239 (10%)

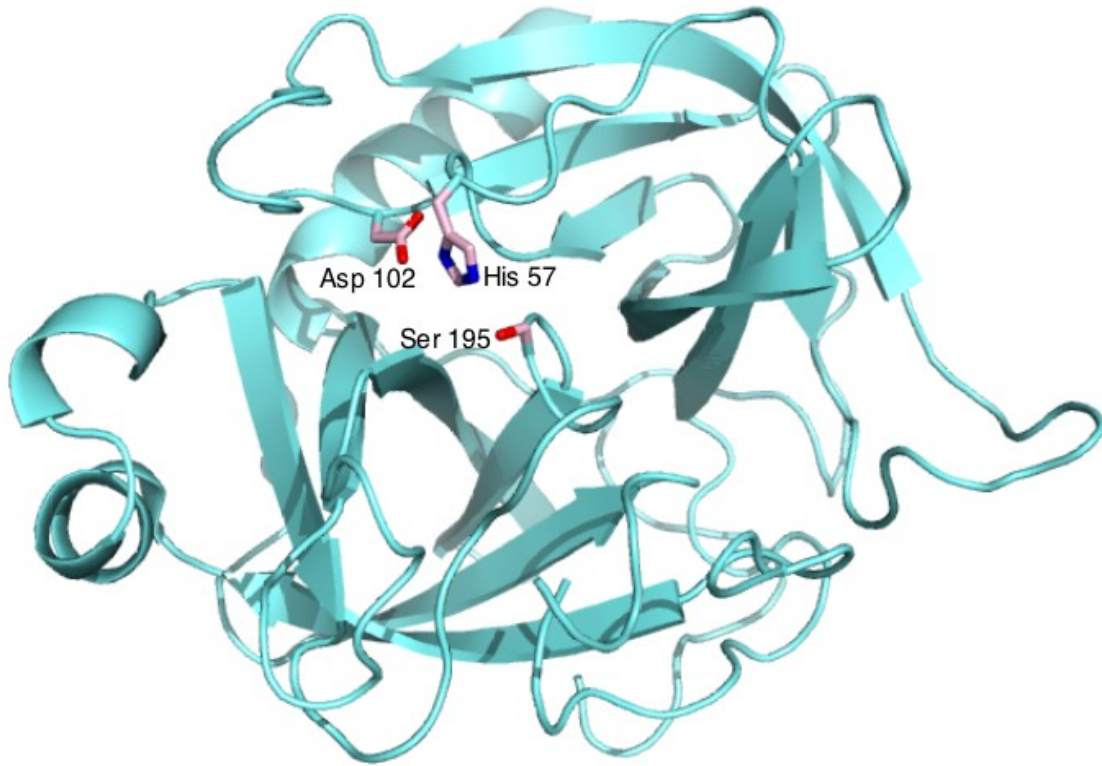
Bovine chymotrypsin

Human neutrophil elastase

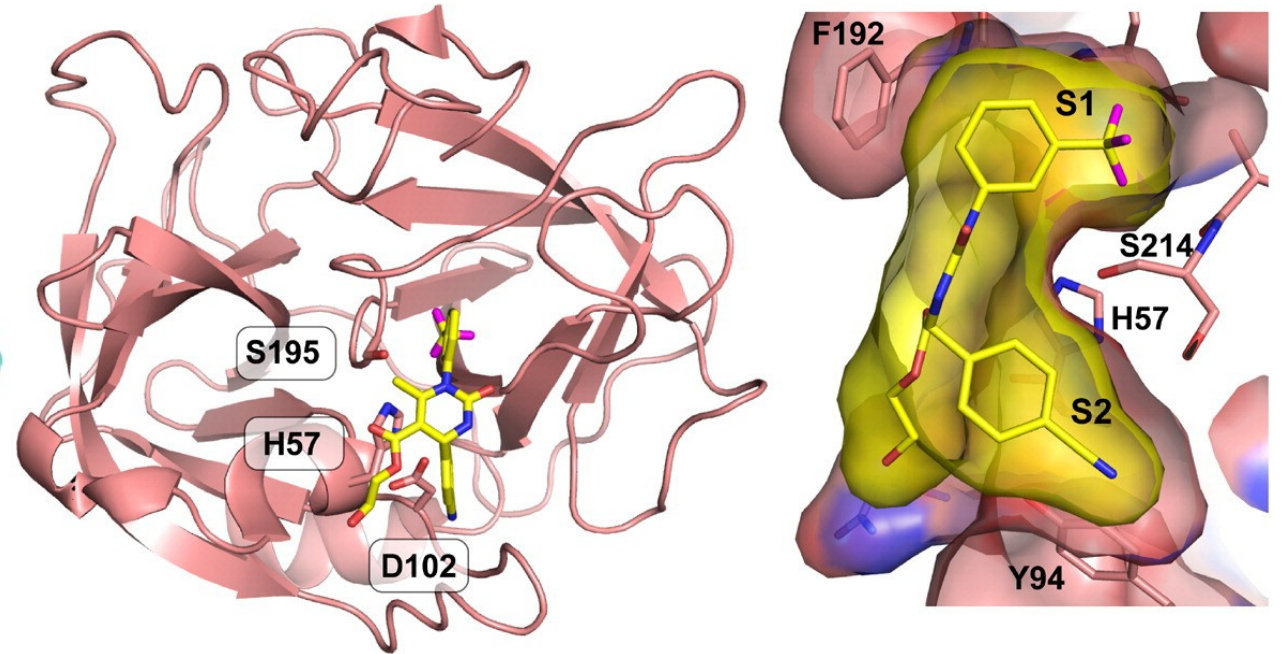
Query	1	VGGEDAIPHSWPWQISLQYLRDNTWRHTCGGTLITPNHVLTAAH	CISNTLT	YRVA--LGK	58
		VGG A PH+WP+ +SLQ LR H CG TLI PN V++AAHC++N V LG			
Sbjct	1	VGGRRARPHAWPFMVSLQ-LRGG---HFCGATLIAPNFVMSAAH	CVANVNVRAVRVVLGA		56
Query	59	NNLEVEDEAGSLYVGVDITFVHEKWNSFLVRND	I ALIKLAETVELSDTIQVACLPEEGSL		118
		+NL + ++ V IF ++ + NDI +++L + ++ +QVA LP +G			
Sbjct	57	HNLSRREPTRQVFA-VQRIF-ENGYDPVNLLND	IVILQLNGSATINANVQVAQLPAQGRR		114
Query	119	LPQDYPCFVTGWGRLYTNGPIAAELQQGLQPVVDYATCSQRDWWGTTVKETMVCAGGDGV			178
		L C GWG L N IA+ LQ+ L V + C + + T+V GV			
Sbjct	115	LGNGVQCLAMGWGLLGRNRGIASVLQE-LNVTVVTSLCRRSNVC-----TLVRGRQAGV			167
Query	179	ISACNGD	SGGPLNCQAENGNDVRGIVSFGSGLSCNTFKKPTVFTRV	SAYIDWINQKLQ	237
		C GD SG PL C N + GI SF G C + P F V+ +++WI+ +Q			
Sbjct	168	---CFGD	SGSPLVC-----NGLIHGIASFVRG-GCASGLYPDAFAPVAQFVNWIDSIIQ		217

Figure 1.48 How Proteins Work (©2012 Garland Science)

sequence alignment



Human neutrophil elastase inhibitor complex

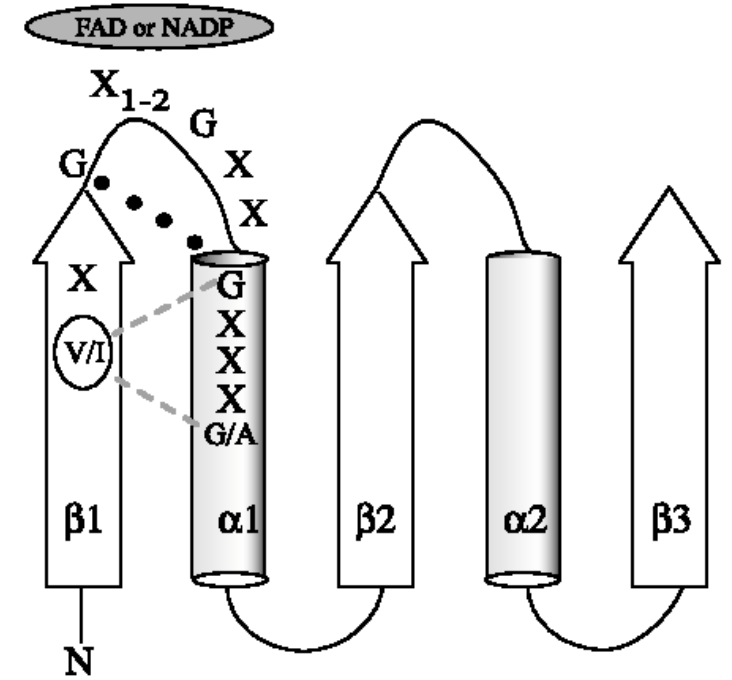
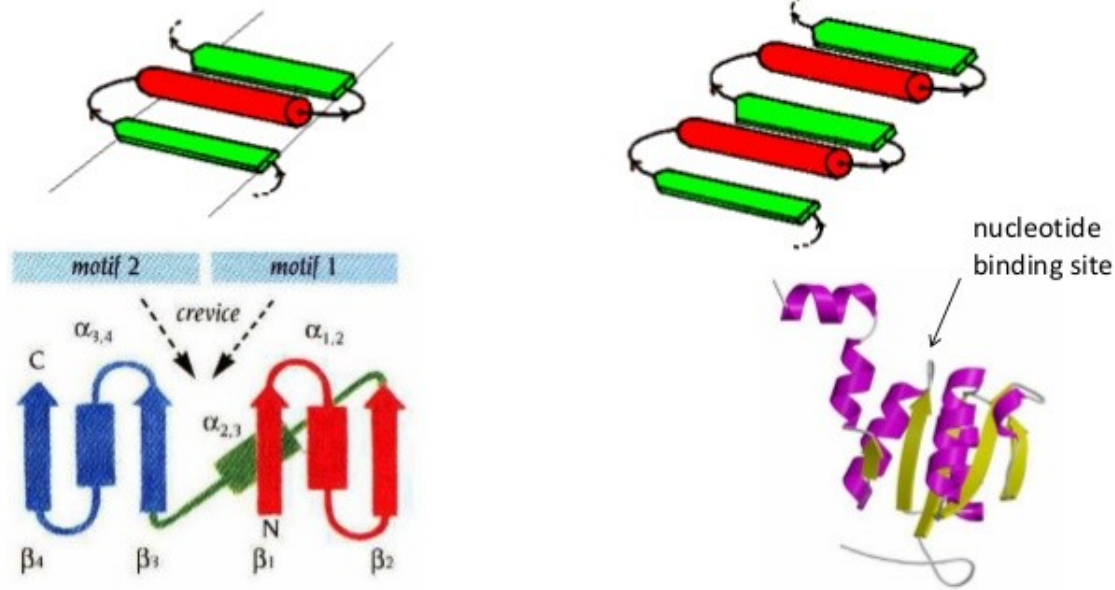


dihydropyrimidone inhibitor

sequence motif

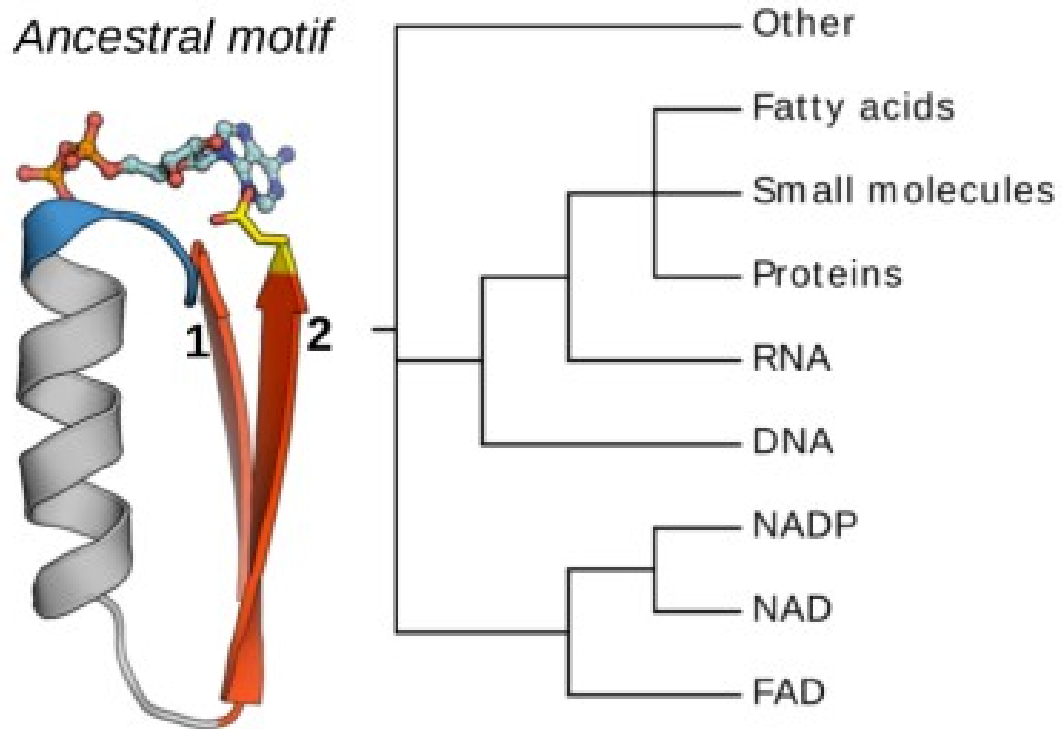
Rossmann Fold

Simple motifs can combine to generate more complex structures e.g. Rossmann fold (=2x $\beta\alpha\beta$ motif with the middle β shared between the two units) binds nucleotides.

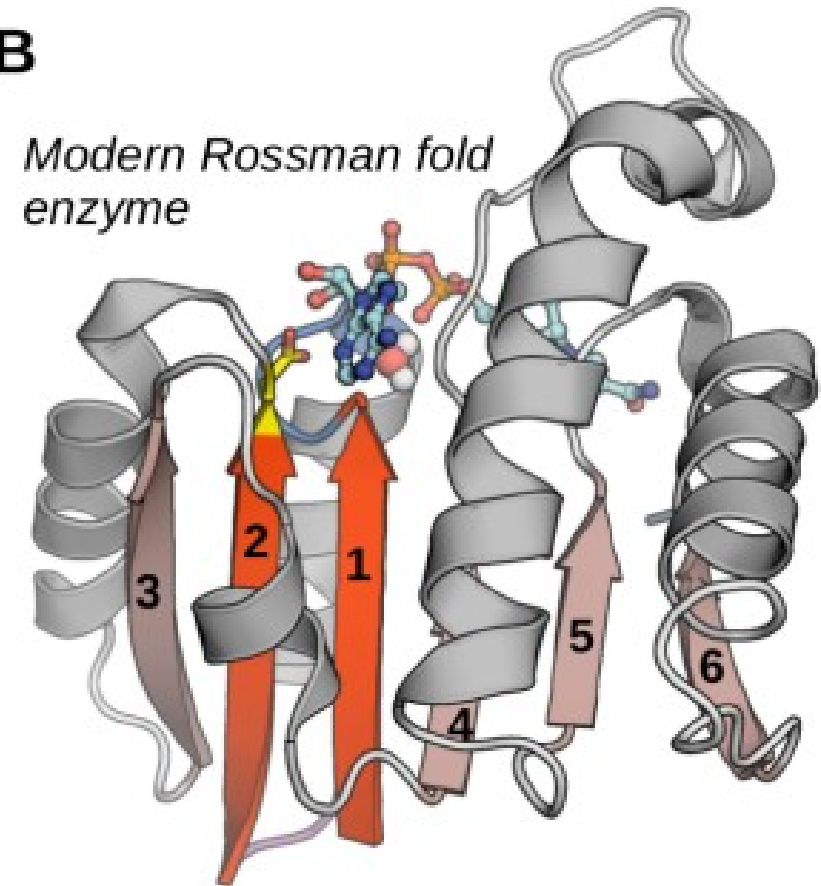


sequence motif

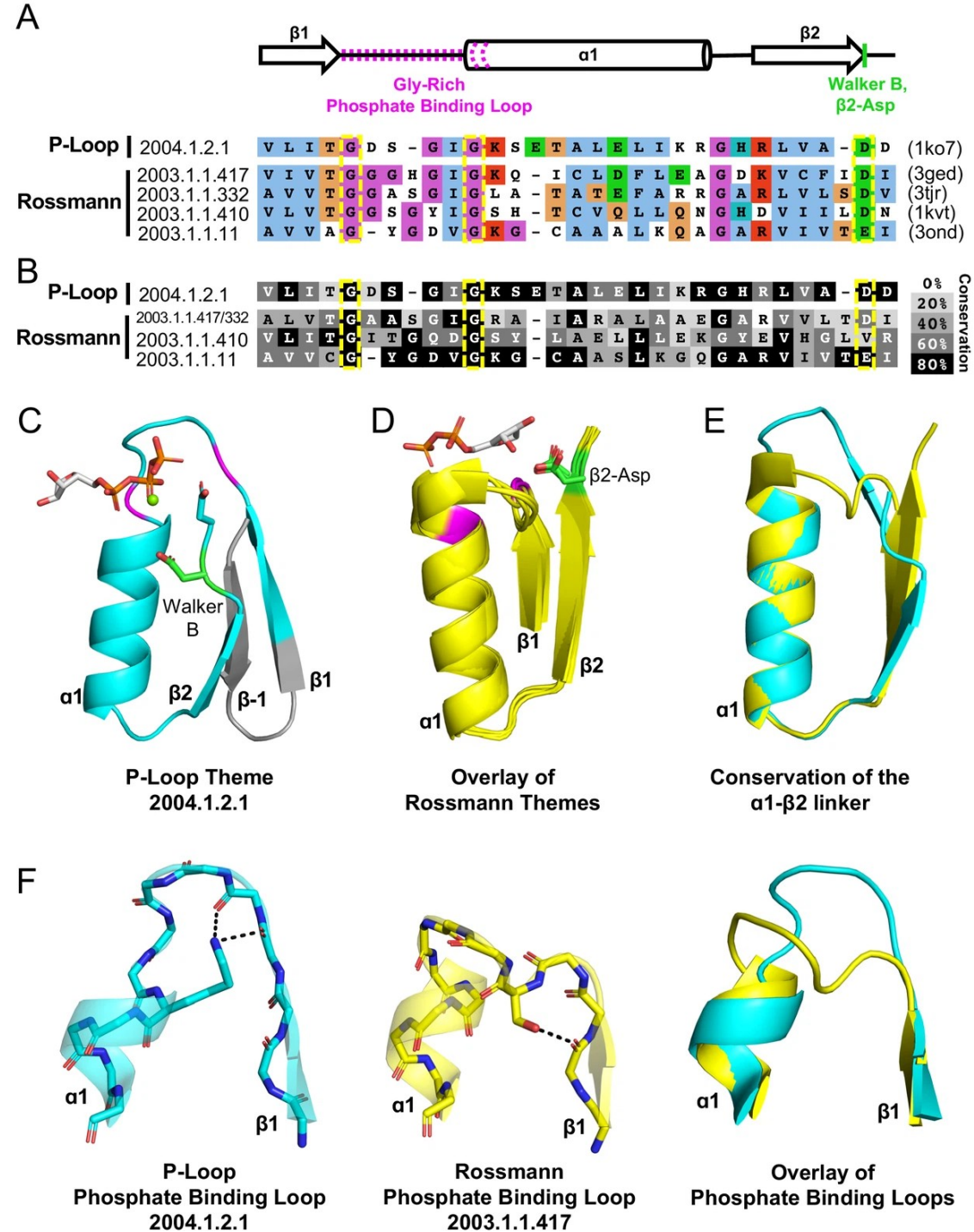
A



B



sequence motif



evolution of proteins

Evolution of cyt c

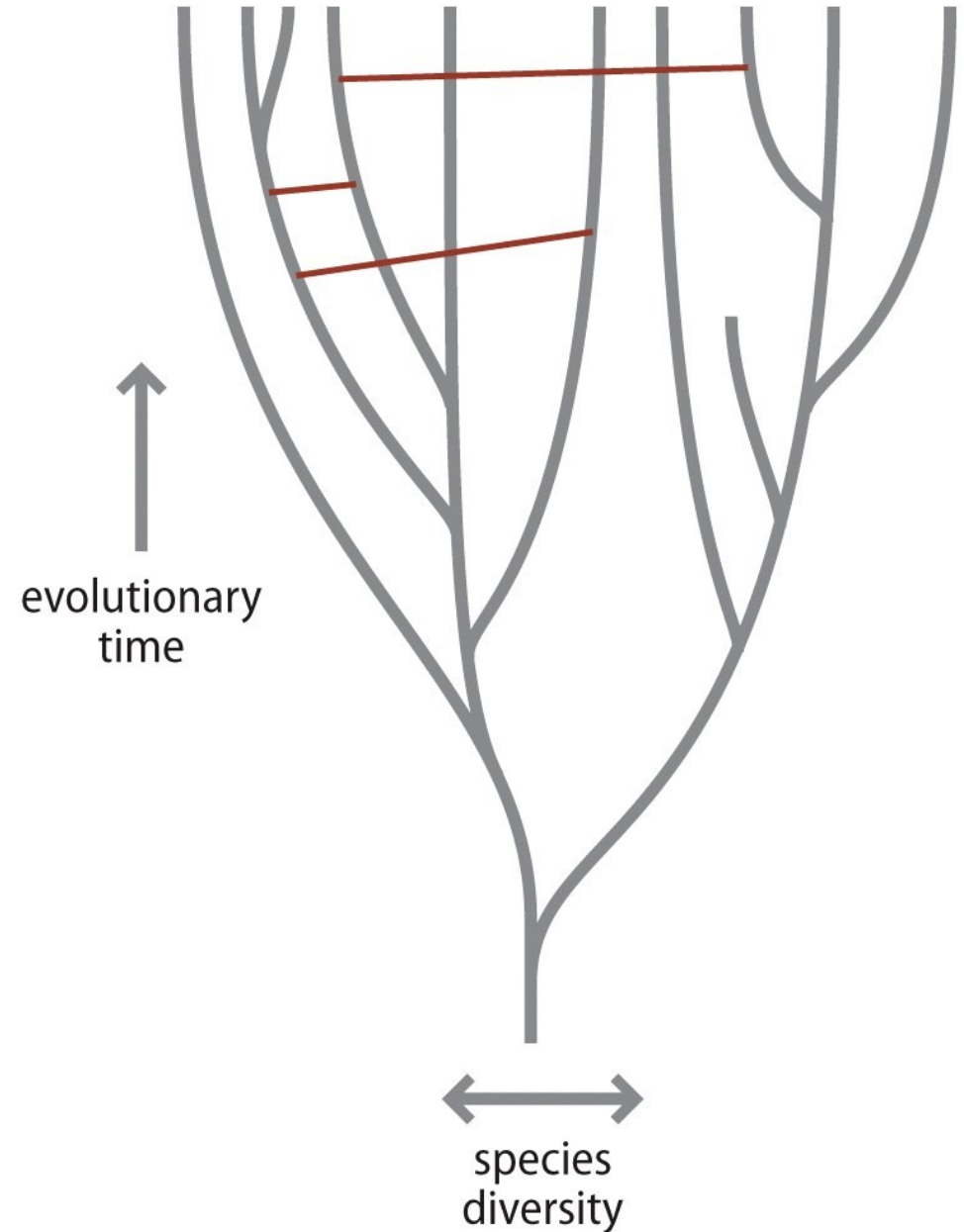
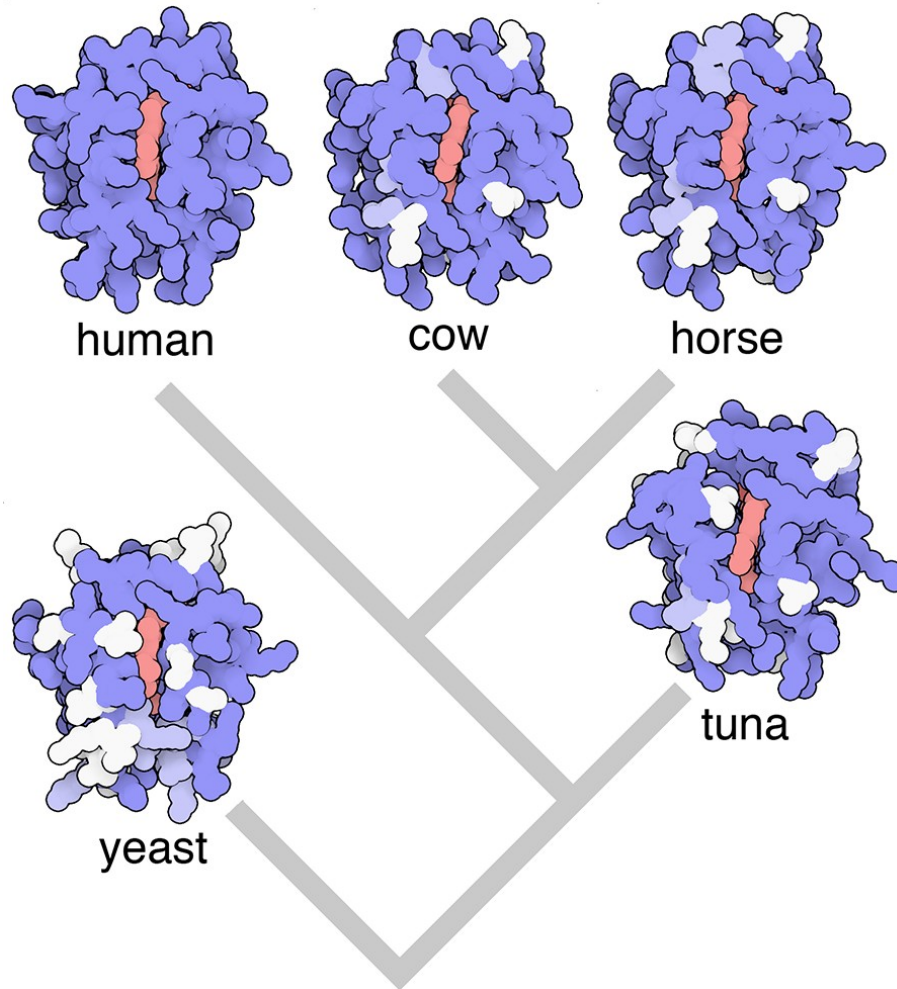


Figure 1.52 How Proteins Work (©2012 Garland Science)

structure conservation

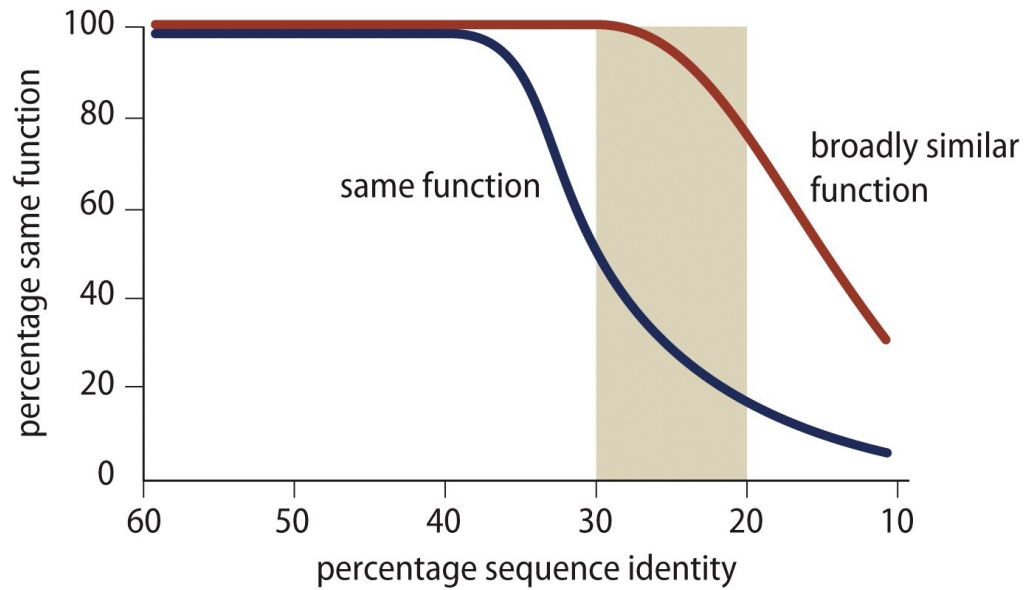


Figure 1.50 How Proteins Work (©2012 Garland Science)

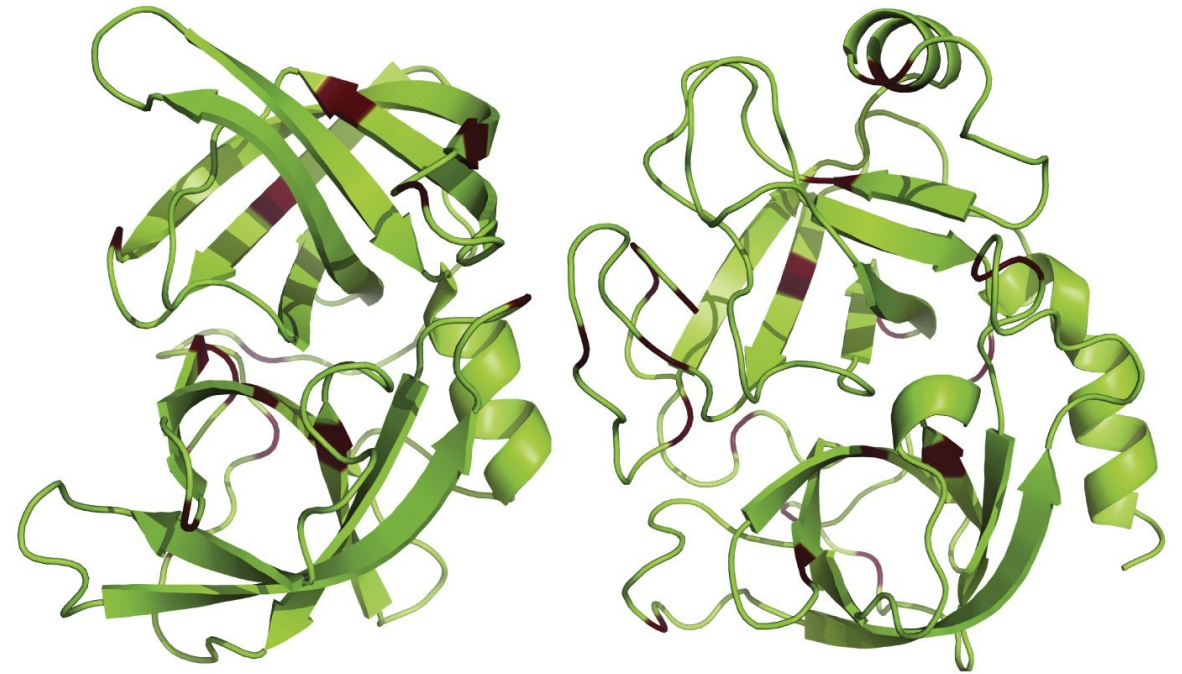


Figure 1.49 How Proteins Work (©2012 Garland Science)

Protease B
Streptomyces griseus

β -trypsin
Bovine

homologous recombination

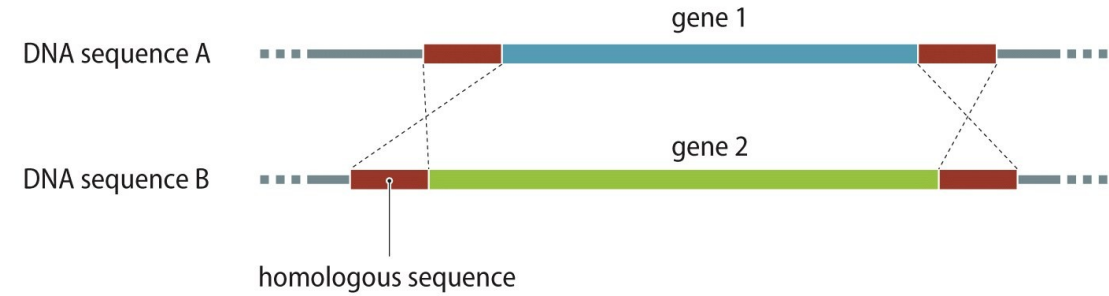
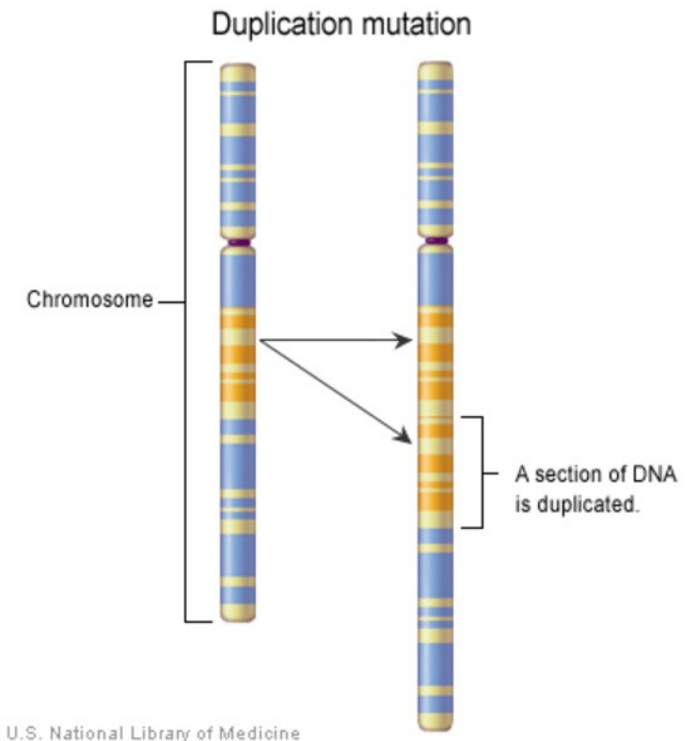
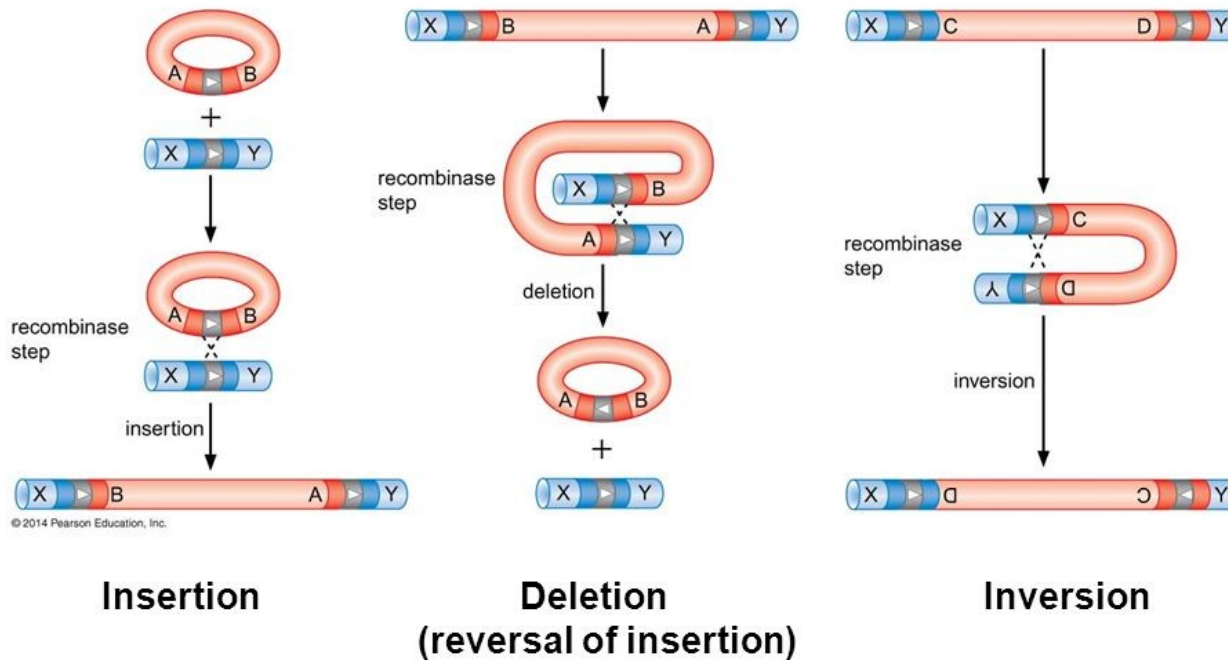


Figure 1.17.1 How Proteins Work (©2012 Garland Science)

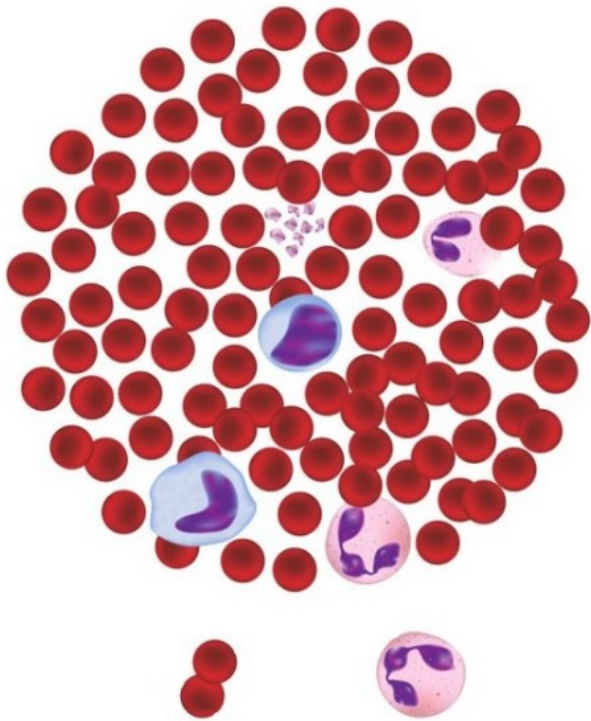
Site-specific recombination either integrates, deletes, or reverses a DNA sequence



homologous recombination

Chronic Myeloid Leukemia

Normal Blood



Erythrocytes

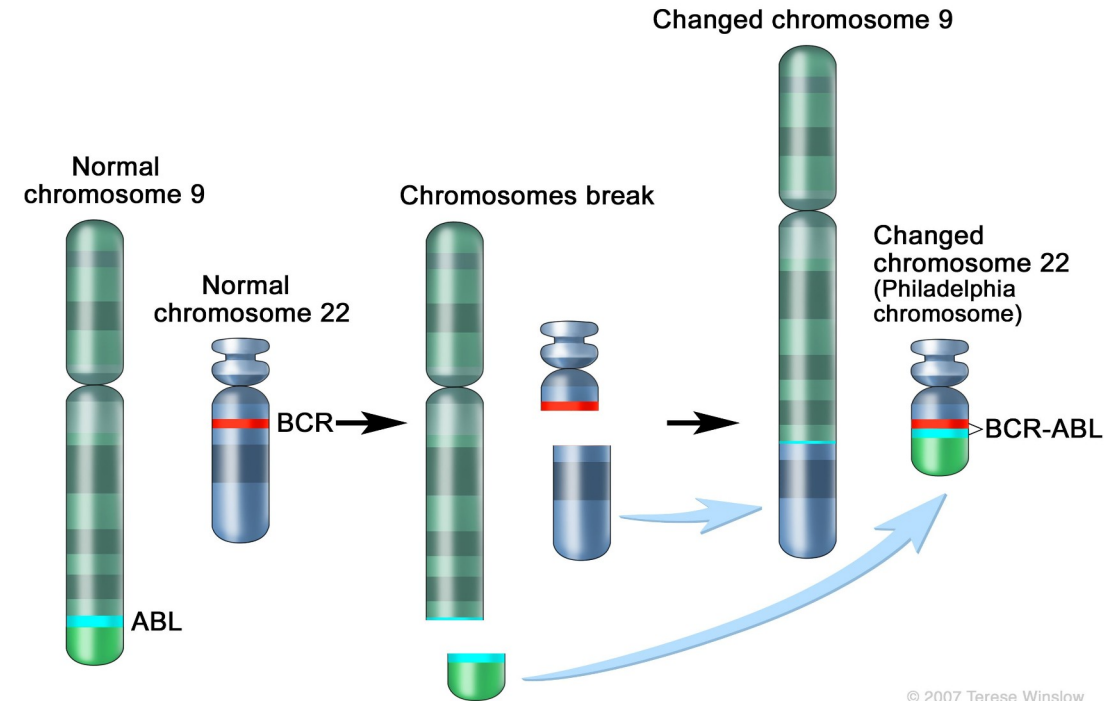
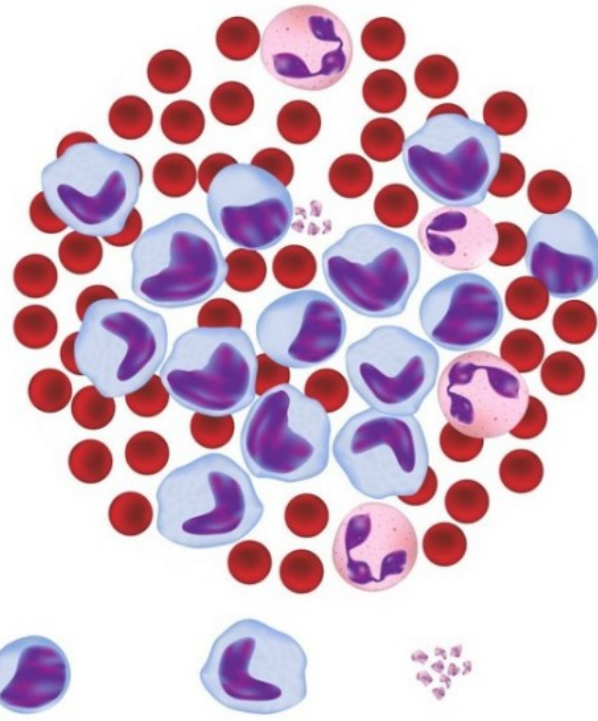
Neutrophil

Lymphocyte

Monocyte

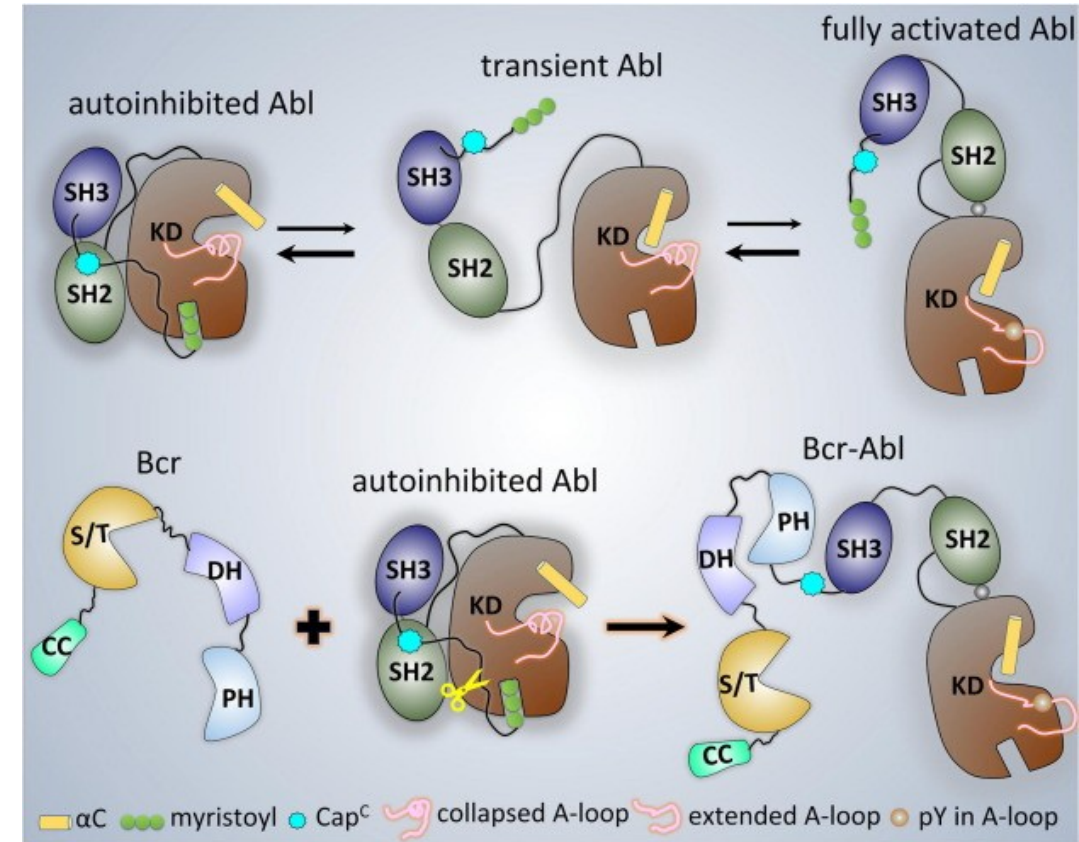
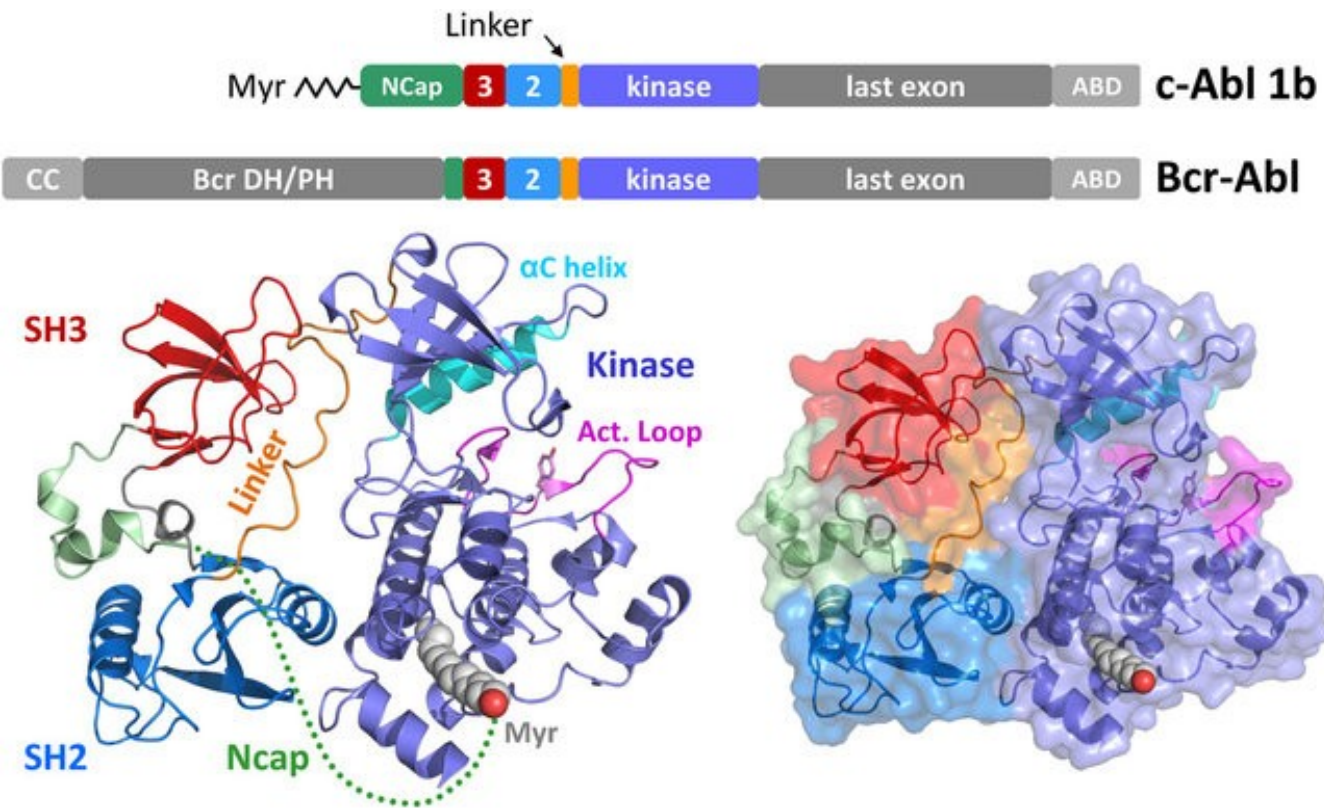
Platelets

Leukemia

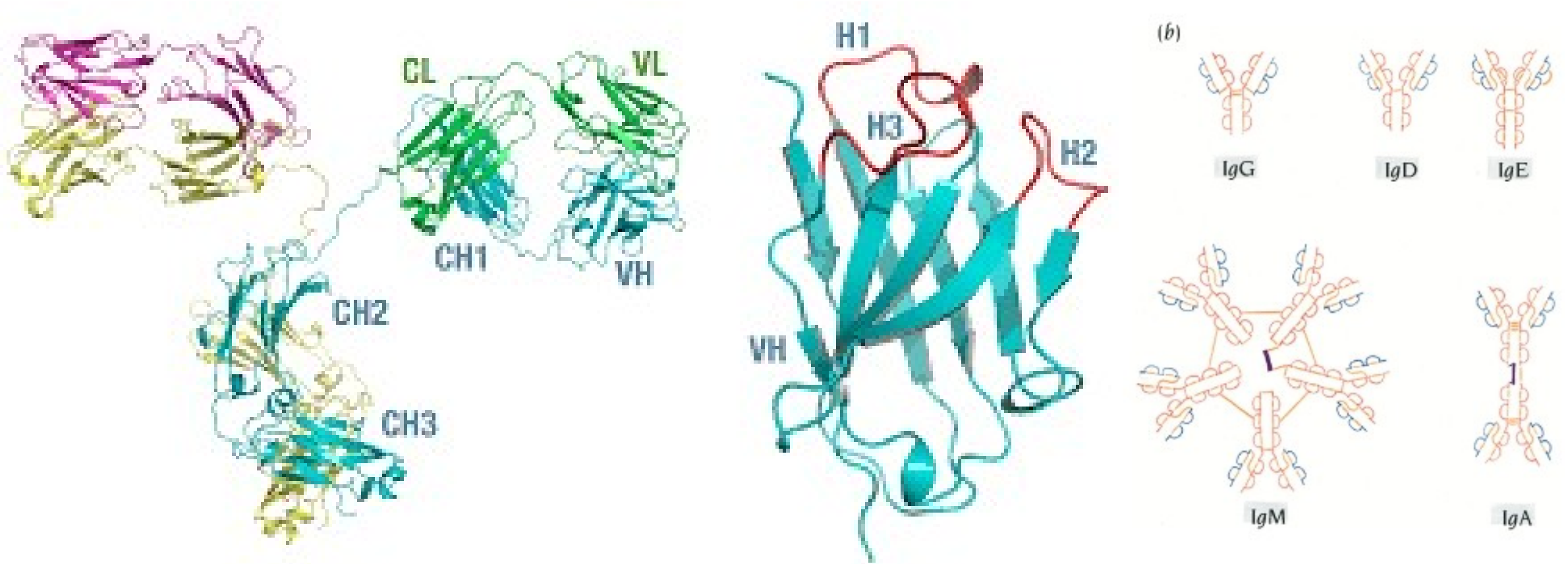


homologous recombination

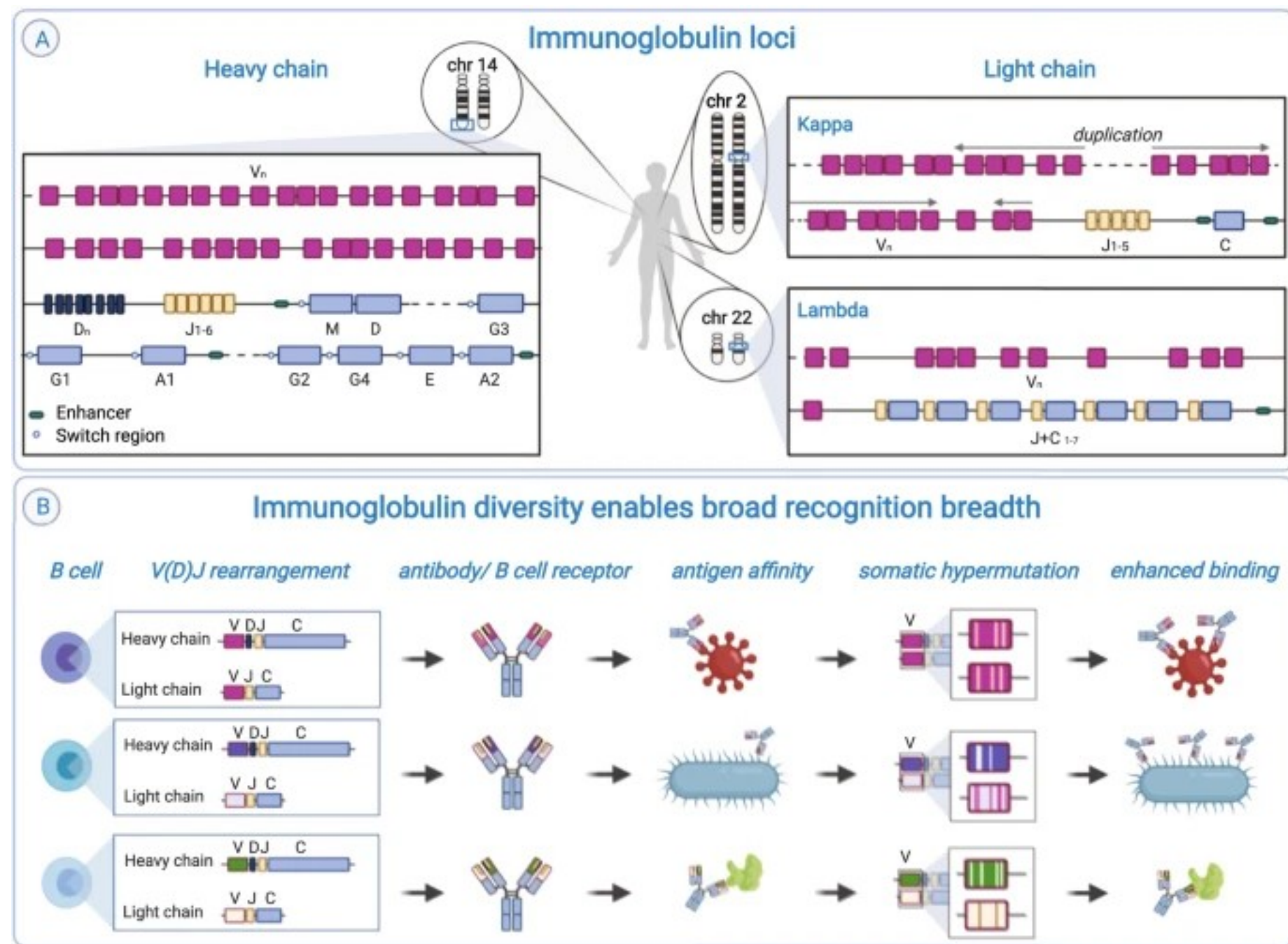
Chronic Myeloid Leukemia



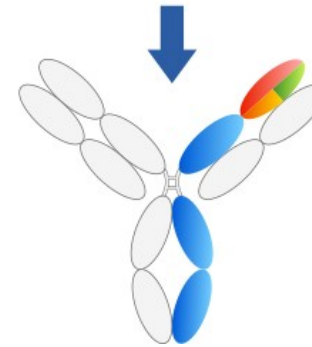
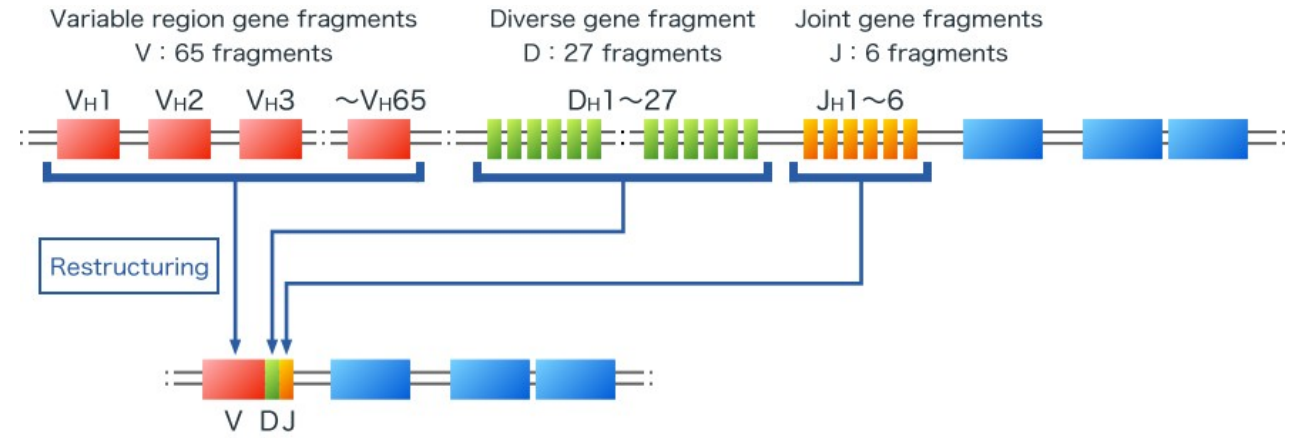
insertion and deletions-antibodies



Antibodies



Diversity of antibodies

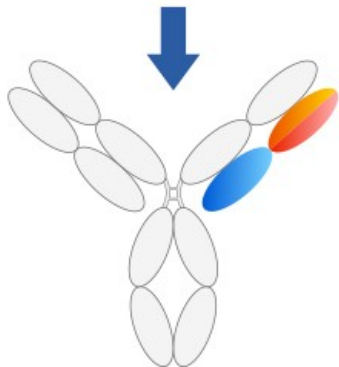
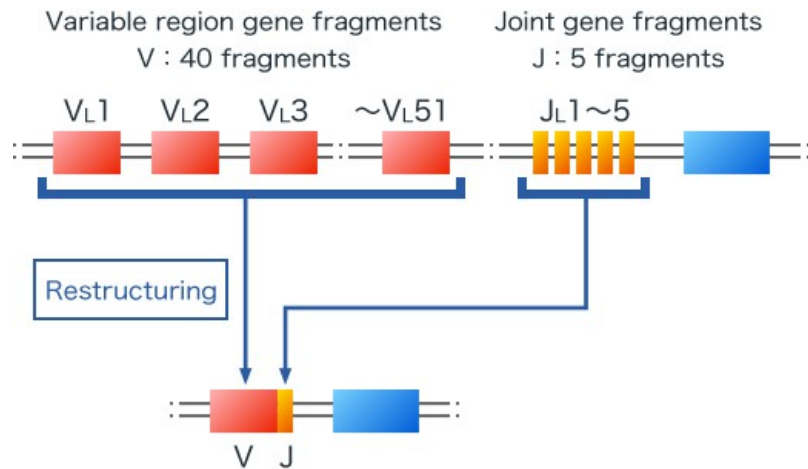


Types of antibodies produced by genes in restructured H chain variable regions

$$65 \times 27 \times 6 = 10,530 \text{ types}$$

fragments fragments fragments

* The figure above is an example of combinations related to diversity



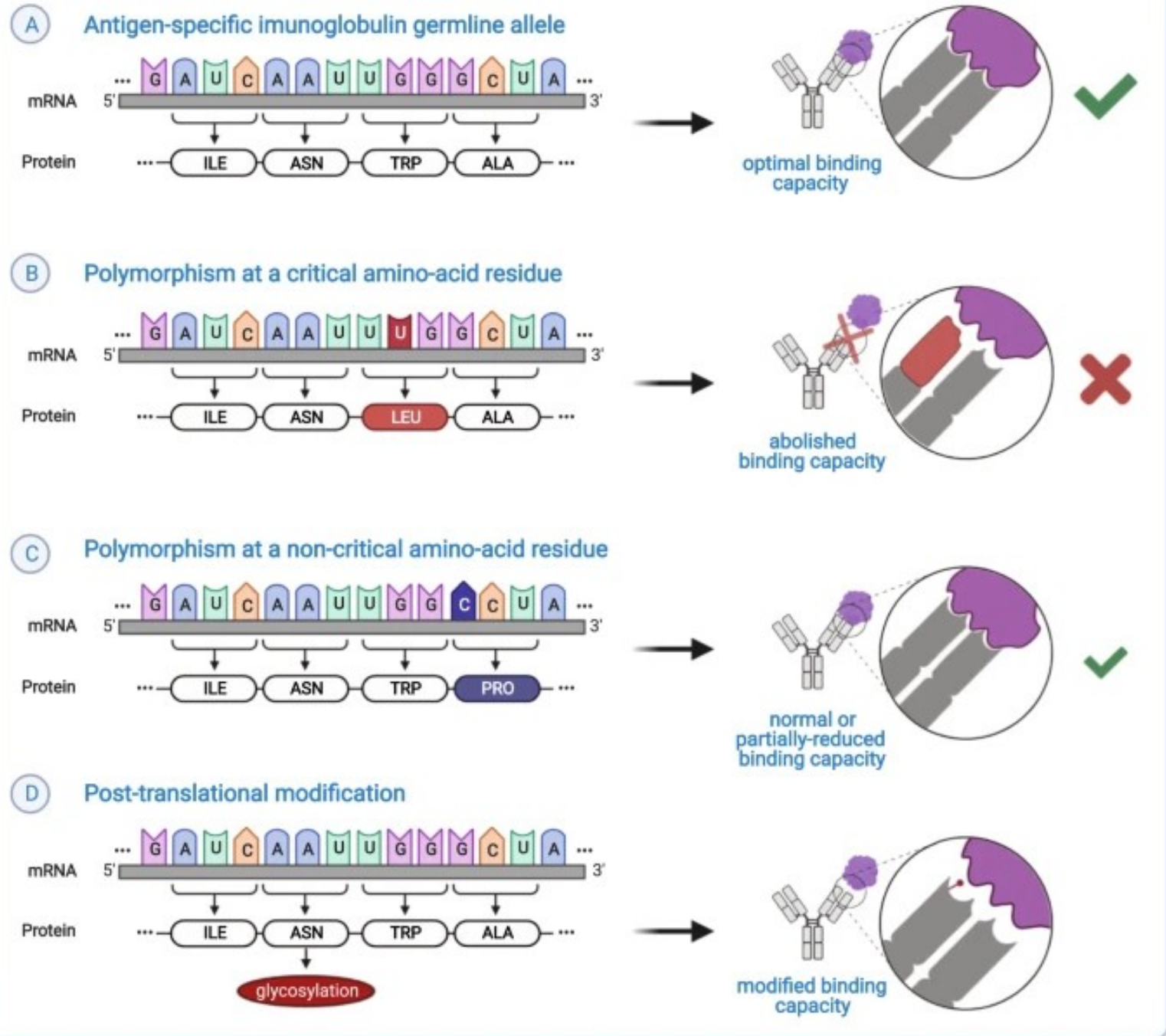
Types of antibodies produced by genes in restructured L chain variable regions

$$40 \times 5 = 200 \text{ types}$$

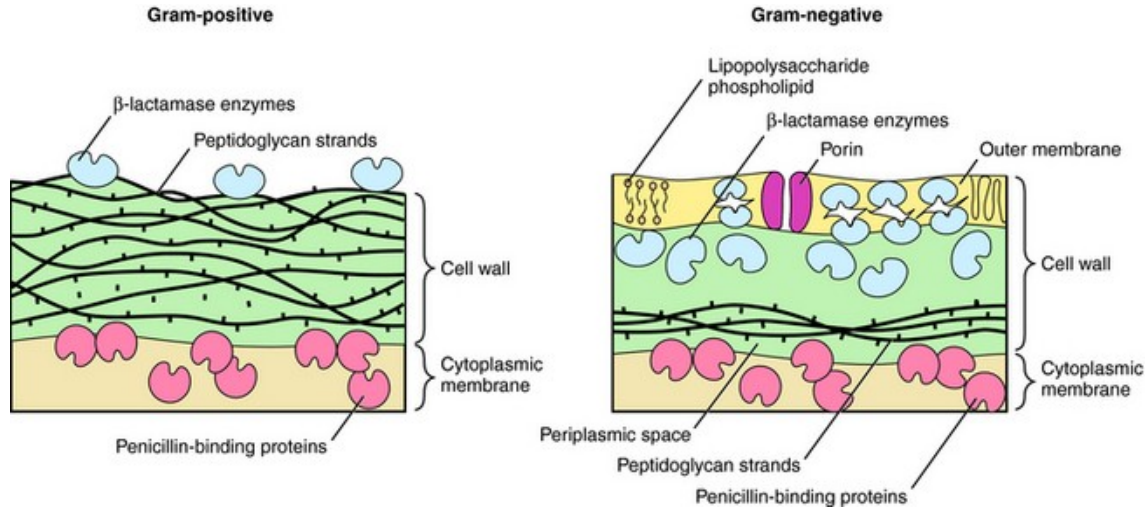
fragments fragments

* The figure above is an example of combinations related to diversity

Antibody specificity

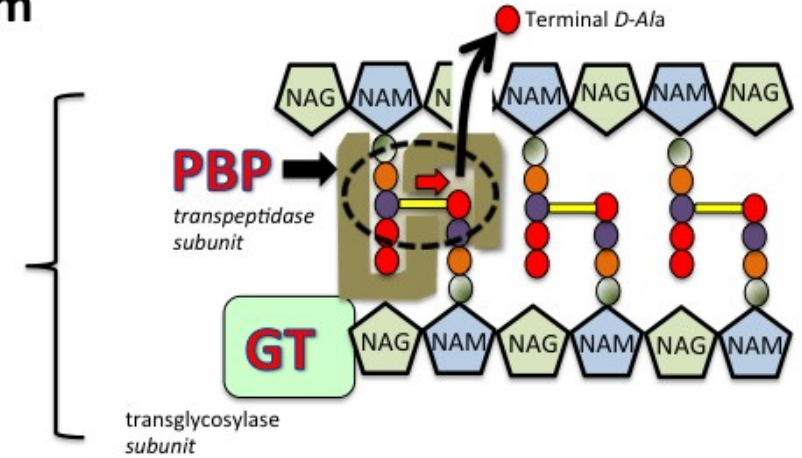


β -lactamases



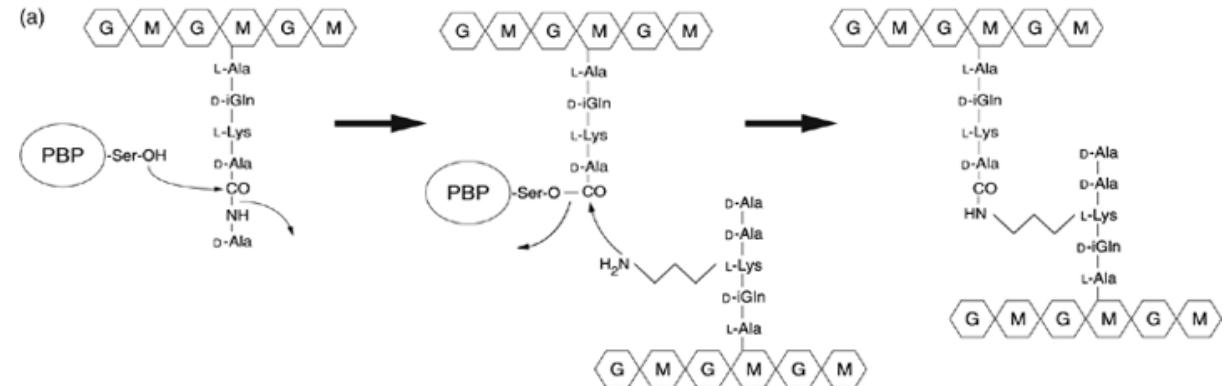
β -lactam mechanism of action

*ABX-free
Cell Wall
Synthesis*

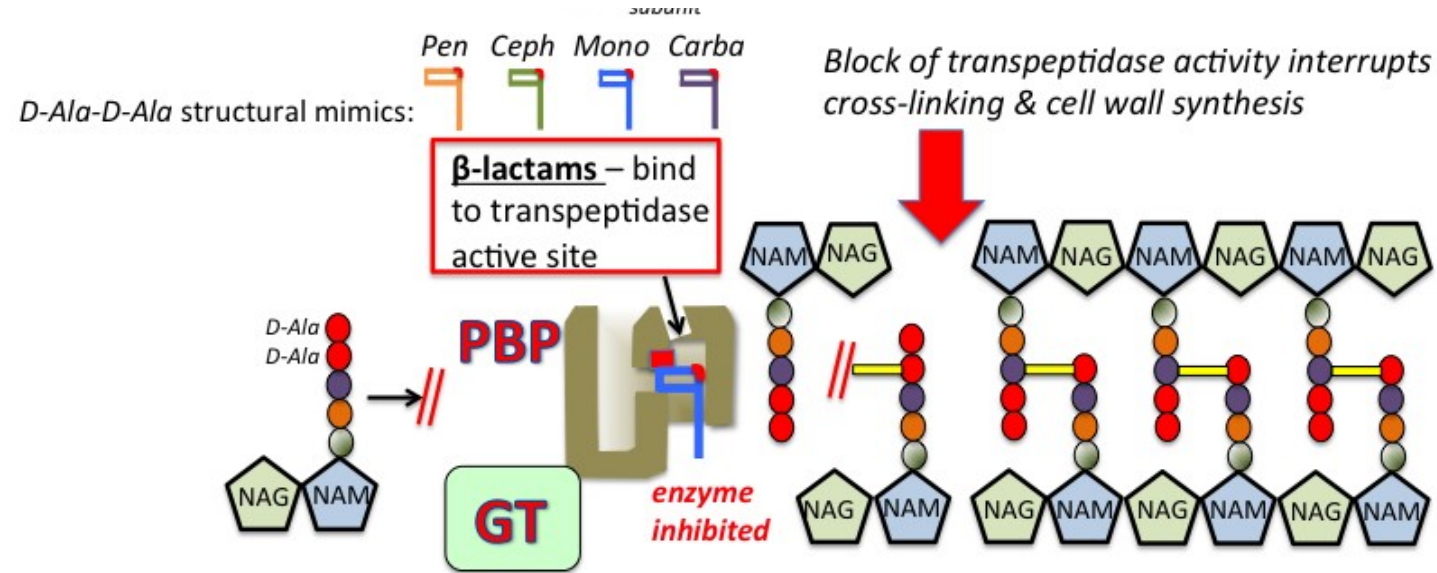
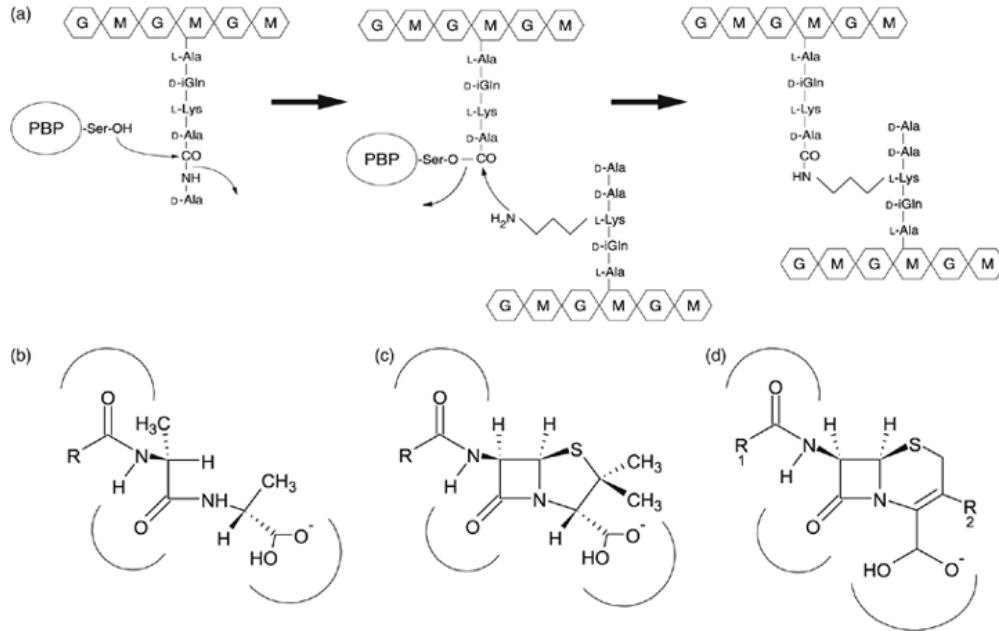


transpeptidase enzymes (also known as Penicillin Binding Proteins; PBP

Glycosyltransferases (GT), which exist as either separate subunits, or tightly associated with transpeptidases (e.g. as is the case for PBP-2) create covalent bonds between adjacent sugar molecules NAM & NAG



β -lactamases



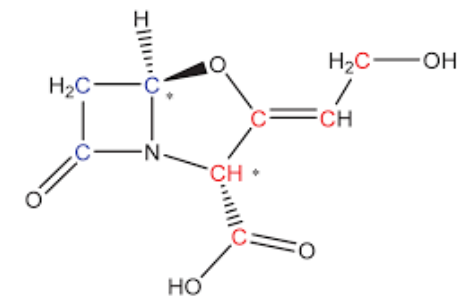
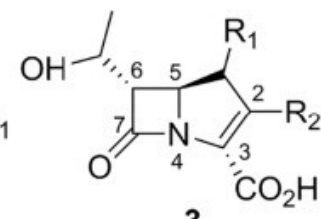
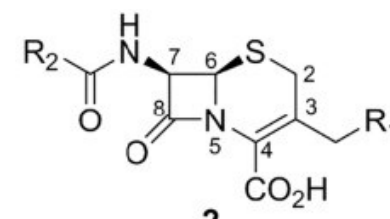
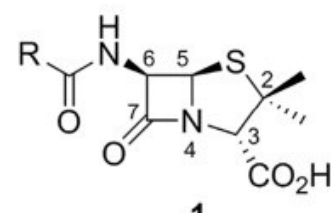
transpeptidase enzymes (also known as Penicillin Binding Proteins; PBP Glycosyltransferases (GT), which exist as either separate subunits, or tightly associated with transpeptidases (e.g. as is the case for PBP-2) create covalent bonds between adjacent sugar molecules NAM & NAG

β -lactamases

Penicillin

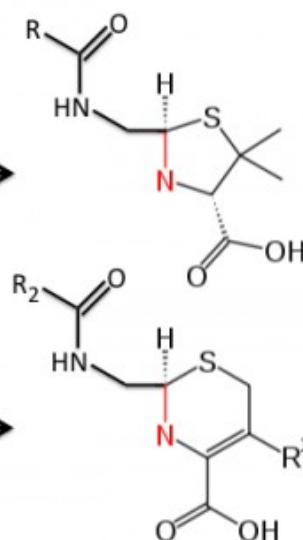
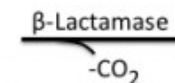
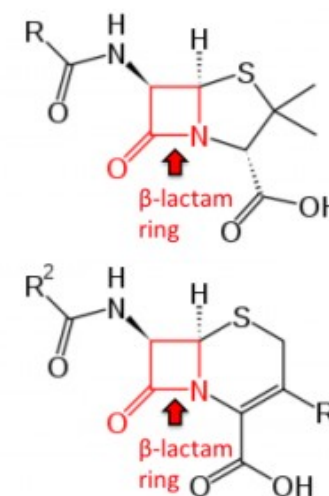
Cephalosporin

(1-methyl) Carbapenem



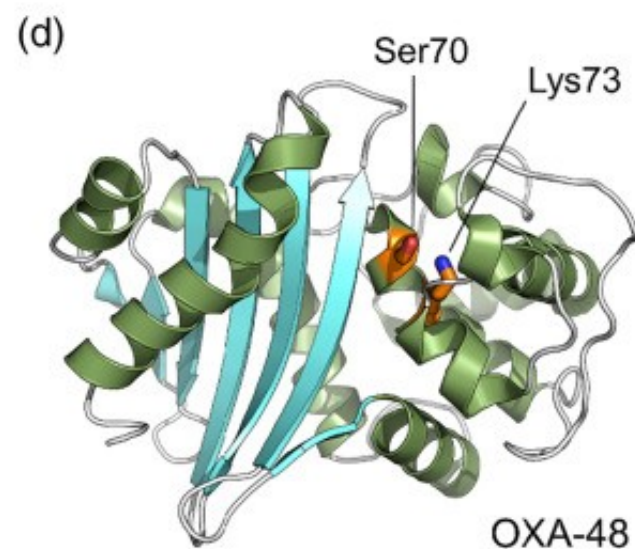
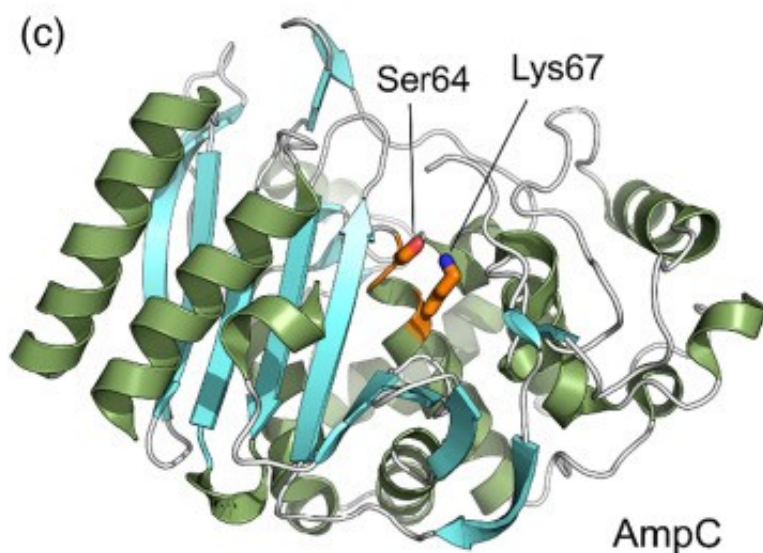
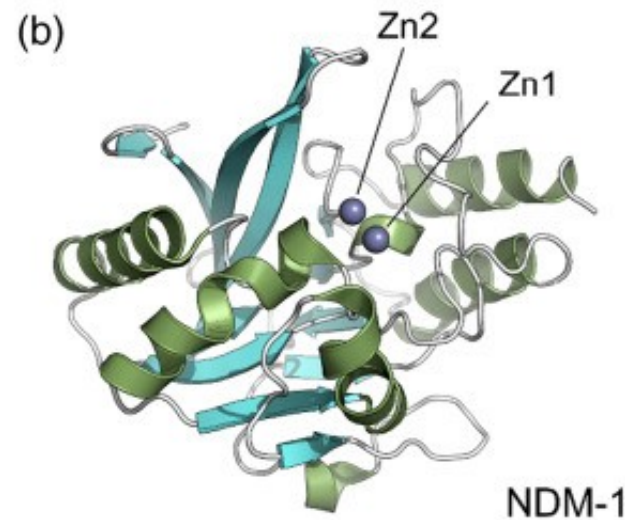
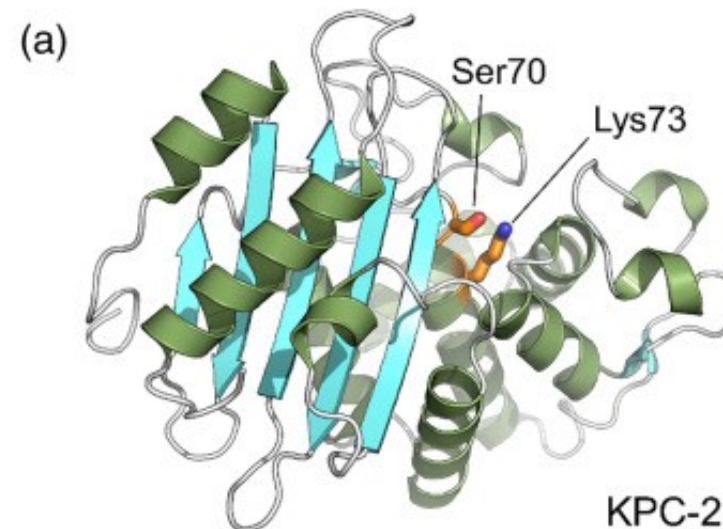
Clavulanic acid

Penicillin

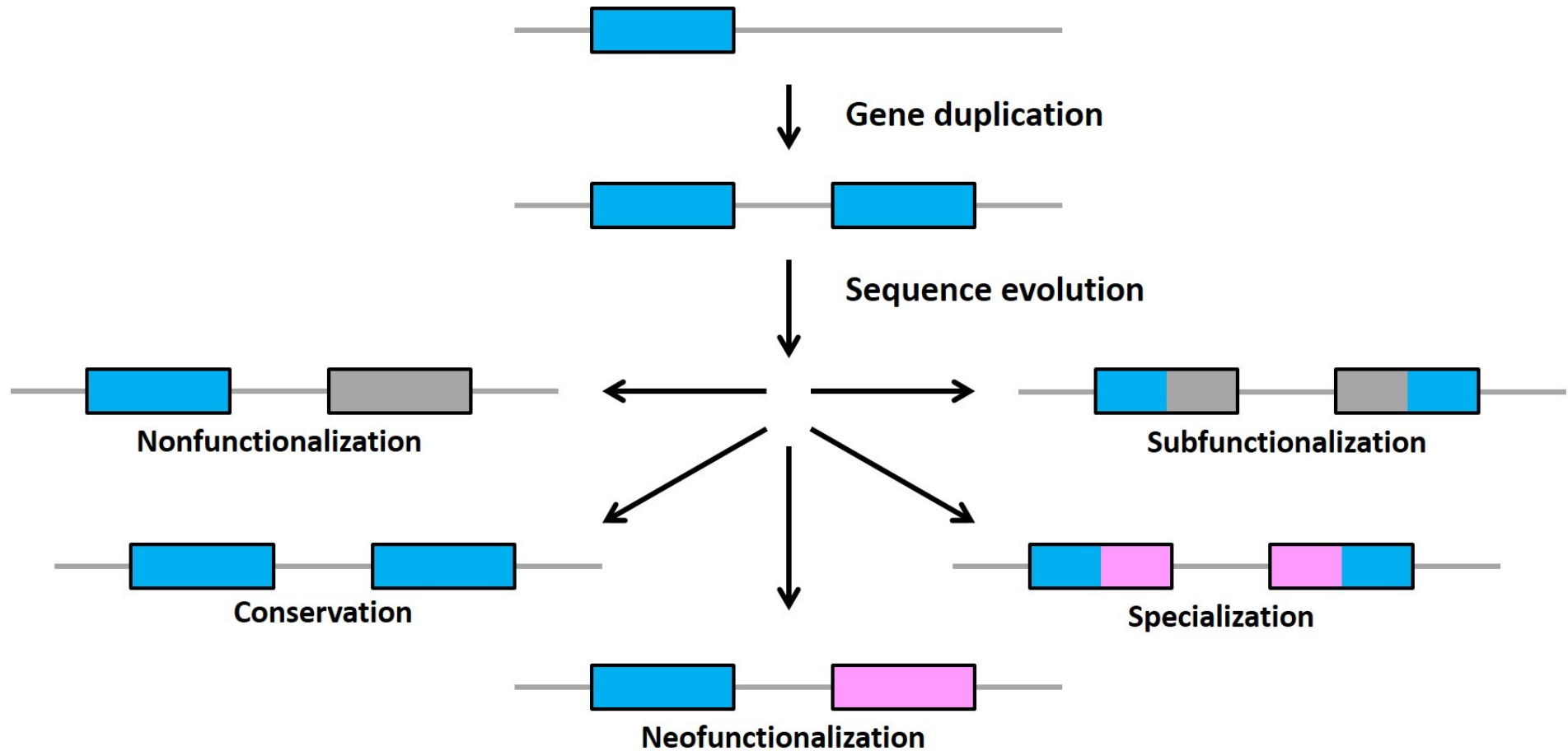


Cephalosporin

inactive metabolites



gene duplication

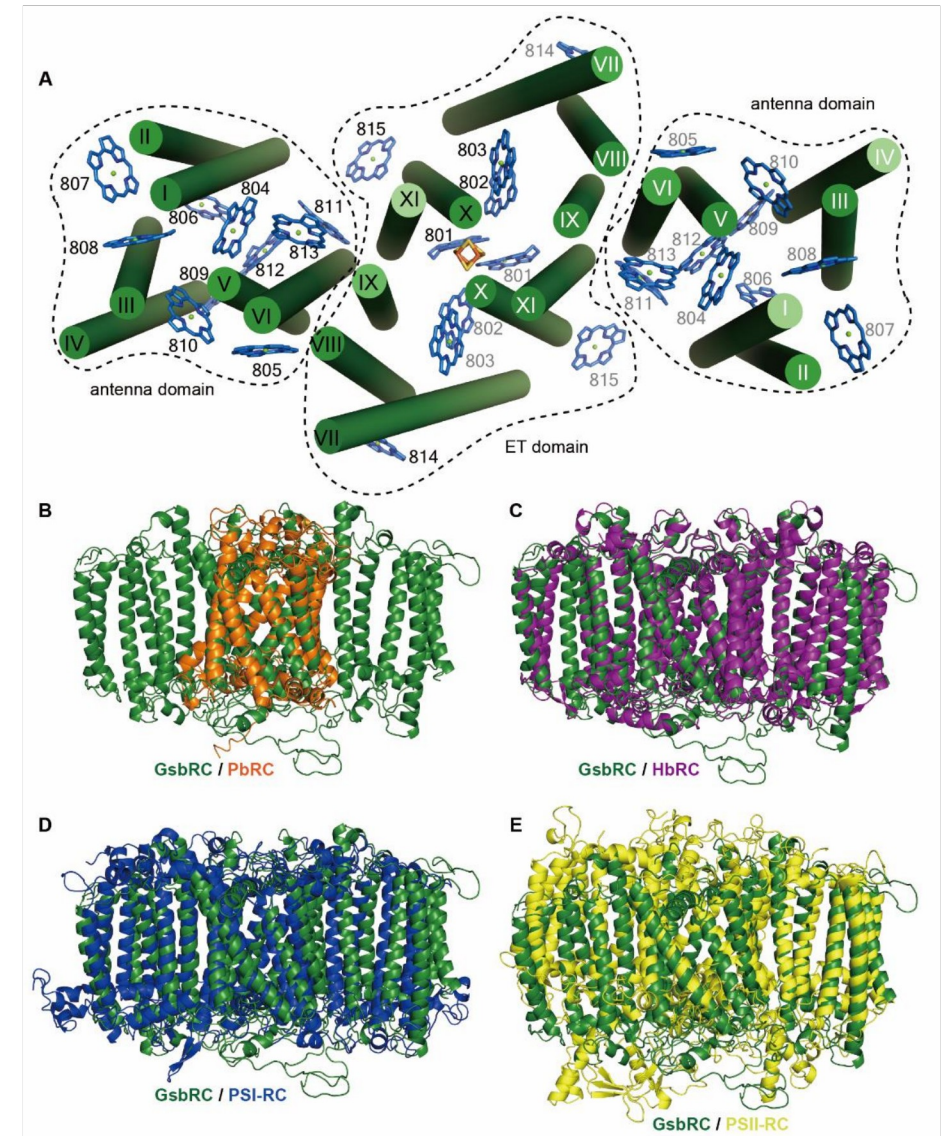
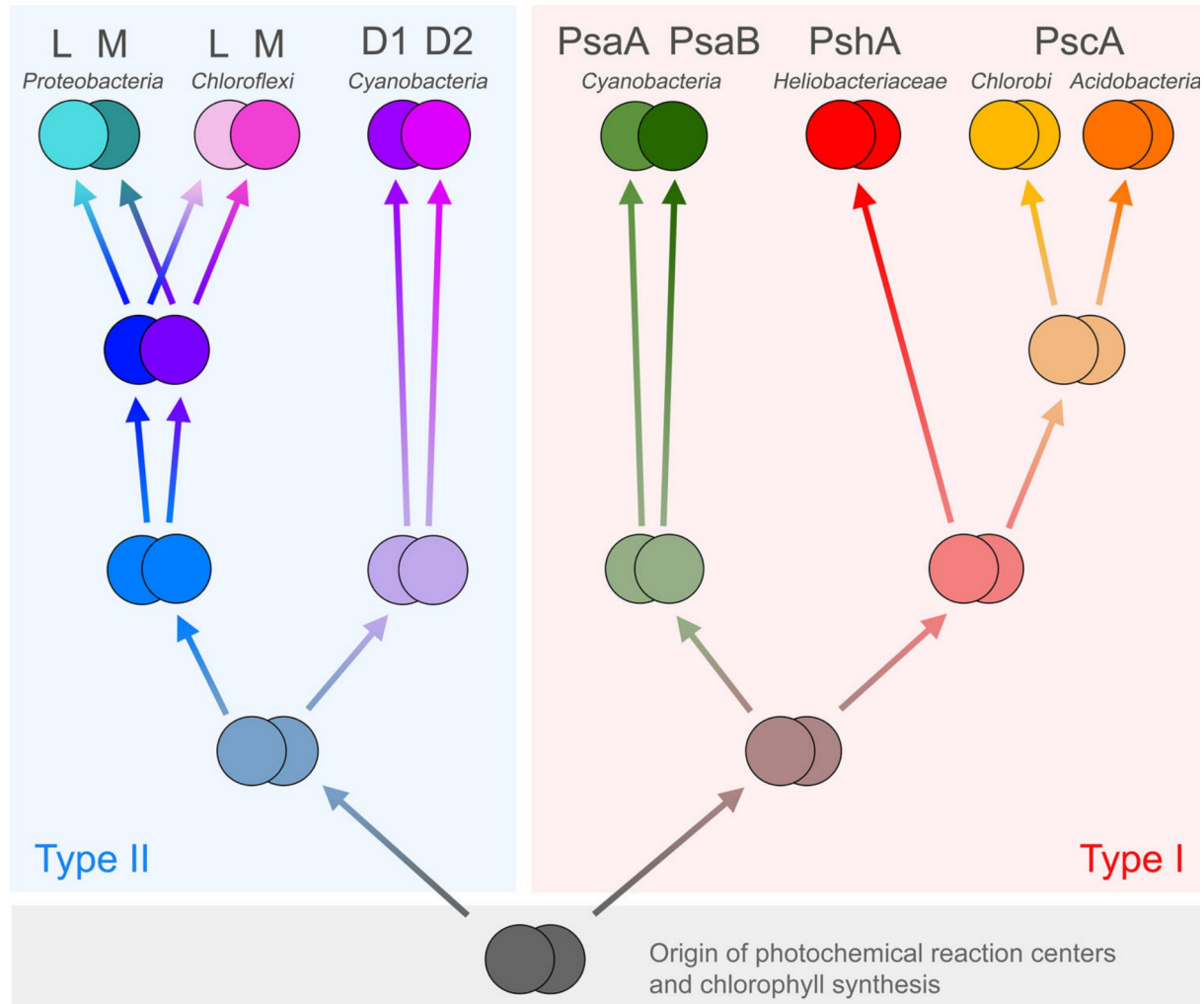


33% of the genes in *Haemophilus influenzae* have arisen from gene duplications

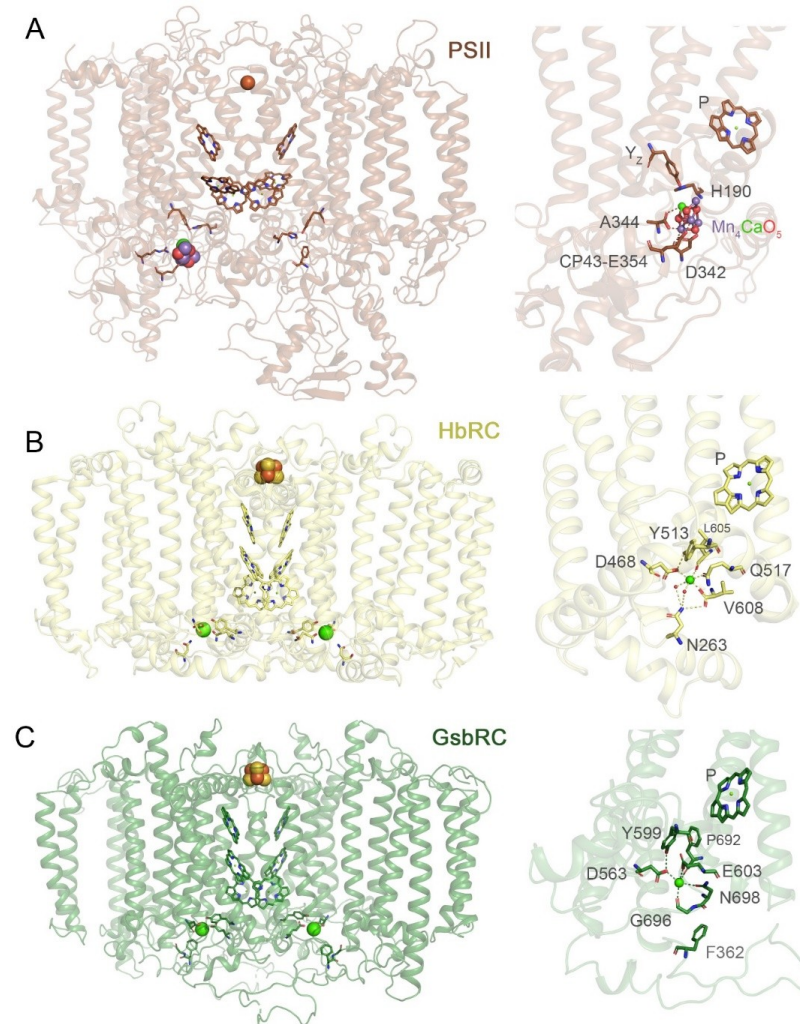
88% of the *Saccharomyces cerevisiae* genome

22% of the

Evolutionary relationships of reaction center proteins



Evolutionary relationships of reaction center proteins



Photosynthesis Research

<https://doi.org/10.1007/s11120-021-00857-9>

modification of duplicated genes

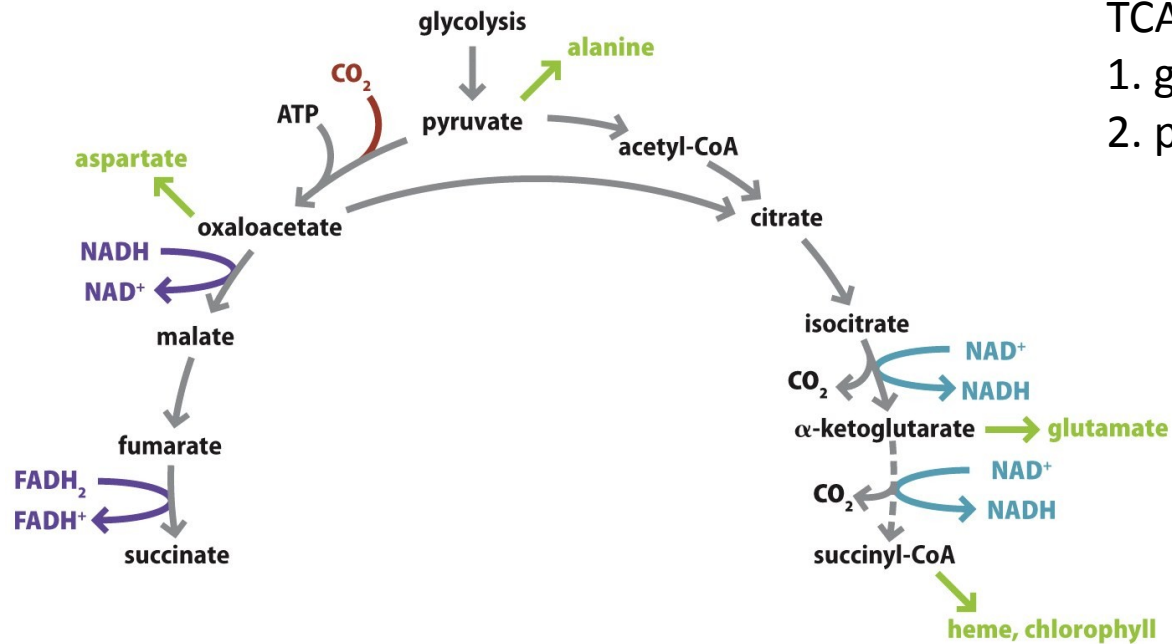


Figure 1.54 How Proteins Work (©2012 Garland Science)

TCA

1. generate metabolic intermediates
2. produce energy

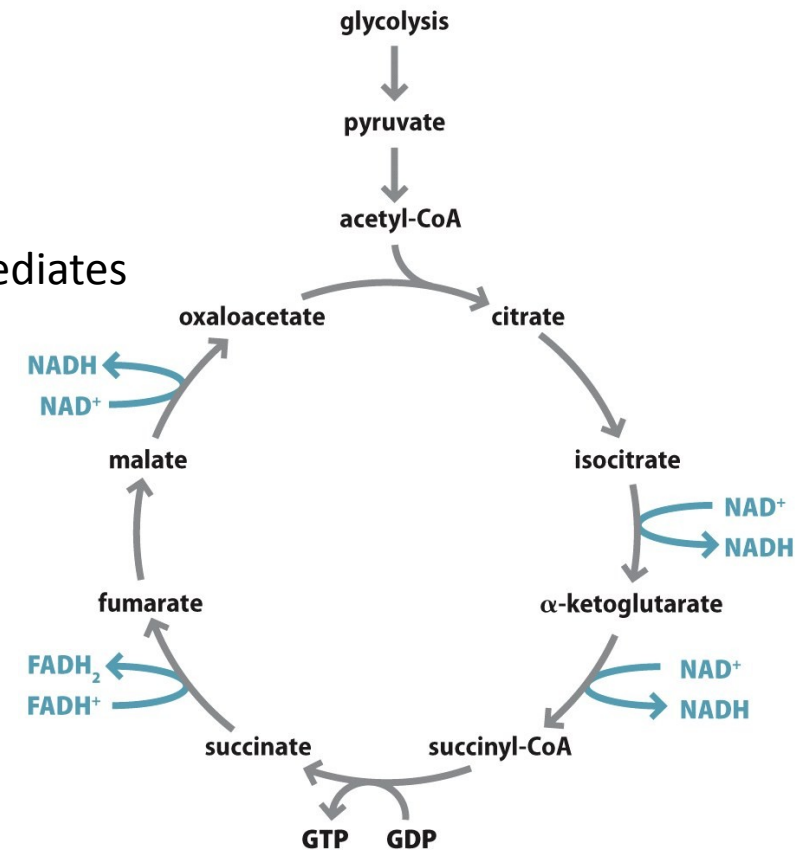
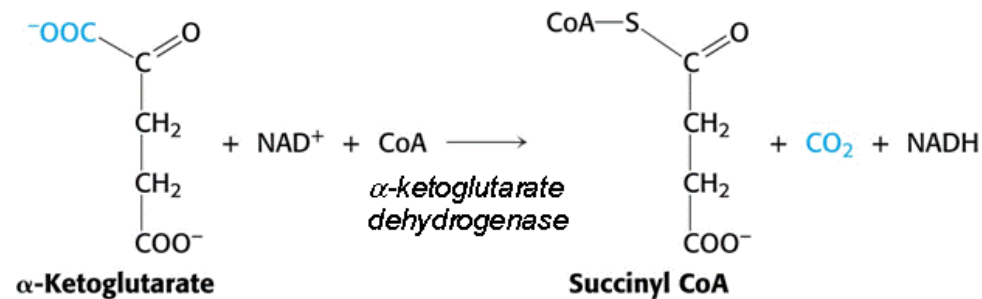
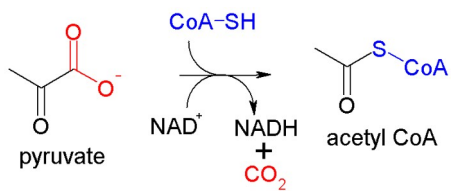


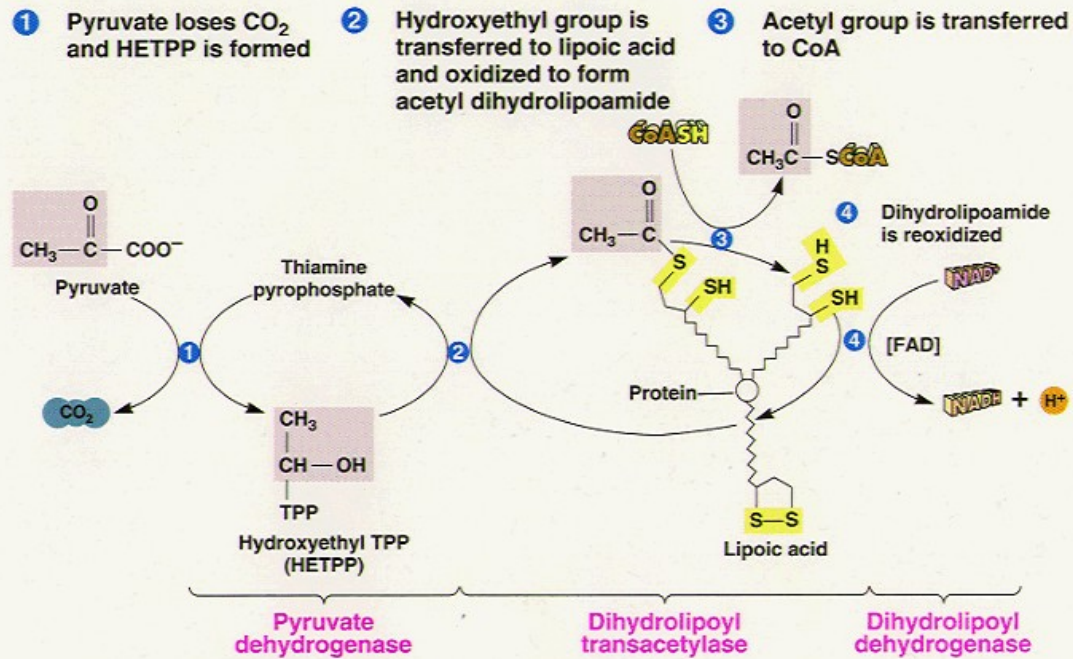
Figure 1.55 How Proteins Work (©2012 Garland Science)

pyruvate dehydrogenase



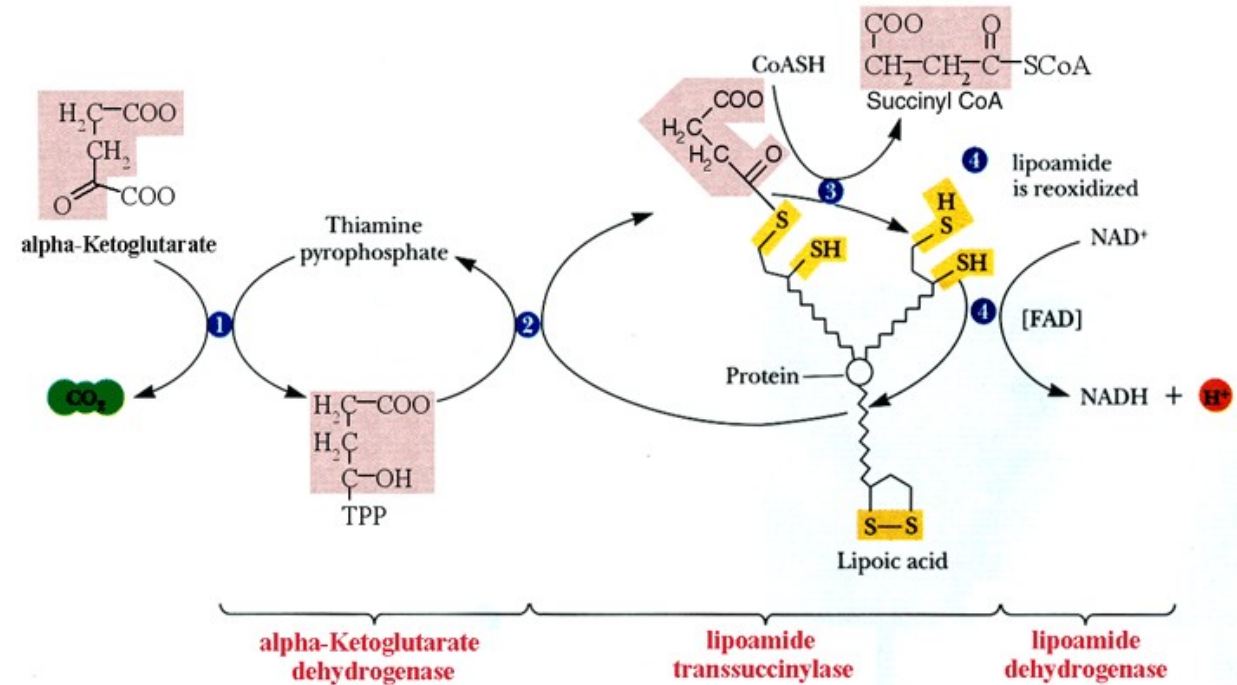
succinyl-CoA synthetase

Mechanisms

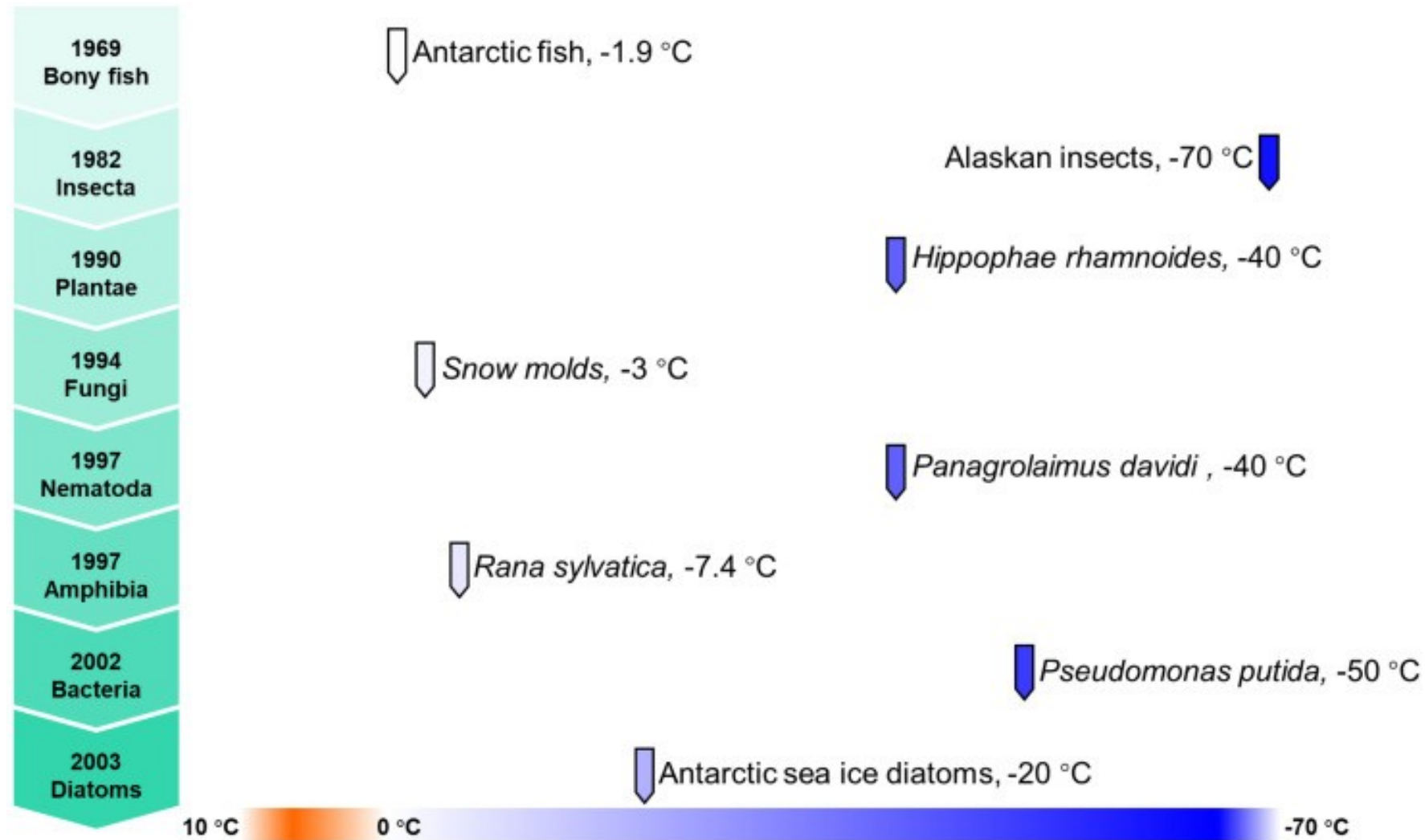


Overhead transparencies to accompany Garrett/Grisham: *Biochemistry*
Transparency 59 Figure 14.41

page 497
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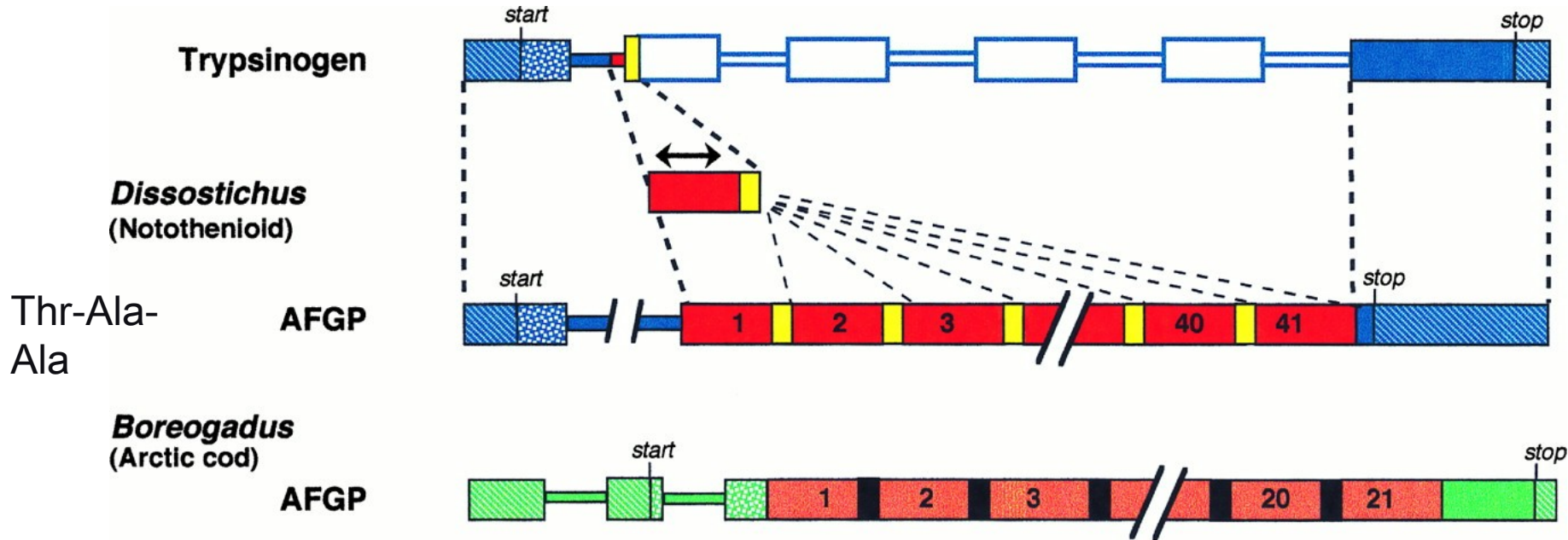
survive in extremely cold weather



modification of duplicated genes

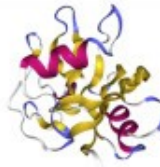
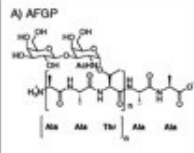
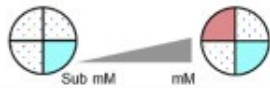
Anti freeze proteins

psychrophilic proteins have
decreased disulphide bonds
decrease of net charge in helix-dipole structures
decrease in protein-solvent interactions
decrease in the number of hydrogen bonds at domain interfaces
a general decrease in the number of hydrophobic interactions
within the core of the protein



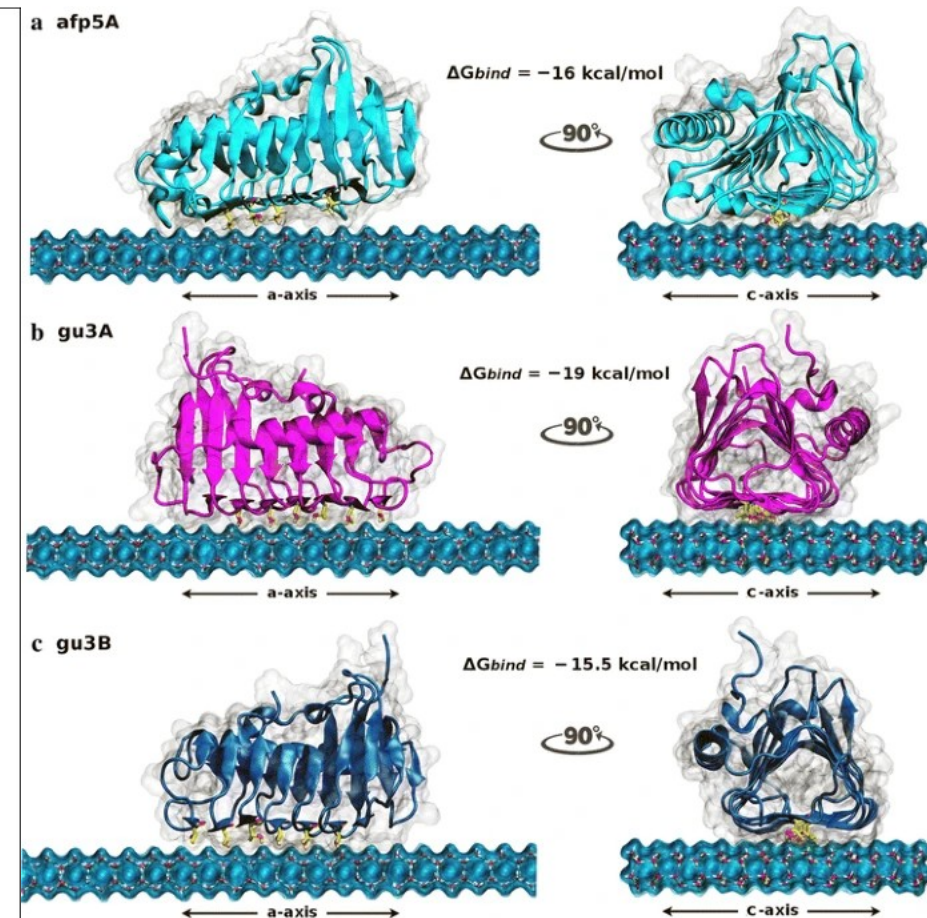
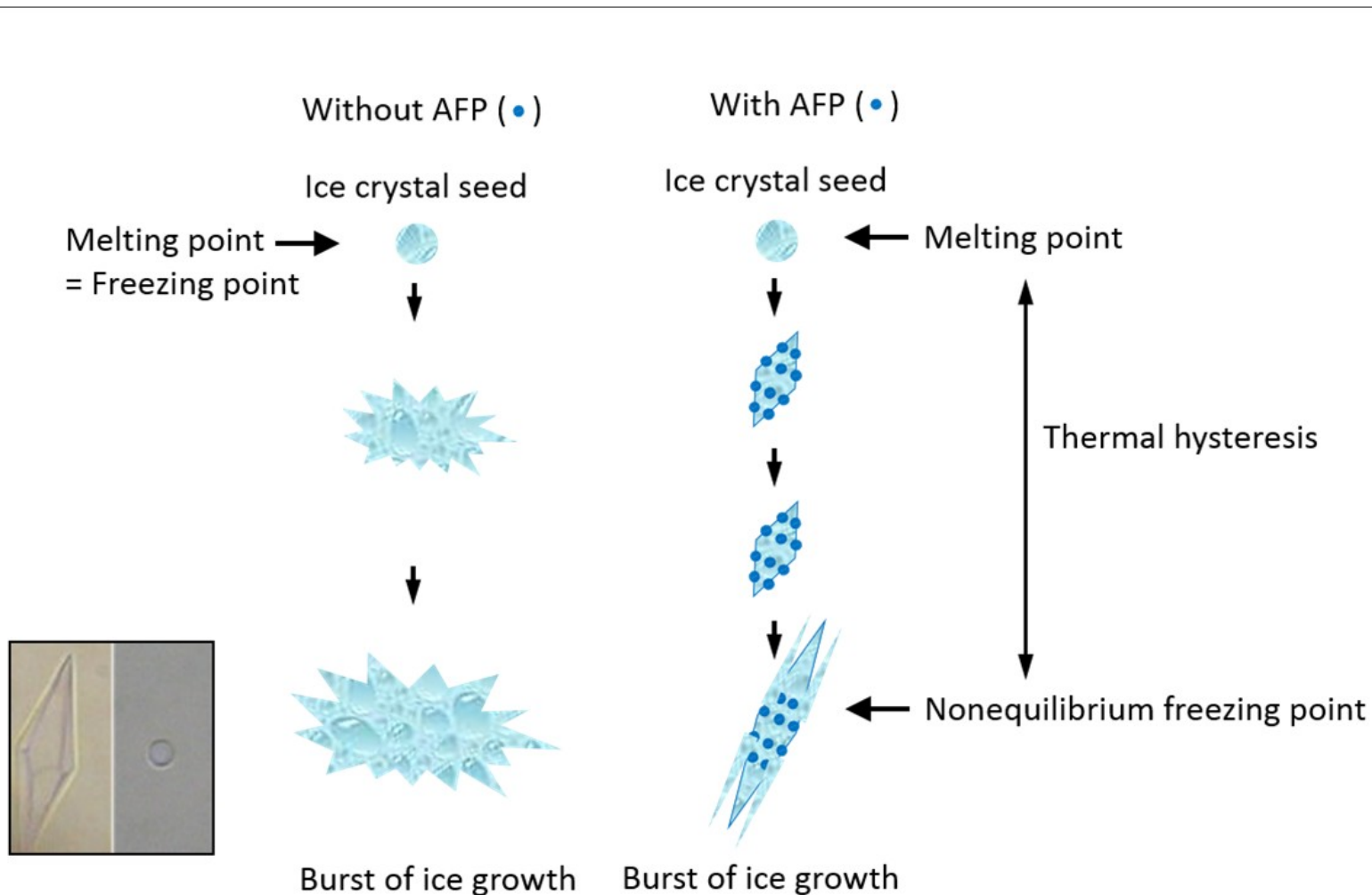
structurally characterized AFPs



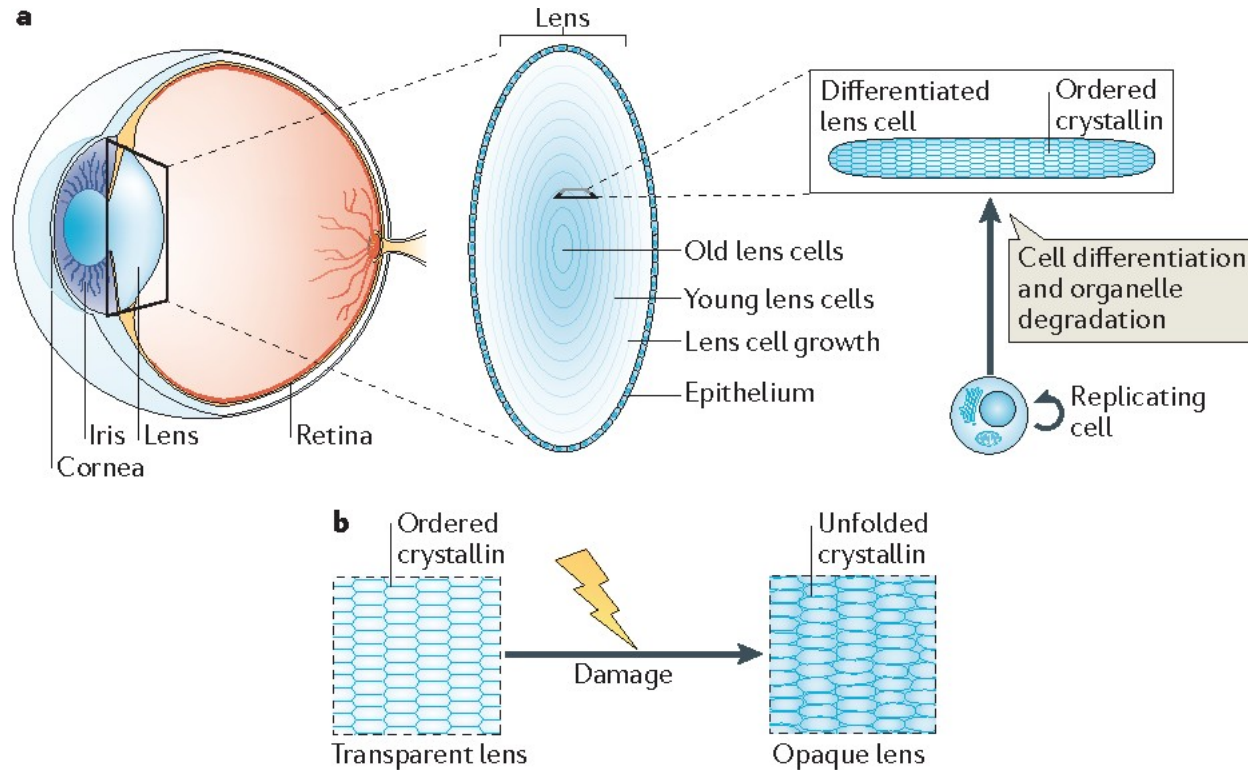
	Fish					Insect	Bacterium	Plant	
	Type I AFP			Type II AFP	Type III AFP	AFGP	DcAFP	MpAFP	LpAFP
Structure element	α -helix, Alanine rich	α -helix, Alanine rich	α -helix, Threonine-(Alanine rich)	Globular; S-S bonds	Globular; β -sandwich	AAT-repeat; Disaccharide	β -solenoid; S-S bonds	β -solenoid	β -solenoid
Representative structure									
Binding plane				 or 					
Natural source	Winter flounder fish (wfAFP1)	Shorthorn sculpin fish (ssAFP1)	Righteye flounder, barfin plaice (bpAFP)	Longsnout Poacher sea raven, rainbow smelt, Atlantic herring	Eel pouts; ocean pout fish	Cods and Antarctic nototheniids	Beetle Dendroides canadensis	Antarctic bacterium Marinomonas primoryensis	Lolium perenne
Thermal hysteresis activity	Moderate	Moderate	Moderate $\rightarrow$ Hyperactive	Moderate	Moderate	Moderate	Hyperactive	Hyperactive	Moderate
Freeze properties	Freeze avoidance						Freeze avoidance; Freeze tolerance	Ice adhesion	Freeze tolerance

The protective function of AFPs benefits from their properties which include ice plane affinity, thermal hysteresis, ice recrystallization inhibition [and transiently binding an organism to ice

Effect



gene sharing



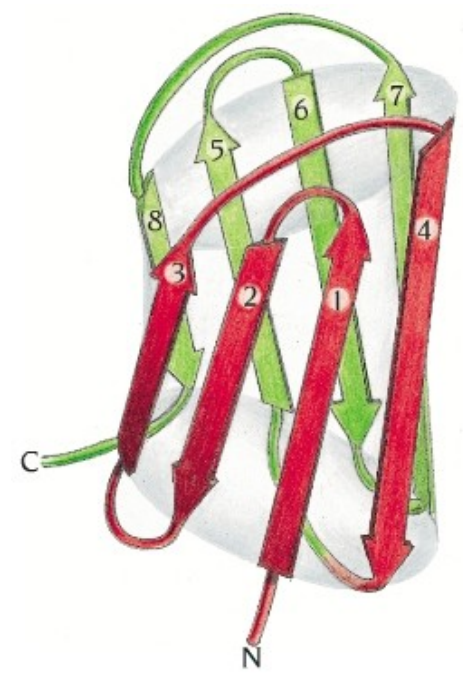
The lens proteins need to have three properties:

they should be soluble enough to create a solution of high refractive index

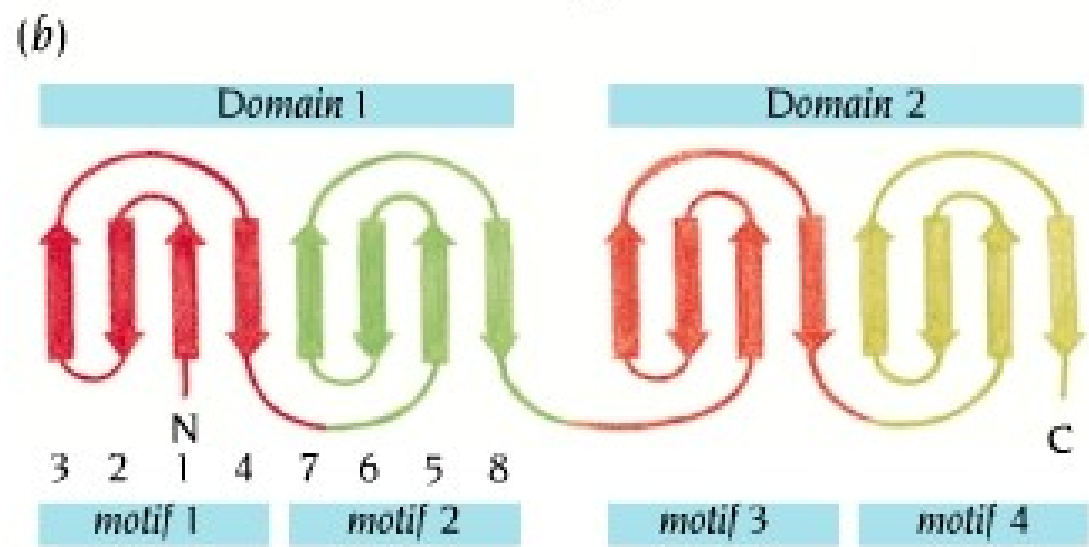
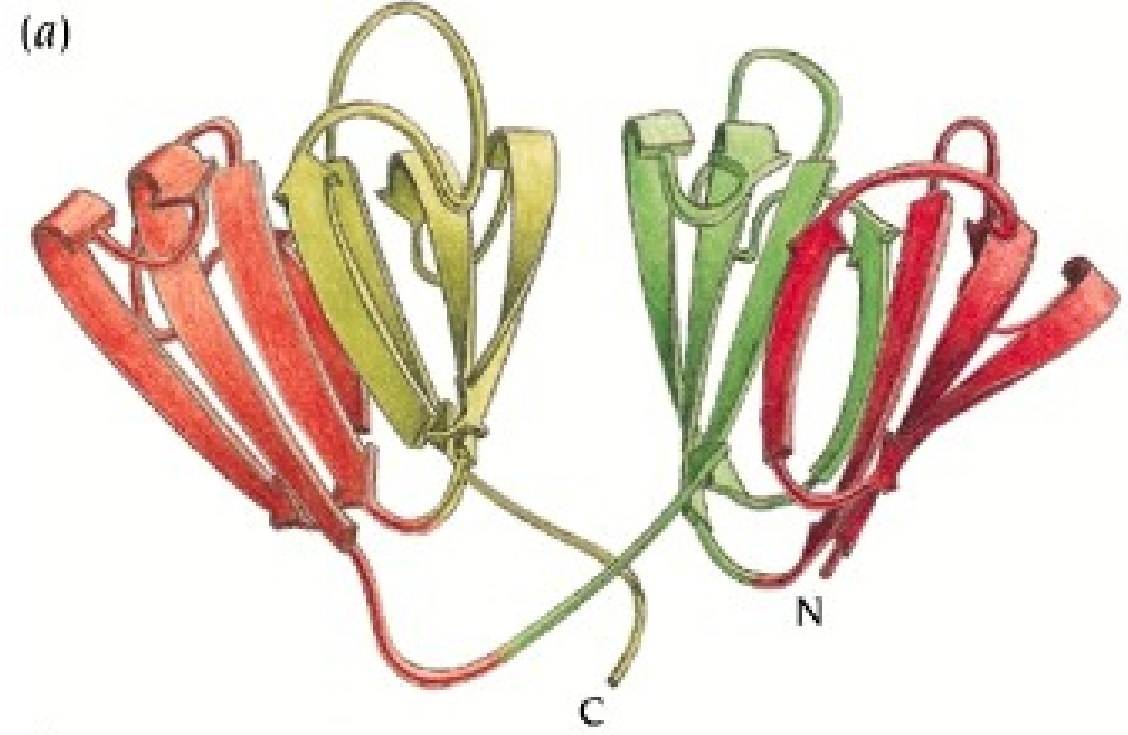
they should remain soluble and transparent throughout the life of the animal

they should be nontoxic in their new location and concentration.

γ crystallin

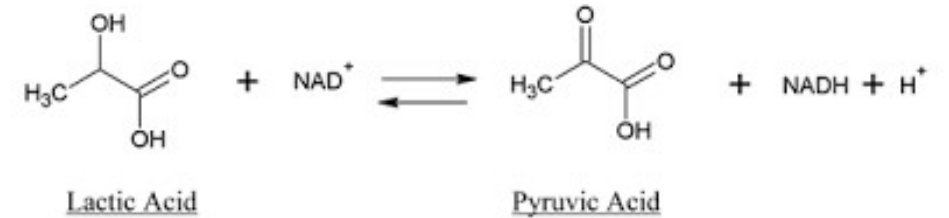


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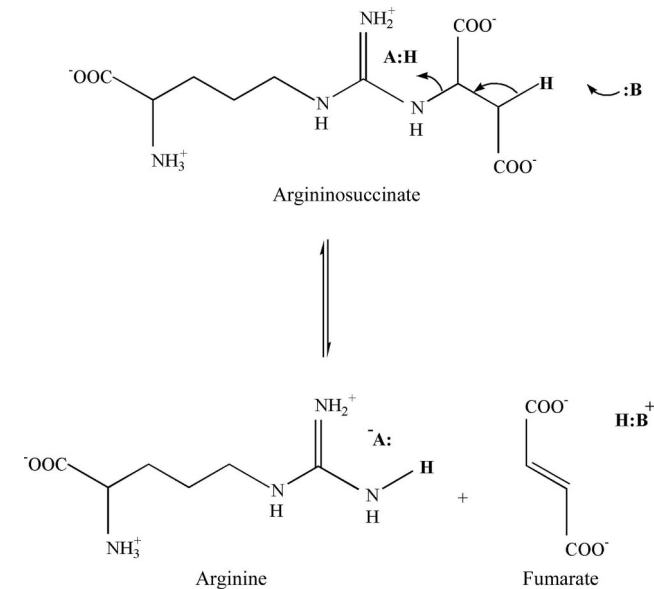
gene sharing



In crocodiles and some birds, ϵ crystallin is identical to lactate dehydrogenase and even retains enzyme activity

$\delta 2$ crystallin, found in all birds and reptiles, is identical to argininosuccinate lyase

$\delta 1$ crystallin, for example, represents a gene duplication of the $\delta 2$ crystallin/argininosuccinate lyase gene with mutations to make it inactive as an enzyme



Convergent and Divergent Evolution

Unrelated proteins can perform the same function (convergent evolution), sometimes using the same mechanism – sometimes using different mechanisms

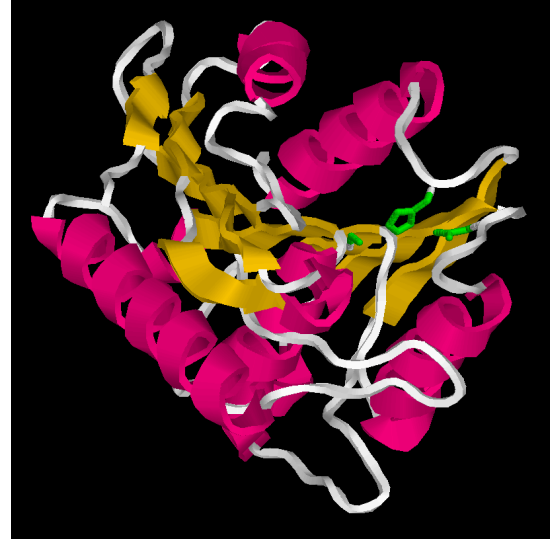
Convergent Evolution



Trypsin



Subtilisin

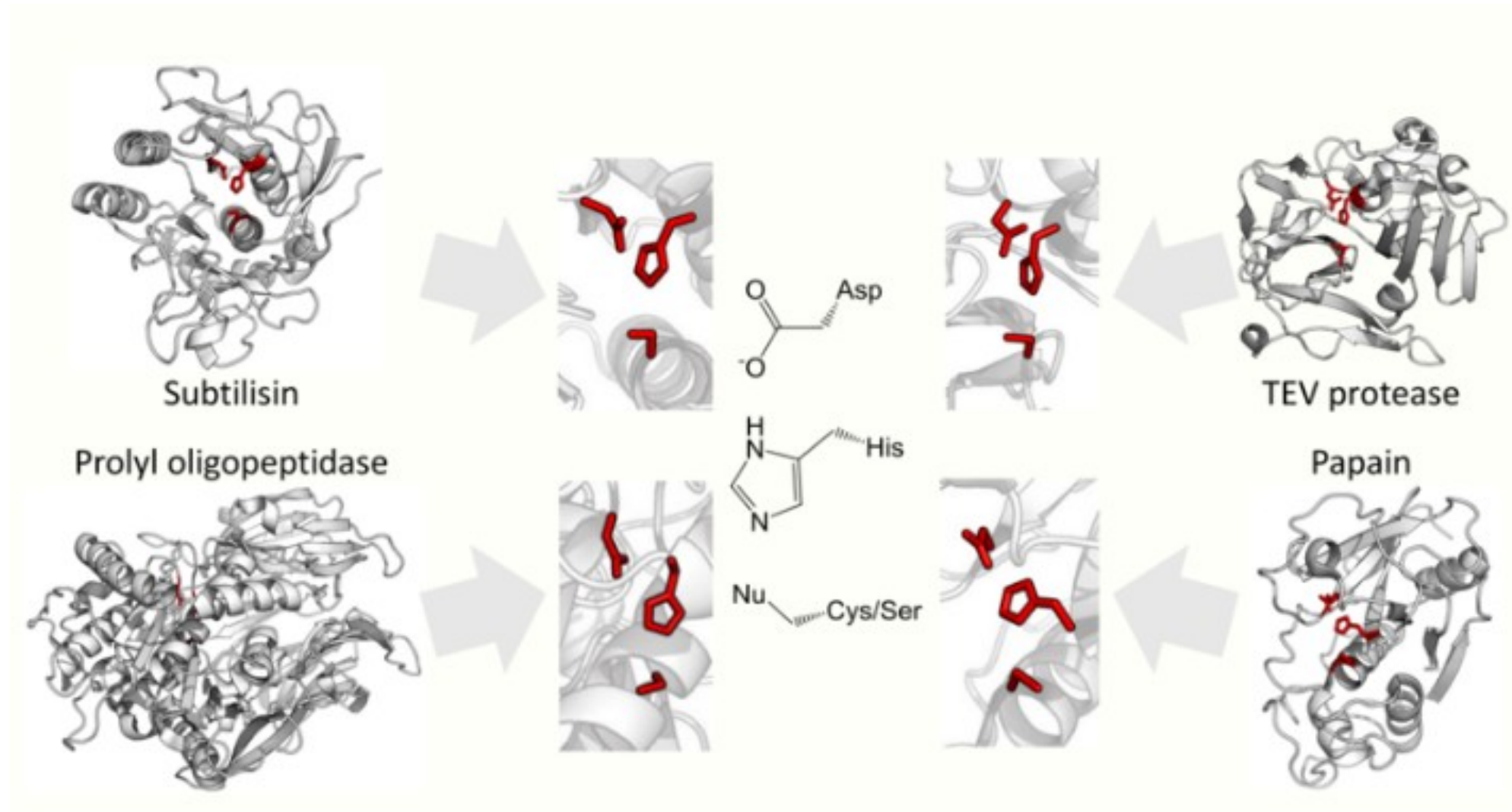


Alpha/beta hydrolase

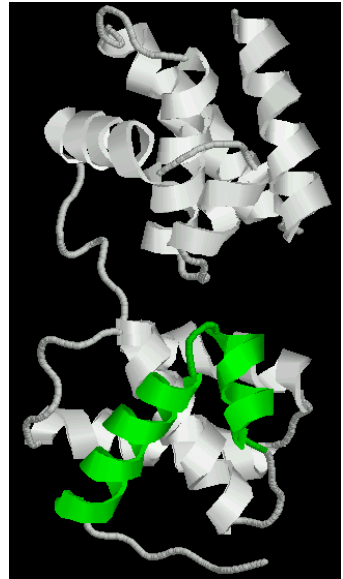
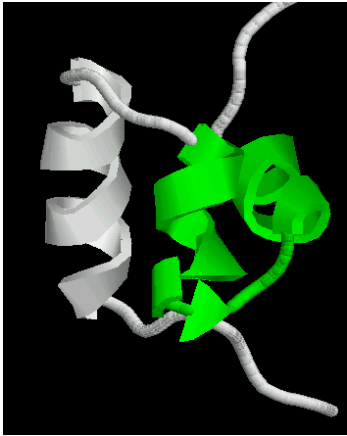


CheB methylesterase

Convergent Evolution



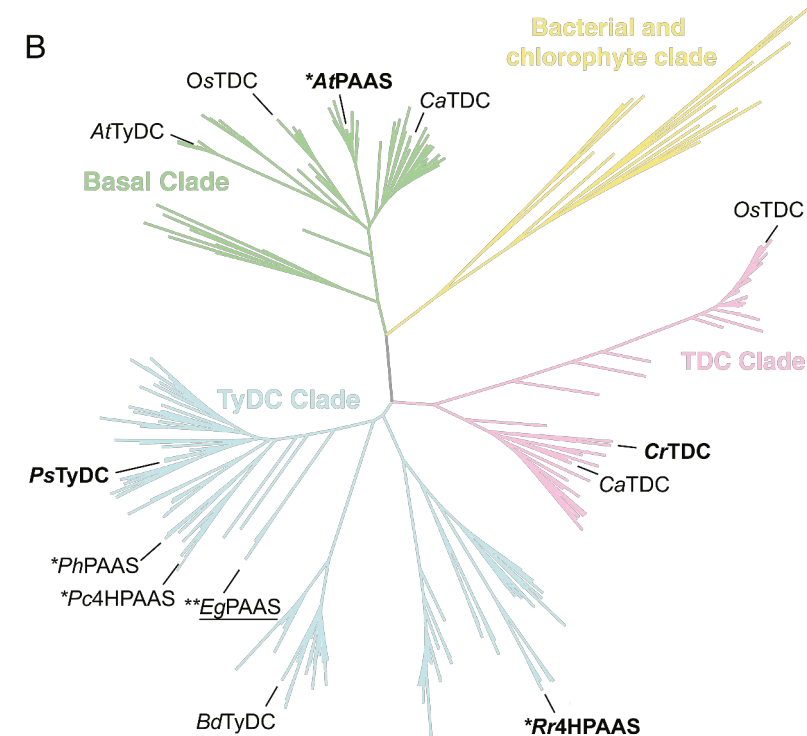
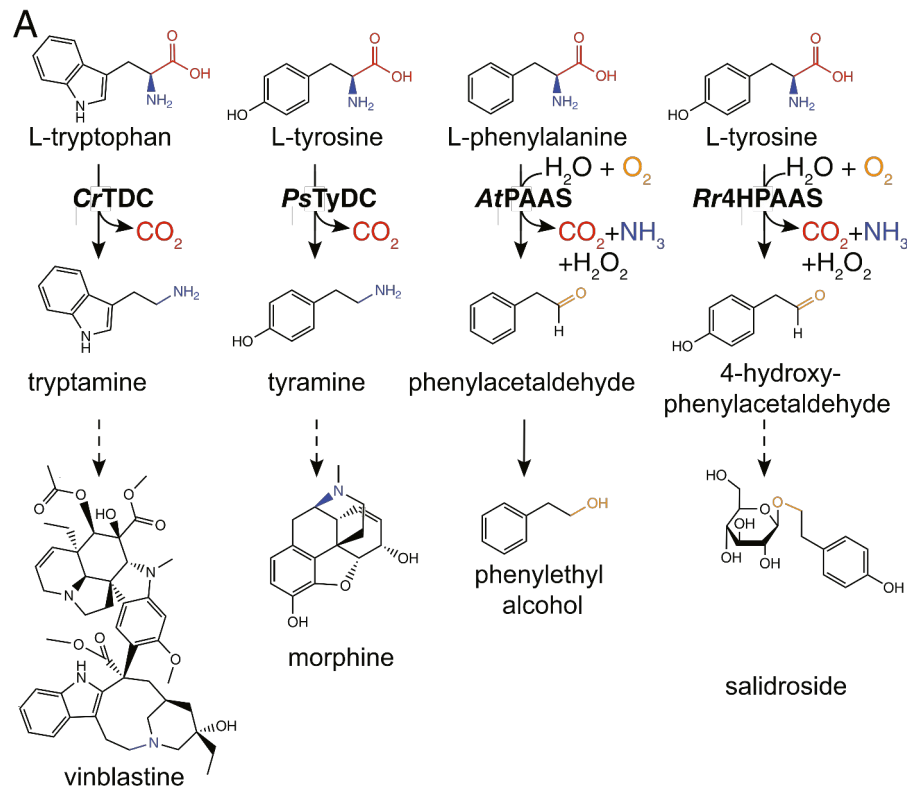
Convergent Evolution

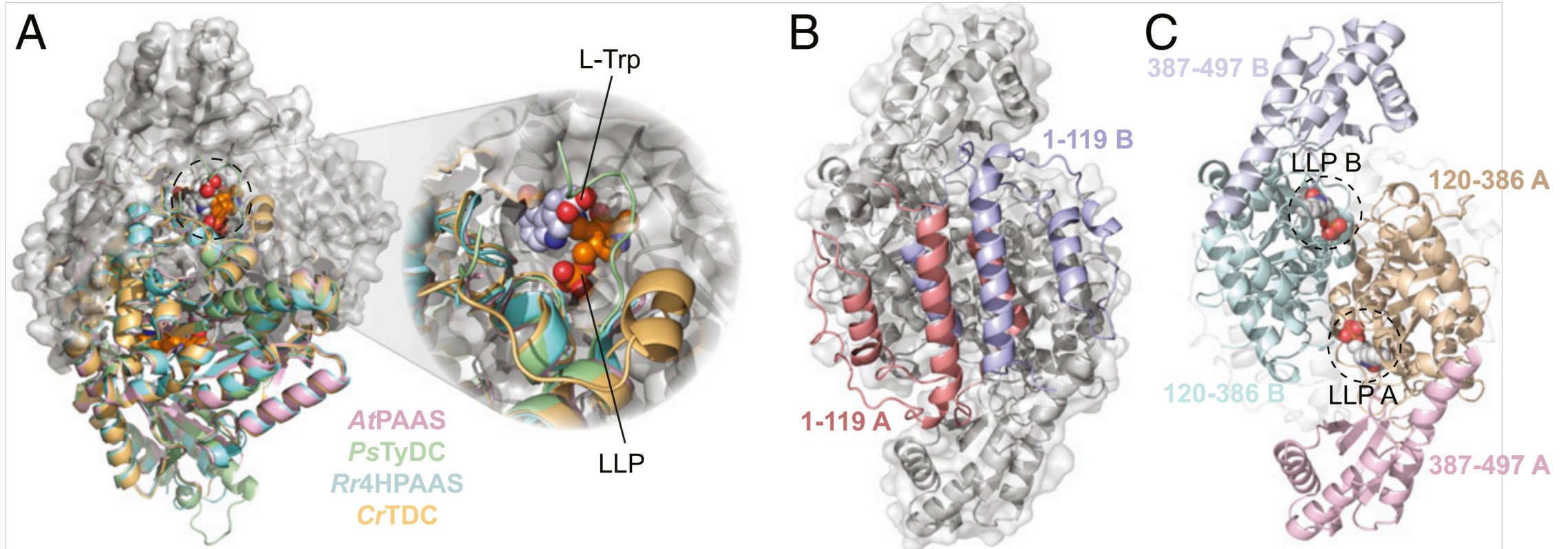


Divergent Evolution

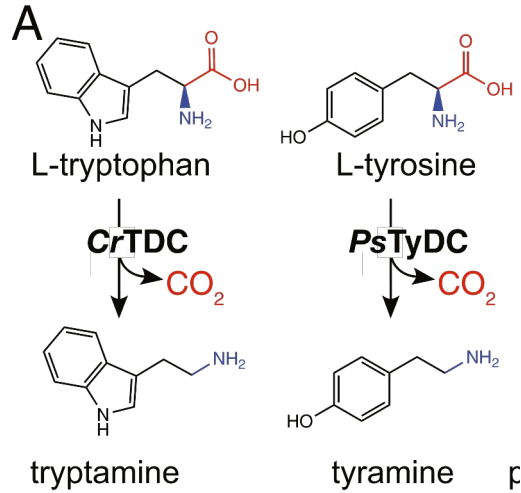
Related proteins can perform different functions – divergent evolution

Pyridoxal 5'-phosphate (PLP)-dependent aromatic L-amino acid decarboxylase (AAAD) family enzymes play important roles in channeling various aromatic L-amino acids into diverse downstream specialized metabolic pathways.

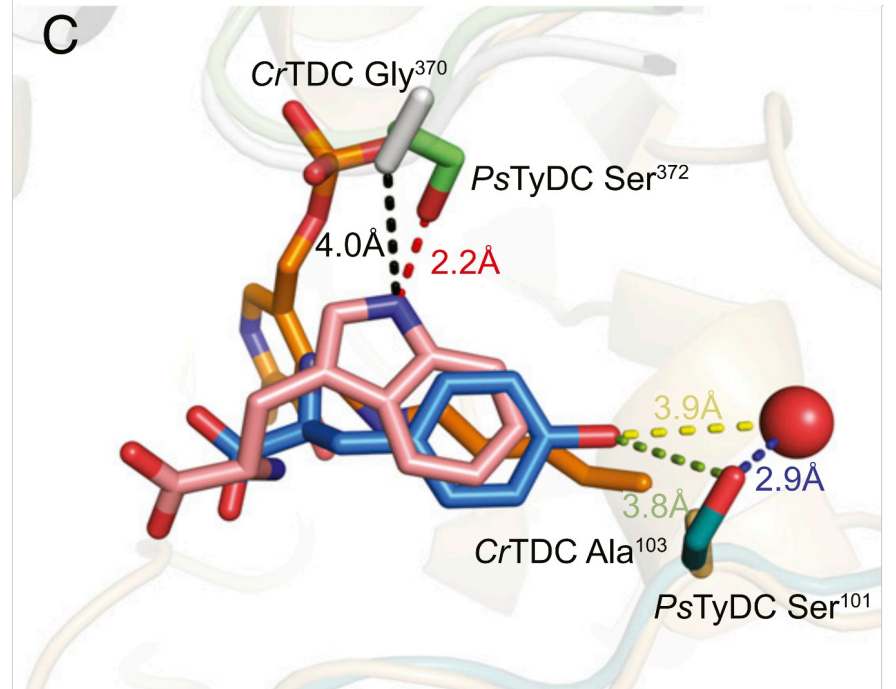
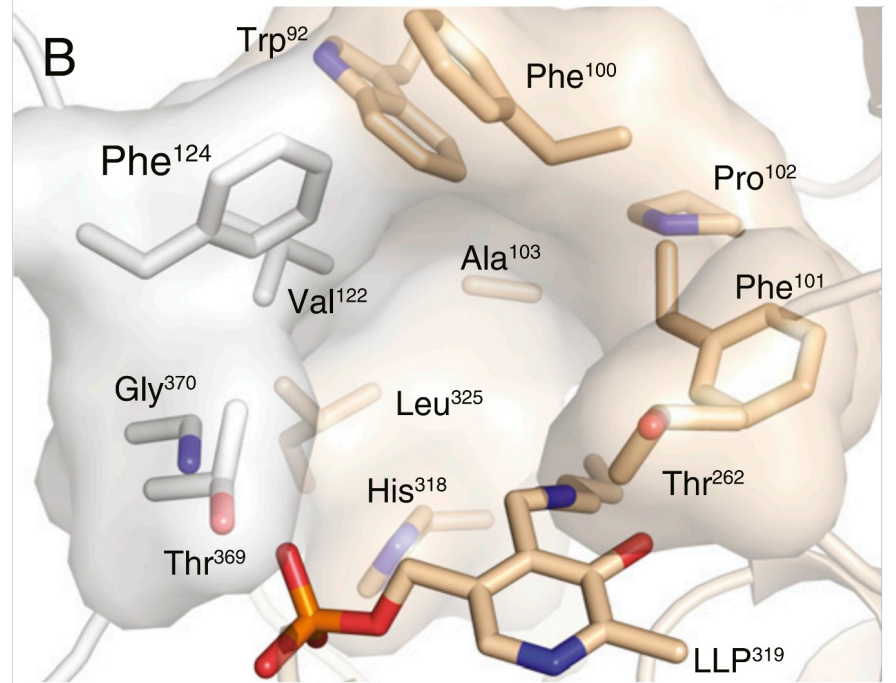




substrate selectivity



The CrTDC active-site pocket

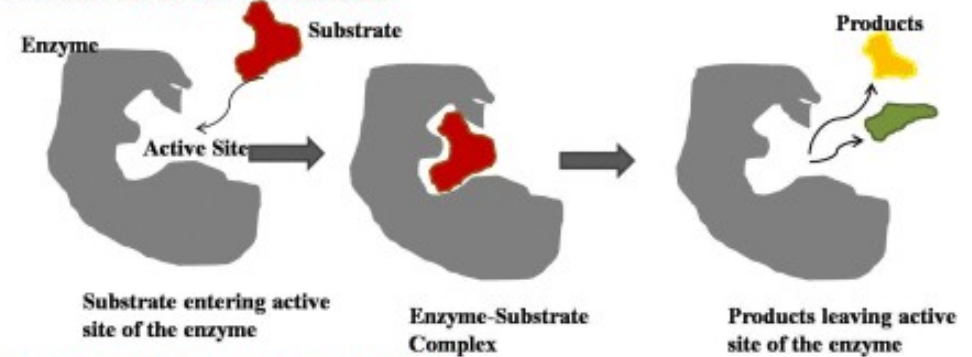


Promiscuous enzymes

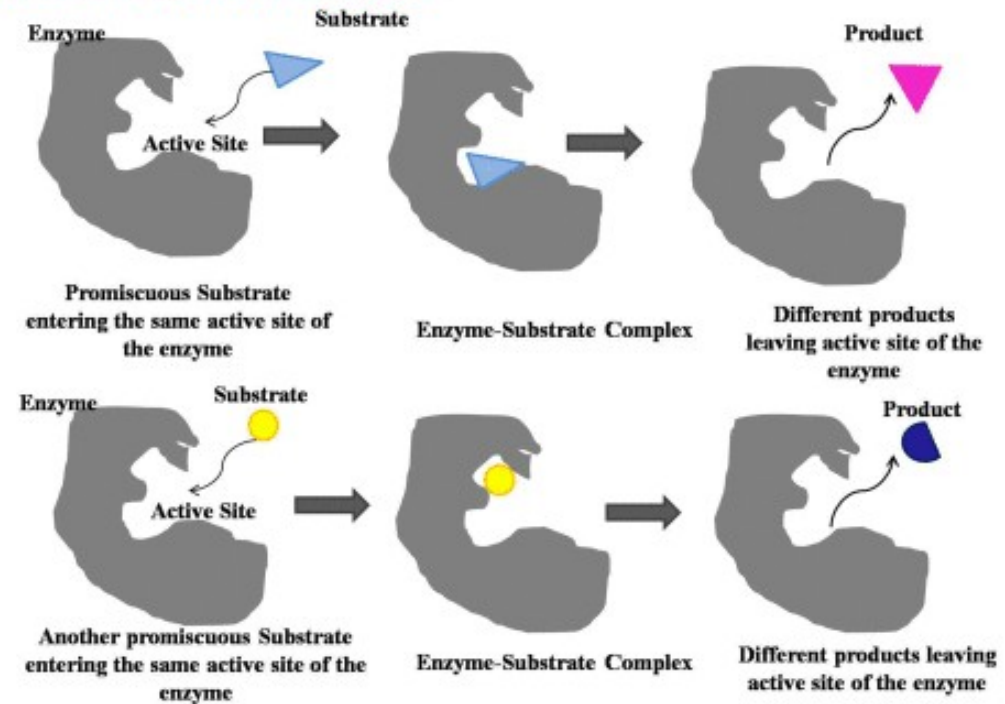
Promiscuous enzymes that catalyze two different reactions

The use the same active site for catalyzing both reactions.

Reaction with a Natural Substrate



Reaction with a Promiscuous Substrate



It is now realized that promiscuity is inherent in design of enzymes: the way enzymes evolved as more complex organisms developed. Just as earlier, biotechnologists benefitted from enzyme specificity, they are fast learning how they can exploit from their "lack of specificity" (catalytic promiscuity) as well.

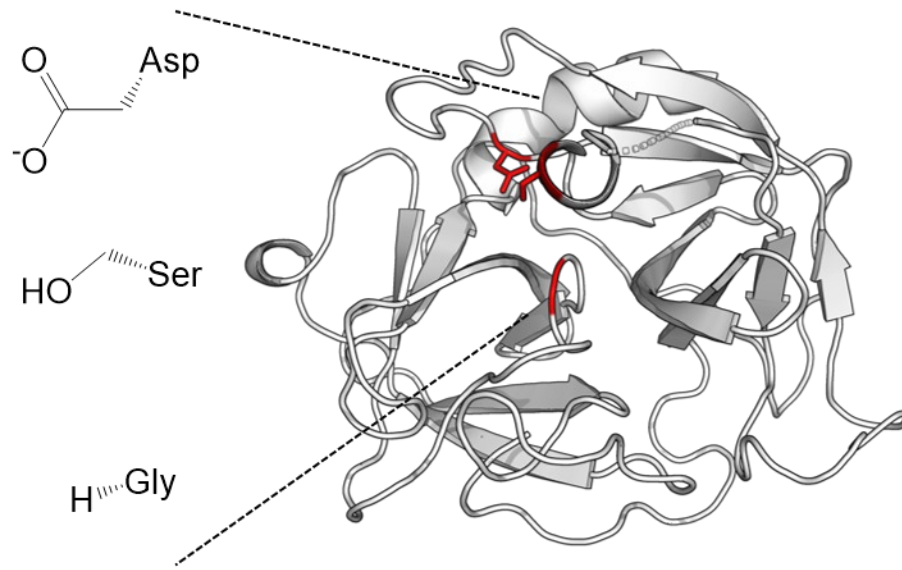
Promiscuous enzymes

TABLE 1.4 Promiscuous enzymes

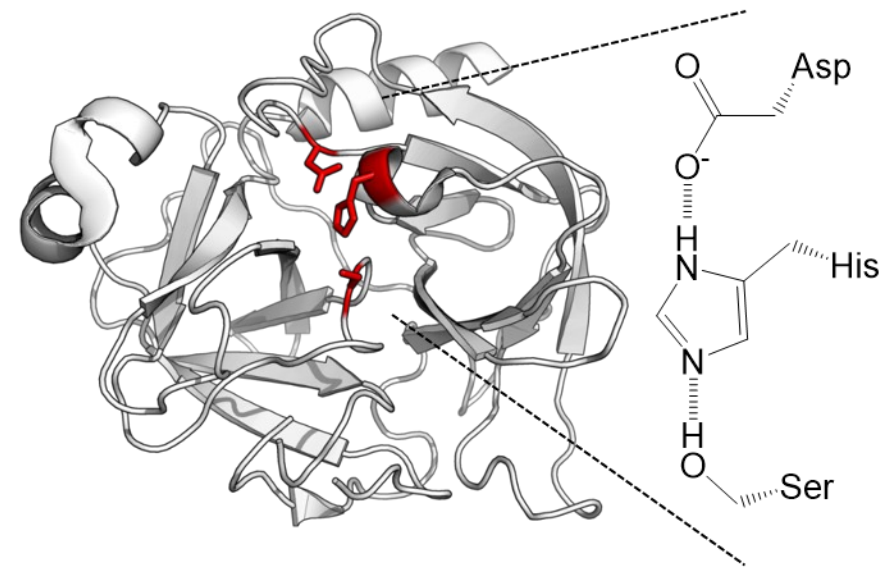
Enzyme	Normal reaction	Promiscuous reaction
α -Chymotrypsin	Peptide hydrolysis	Hydrolysis of esters and phosphate triesters
Alkaline phosphatase	Phosphate monoester hydrolysis	Hydrolysis of phosphate diesters, phosphonate monoesters, and sulfate esters; phosphate oxidation
Arylsulfatase A	Sulfate ester hydrolysis	Hydrolysis of phosphate diesters
Phosphonate monoester hydrolase	Phosphonate monoester hydrolysis	Hydrolysis of phosphate monoesters, sulfate monoesters, phosphate diesters, and sulfonates
Exonuclease III	DNA phosphate diester hydrolysis	DNA phosphate monoester hydrolysis
Phosphotriesterase	Phosphate triester hydrolysis	Hydrolysis of phosphate diesters, esters, and lactones
Urease	Urea hydrolysis	Phosphoramidite hydrolysis
Dihydroorotase	Hydrolysis of dihydroorotate	Phosphate triester hydrolysis

(Taken from Table 3.2 in A.J. Kirby and F. Hollfelder, From Enzyme Models to Model Enzymes. Cambridge, UK: Royal Society of Chemistry, 2009.)

Promiscuous enzymes



Azurocidin 1



Chymotrypsin

This protein is homologous to a number of serine proteases that are involved in protecting the cell against attacking bacteria, but it has lost its protease activity and instead binds to lipopolysaccharide on the bacterial cell wall, forming a bridge that activates recognition and attack by the immune system

moonlighting proteins

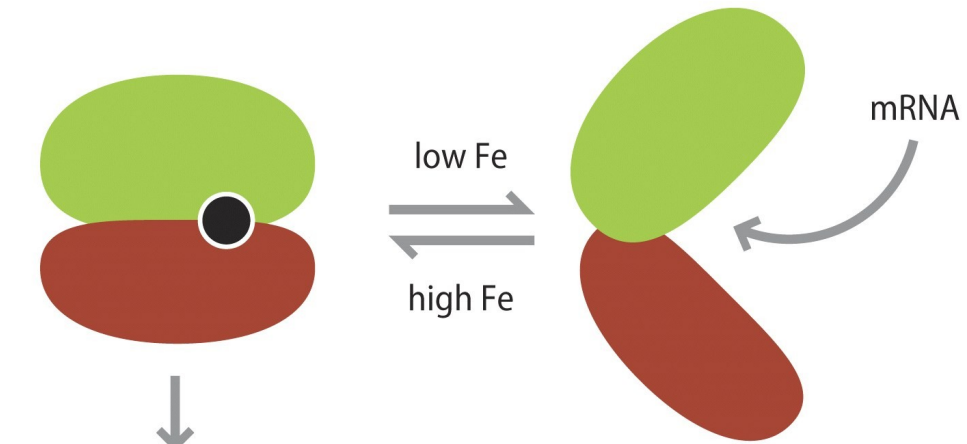
Moonlighting proteins that have two or more quite different functions:

In most cases, the second function is not enzymatic.

TABLE 1.5 Enzymes with a moonlighting nonenzymatic function		
Enzyme	Function	Second function
Cytochrome c	Electron carrier	Apoptosis
PutA	Proline dehydrogenase	Transcriptional repressor
Phosphoglucose isomerase	Glycolytic enzyme	Cytokine
Phosphoglycerate kinase	Glycolytic enzyme	Cytokine
Thymidine phosphorylase	Biosynthetic enzyme	Endothelial growth factor
Aconitase	TCA cycle enzyme	Iron-responsive element binding protein
Thymidylate synthase	Biosynthetic enzyme	Translation inhibitor
Band 3 ion exchanger	Cl ⁻ /HCO ₃ ⁻ antiporter	Regulator of glycolysis
FtsH	Metalloprotease	Chaperone
birA	Biotin synthetase	Bio operon repressor
Lactate dehydrogenase	Glycolytic enzyme	Eye lens crystallin
ARGONAUTE4	RNAse to make siRNA	Chromatin remodeling
Cyclophilin	Peptidyl proline <i>cis/trans</i> isomerase	Regulator of calcineurin
Enolase	Glycolytic enzyme	Mitochondrial import
Enolase	Glycolytic enzyme	Transcriptional regulation [131]
Hexokinase	Glycolytic enzyme	Apoptosis repressor [132]
Galectin-1	Lectin (saccharide binding)	Protein:protein interaction

Table 1.5 How Proteins Work (©2012 Garland Science)

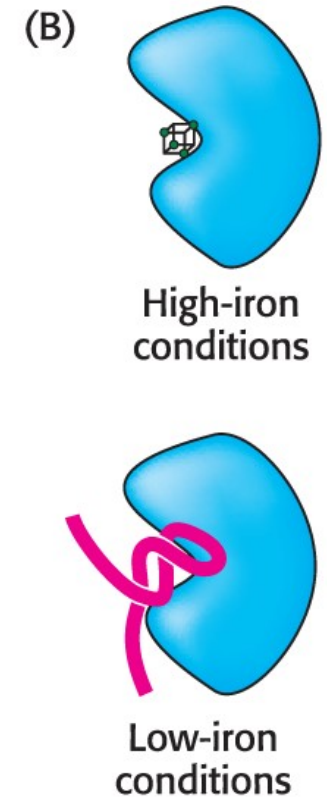
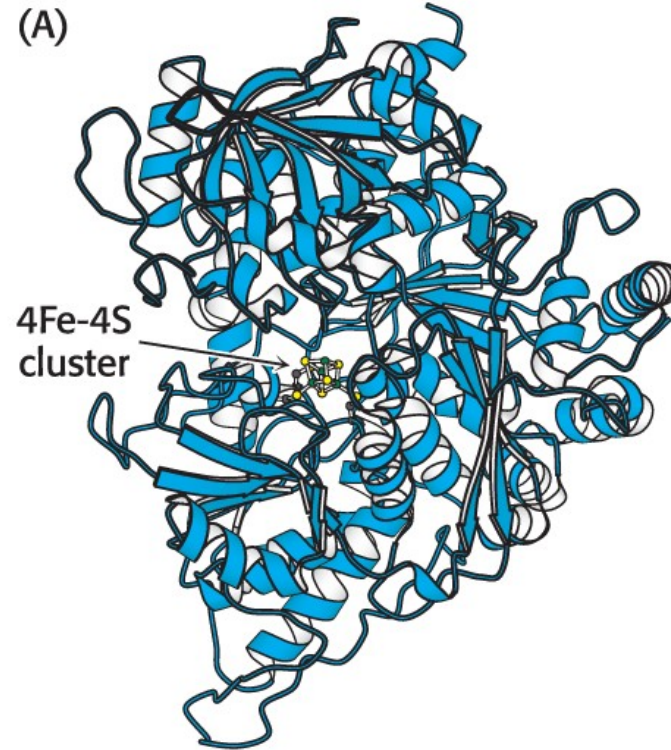
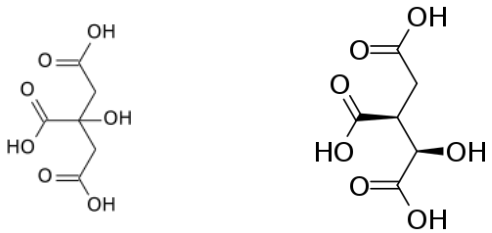
aconitase



aconitase enzyme

citrate $\longrightarrow$ isocitrate

Figure 1.59 How Proteins Work (©2012 Garland Science)



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Genes Associated with Iron Metabolism Are Translationally Regulated in Animals

Iron is a key component of many important proteins, including hemoglobin and cytochromes.

However, iron is also capable of generating destructive reactive oxygen species, so iron transport and storage must be carefully regulated.

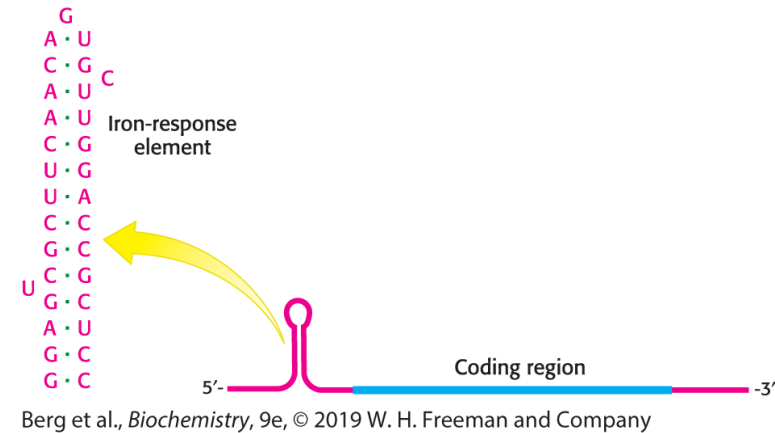
Important proteins in iron metabolism are transferrin, a blood protein that transports iron; transferrin receptor, a membrane protein that binds iron-rich transferrin and facilitates its entry into the cell; and ferritin, an iron-storage protein in the cell.

Ferritin mRNA contains a stem-loop structure in its 5' untranslated region called the iron response element (IRE).

In the absence of iron, the protein IRE-binding protein (IRP) binds to the IRE and prevents translation.

When present, iron binds the IRP, causing it to dissociate from the IRE and thereby allowing translation to occur.

Ferritin mRNA



Genes Associated with Iron Metabolism Are Translationally Regulated in Animals

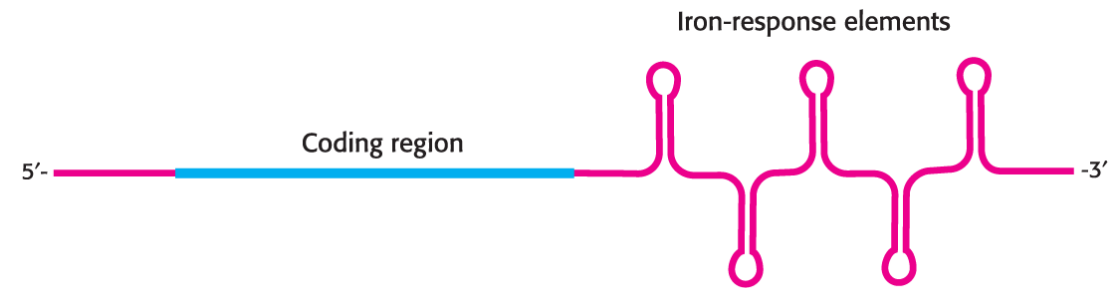
Transferrin-receptor mRNA also has several IREs, located in the 3' untranslated region.

When little iron is present, IRP binds to the IRE, allowing the mRNA to be translated.

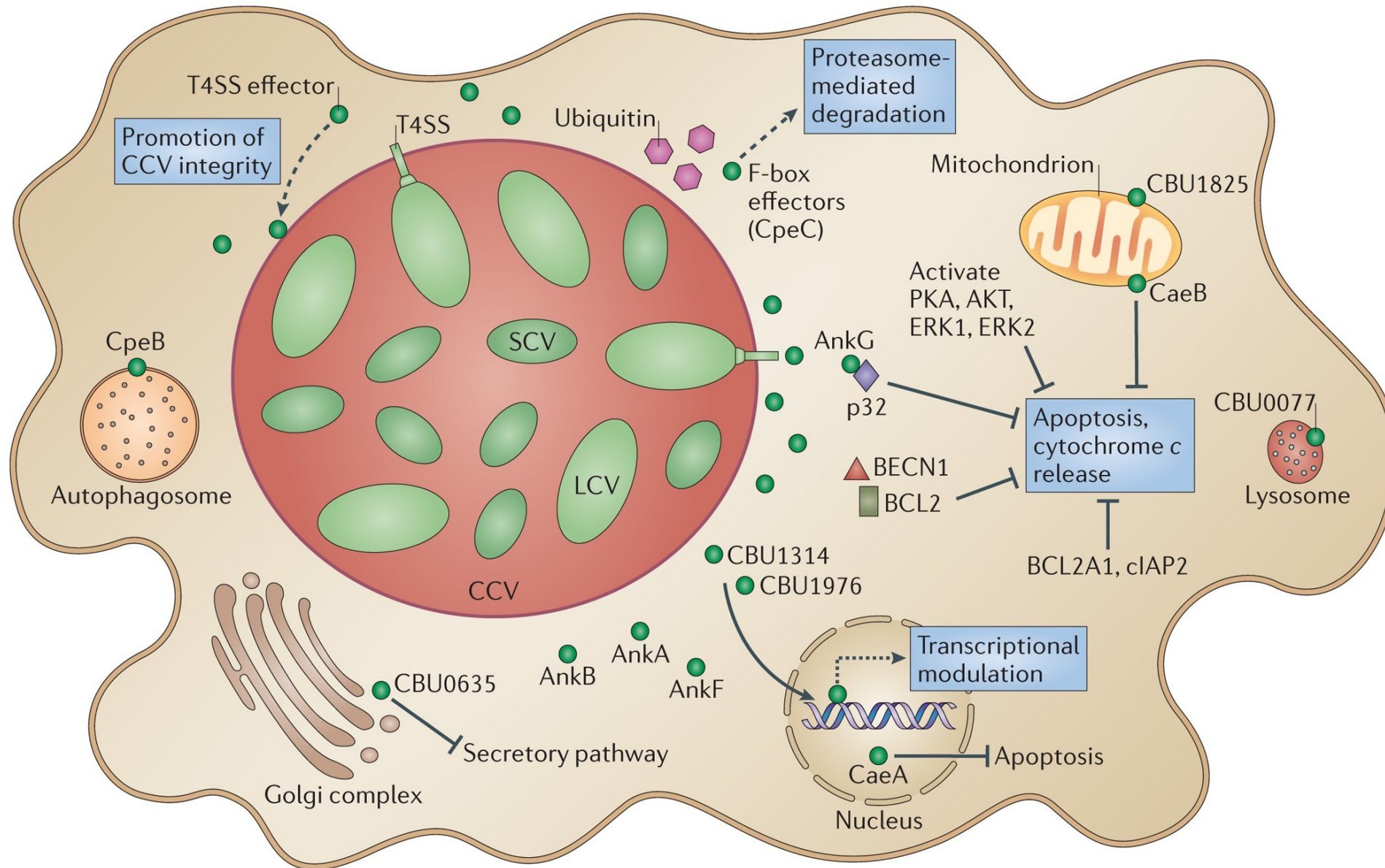
When present, iron binds to the IRP, causing it to dissociate from the transferrin-receptor mRNA. Devoid of the IRP, the receptor mRNA is degraded.

IRP is an active aconitase that requires iron and undergoes a conformational change when not bound to iron; therefore, it can serve as an iron sensor.

Transferrin-receptor mRNA



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Proteins began in an RNA world

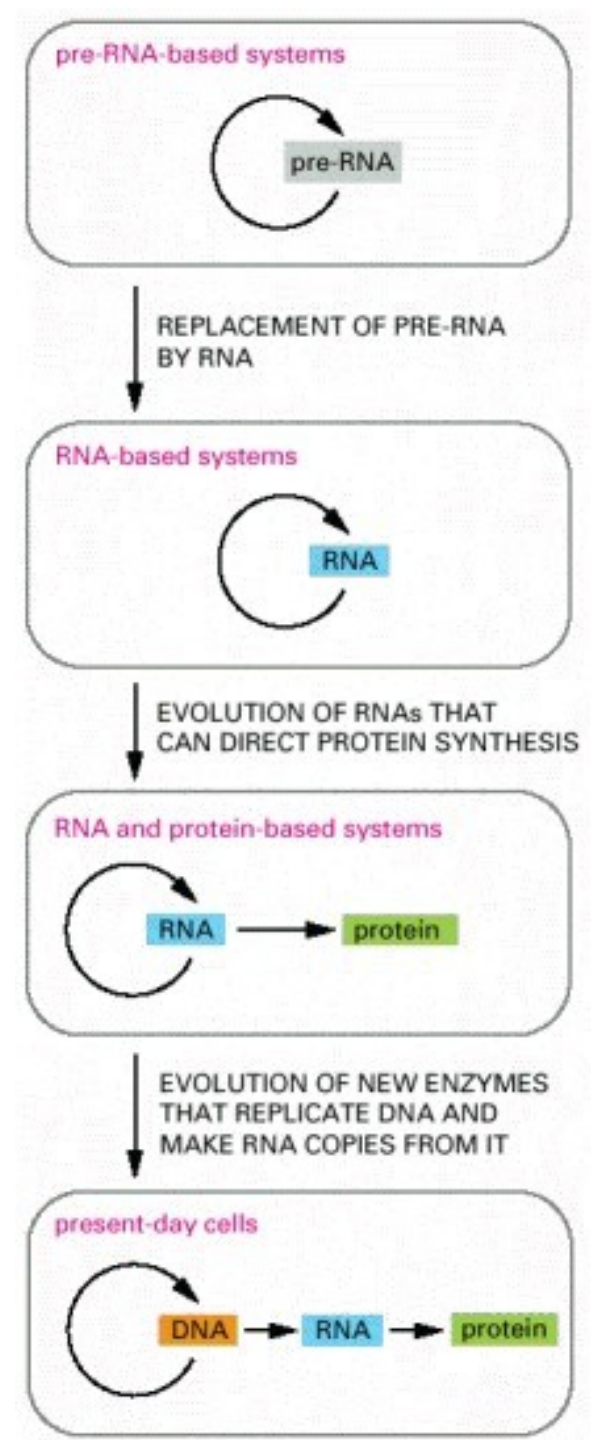
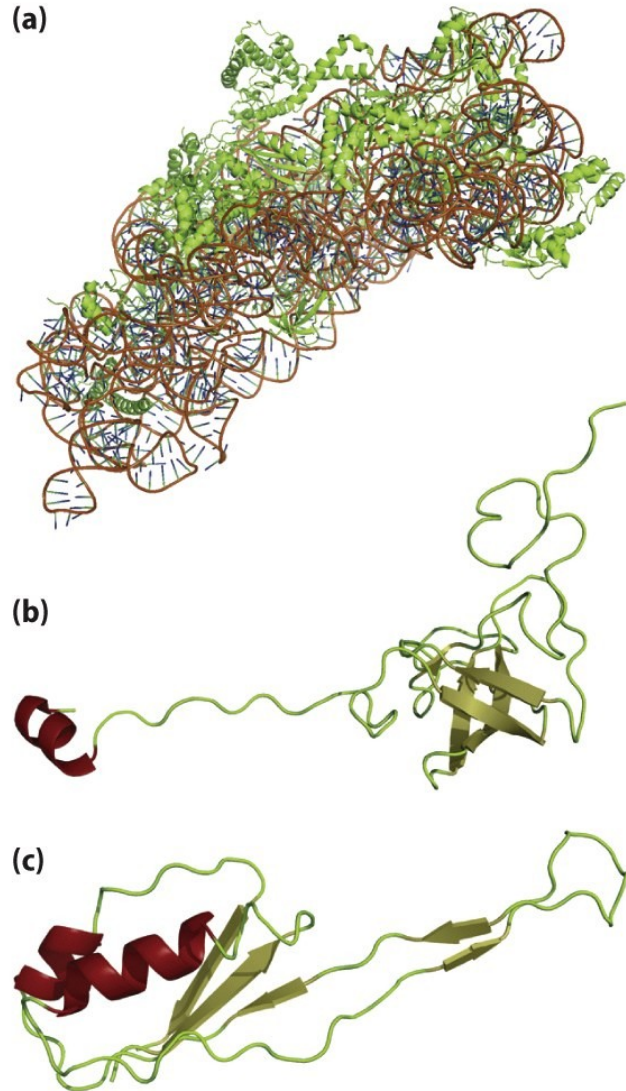


Figure 1.62 How Proteins Work (©2012 Garland Science)