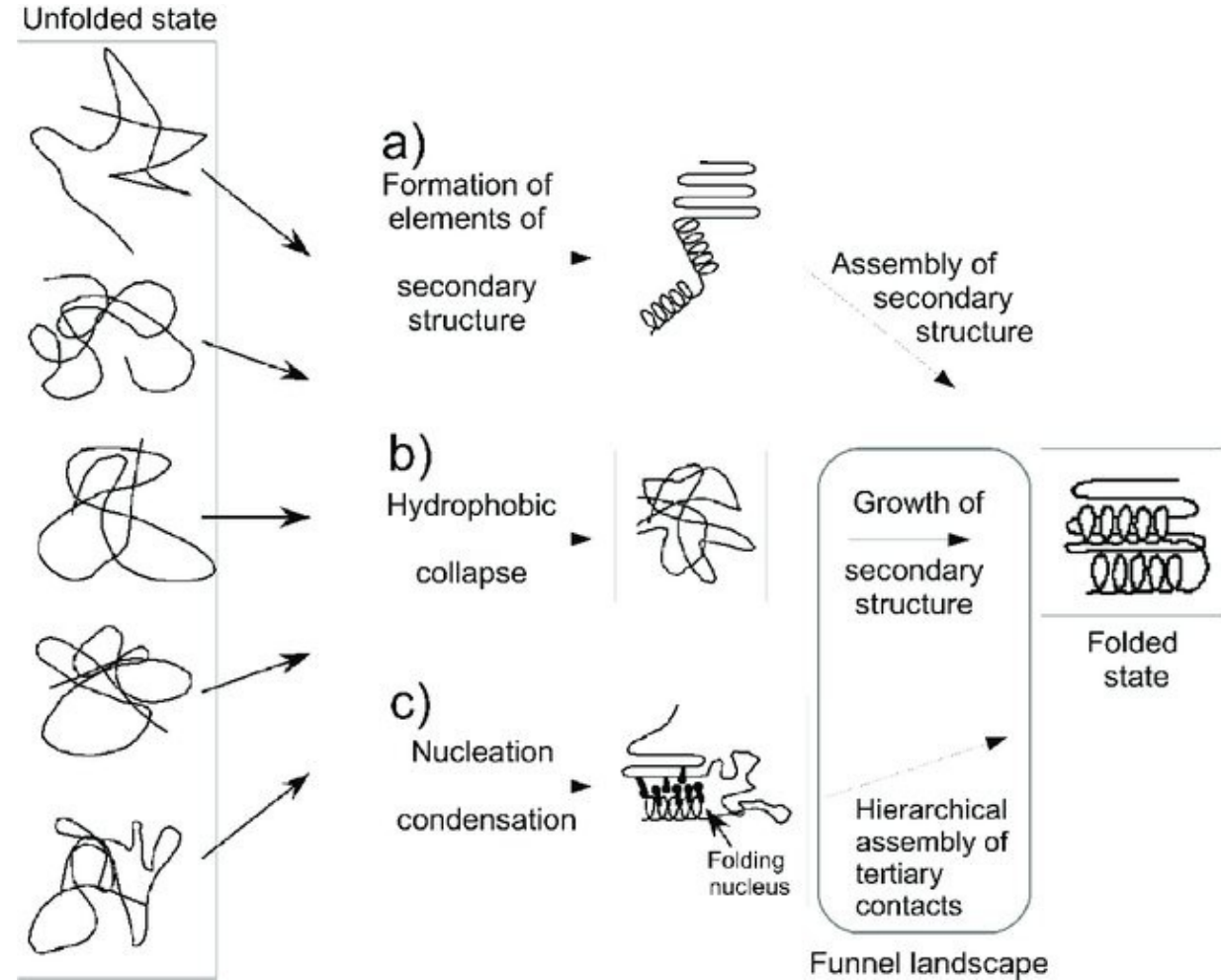
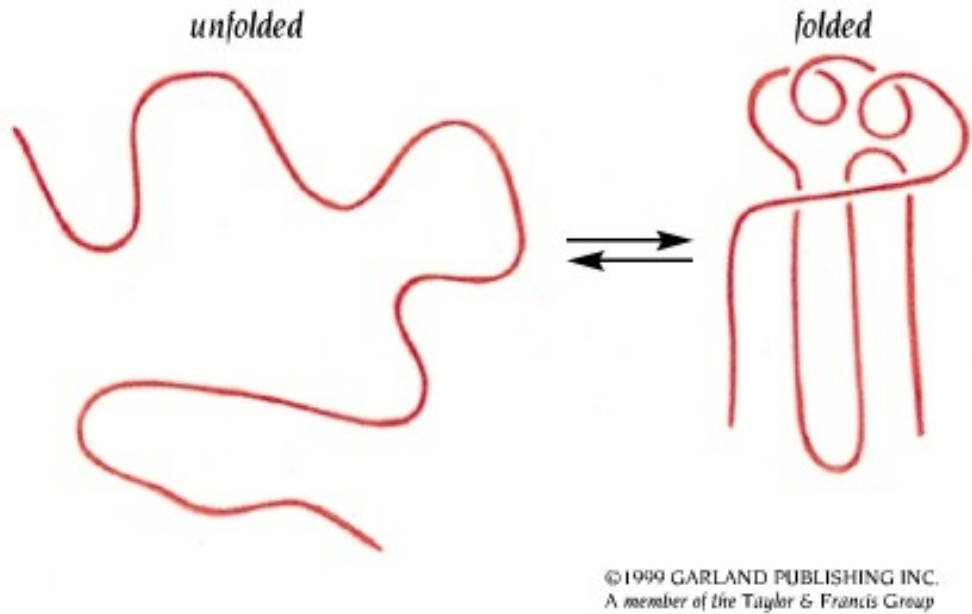


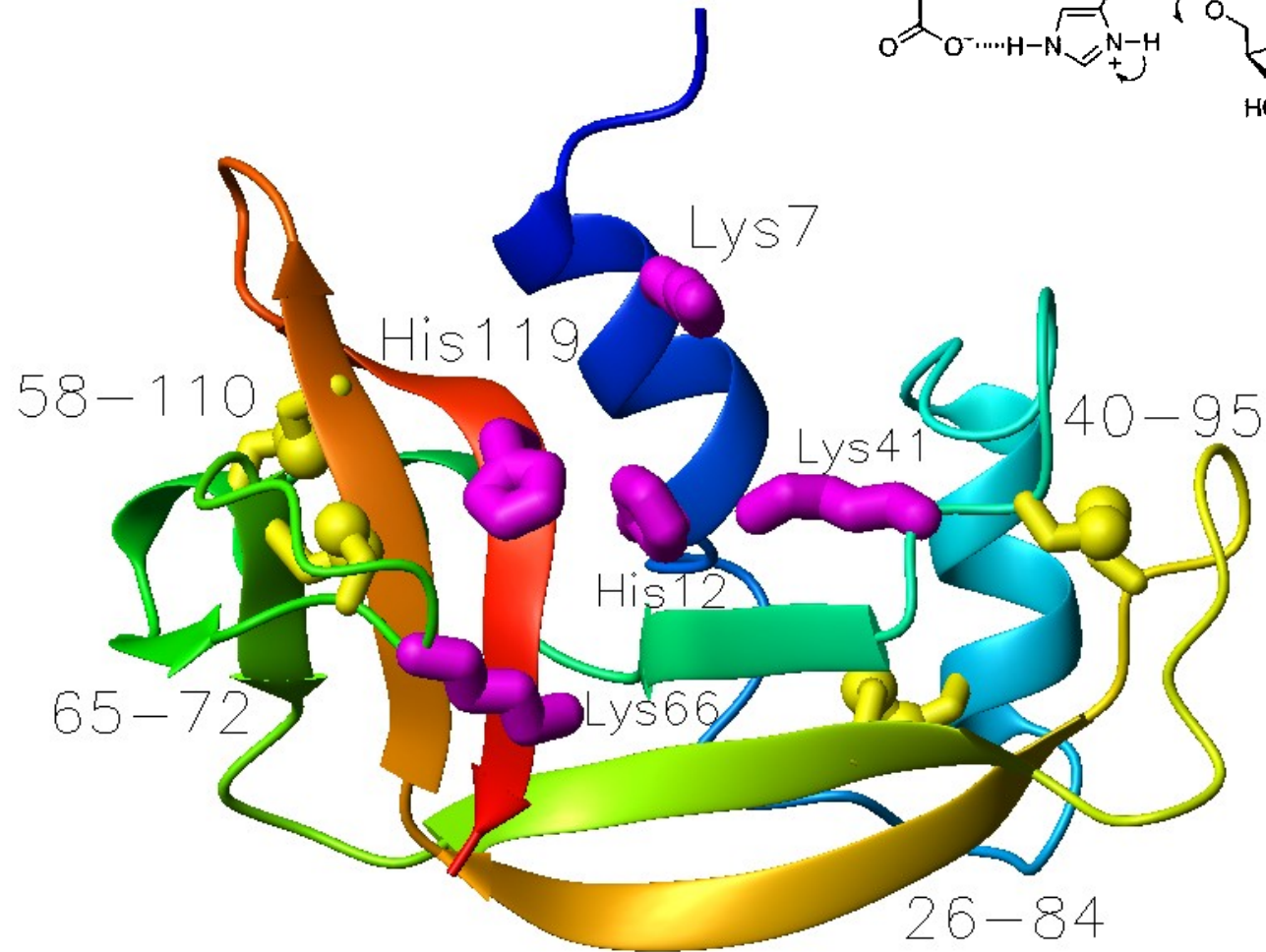
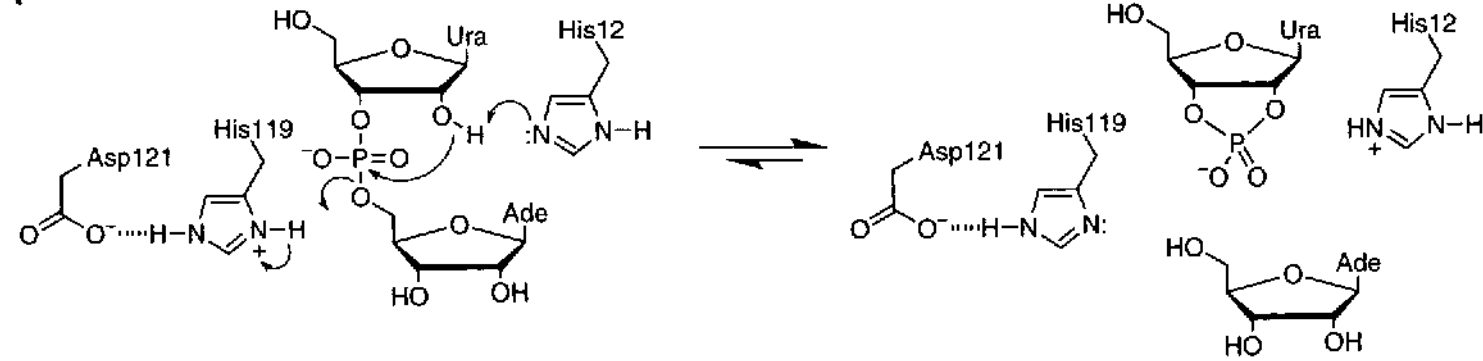
Protein folding



Protein folding

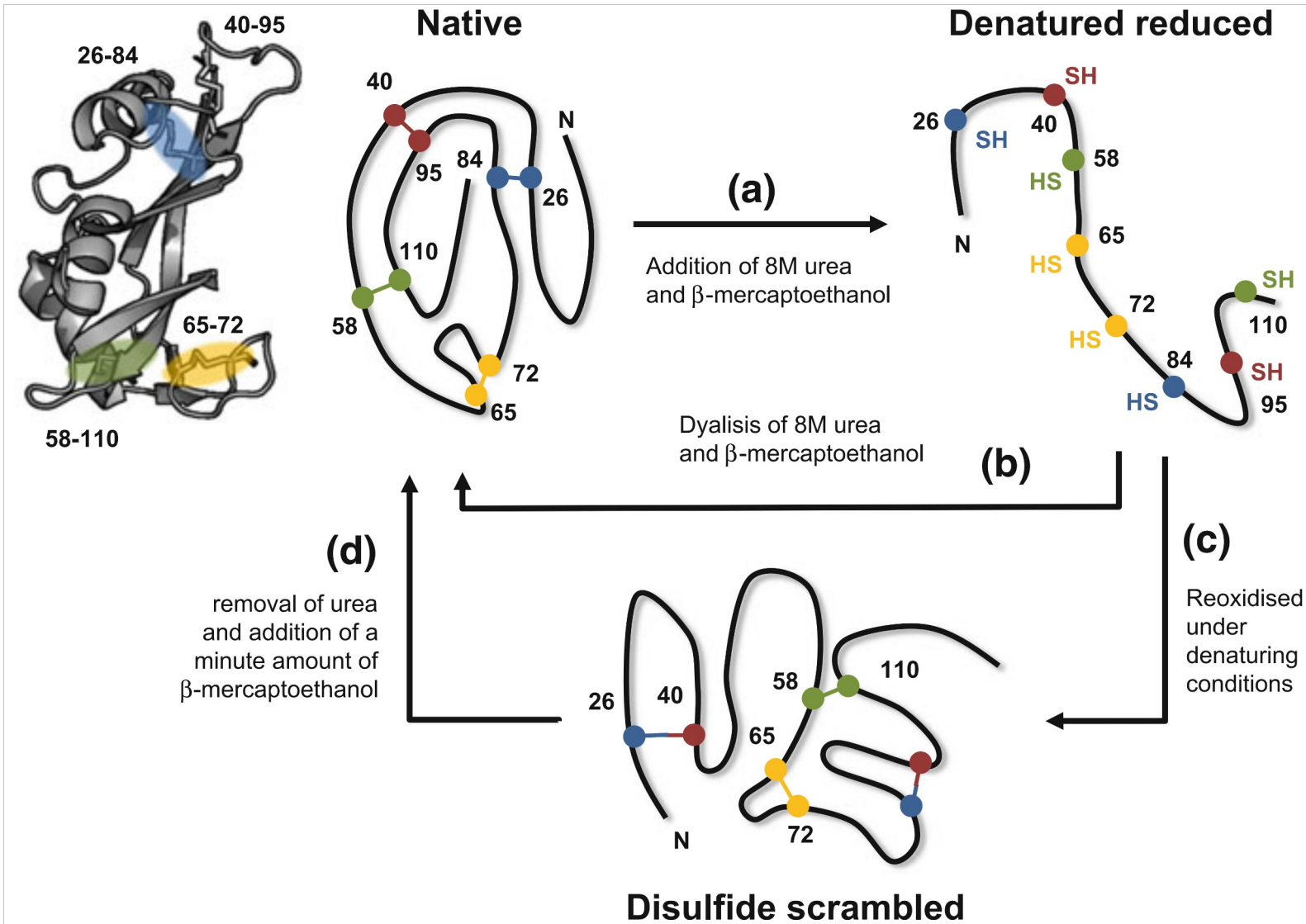
ribonuclease A

A



Protein folding

Anfinsen experiment



Λάθη συμβαίνουν in vitro και, πιθανώς, και in vivo

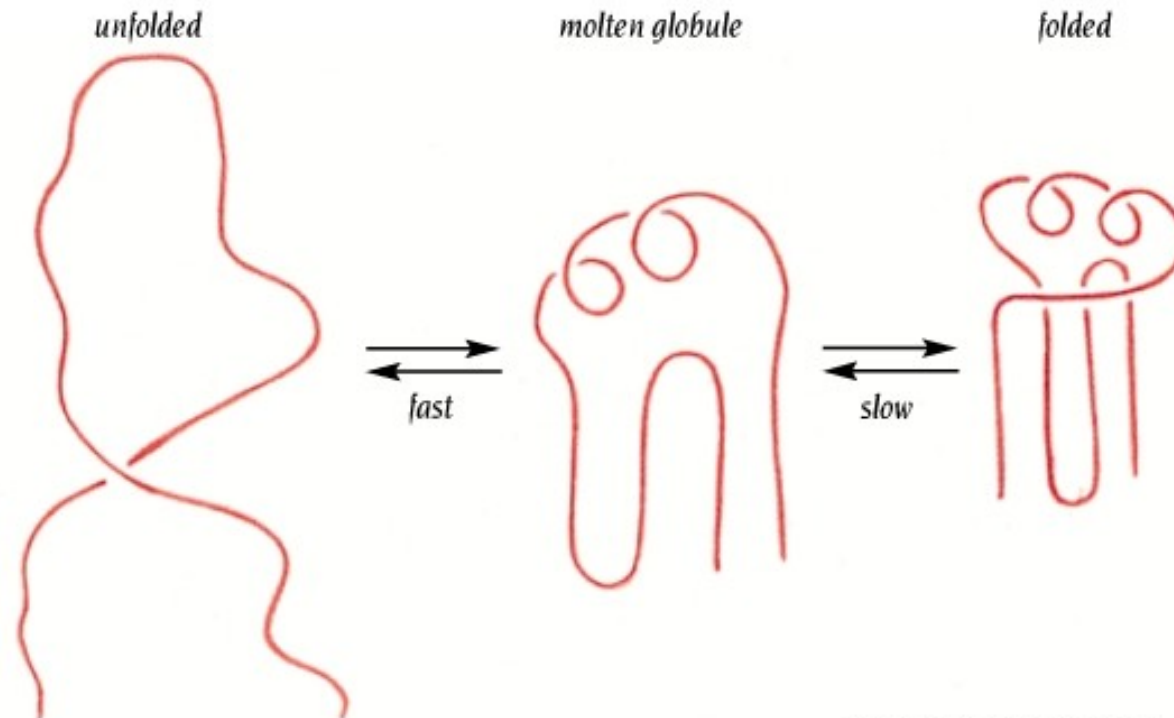
protein disulfide isomerase (PDI) καταλύει την αναγωγή των λανθασμένων δισουλφιδικών δεσμών και επιτρέπει σε μια πρωτεΐνη που έχει παγιδευτεί σε λανθασμένη διαμόρφωση να ξεδιπλωθεί και να προσπαθήσει ξανά.

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

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



The thermodynamic hypothesis

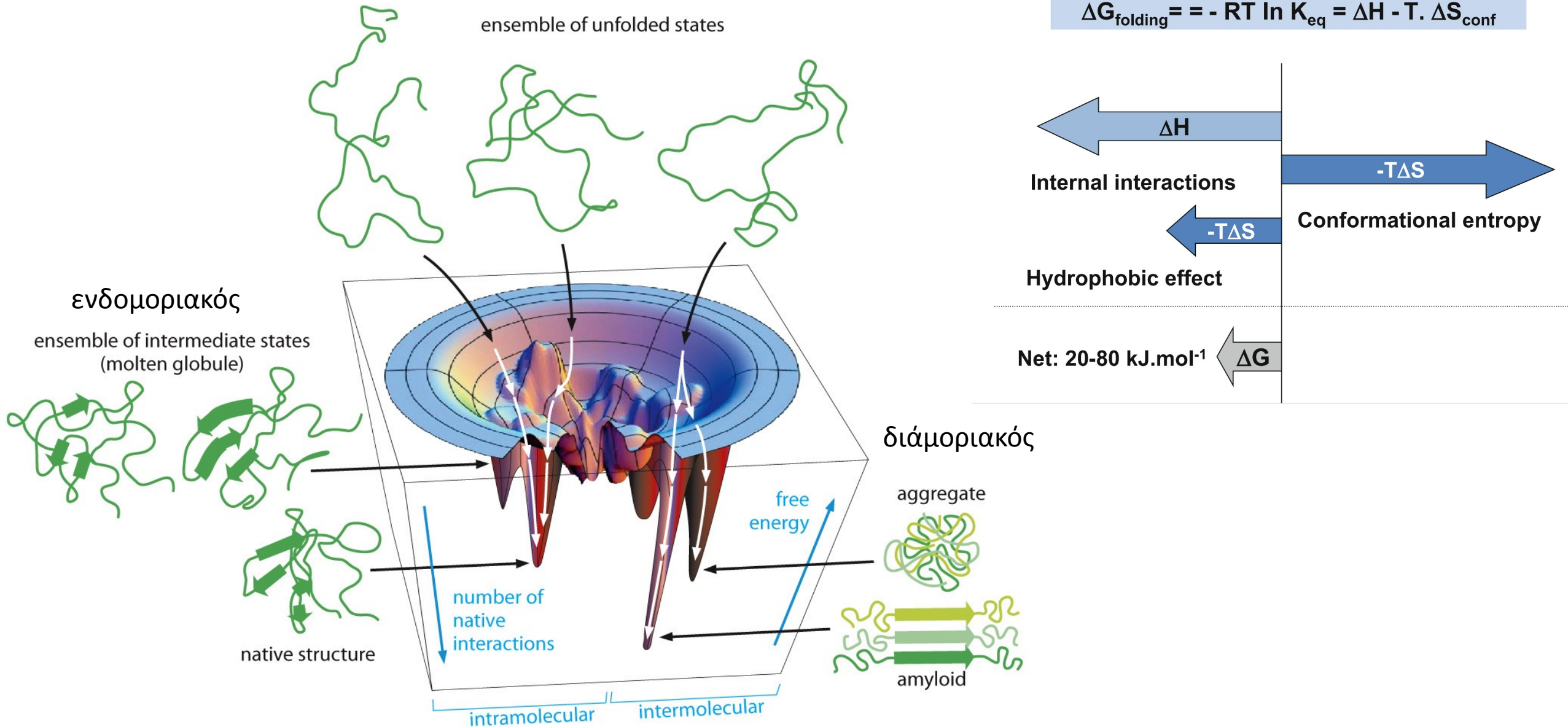


Figure 1.12 Molecular Biology of Assemblies and Machines (© Garland Science 2016)

Energy landscapes

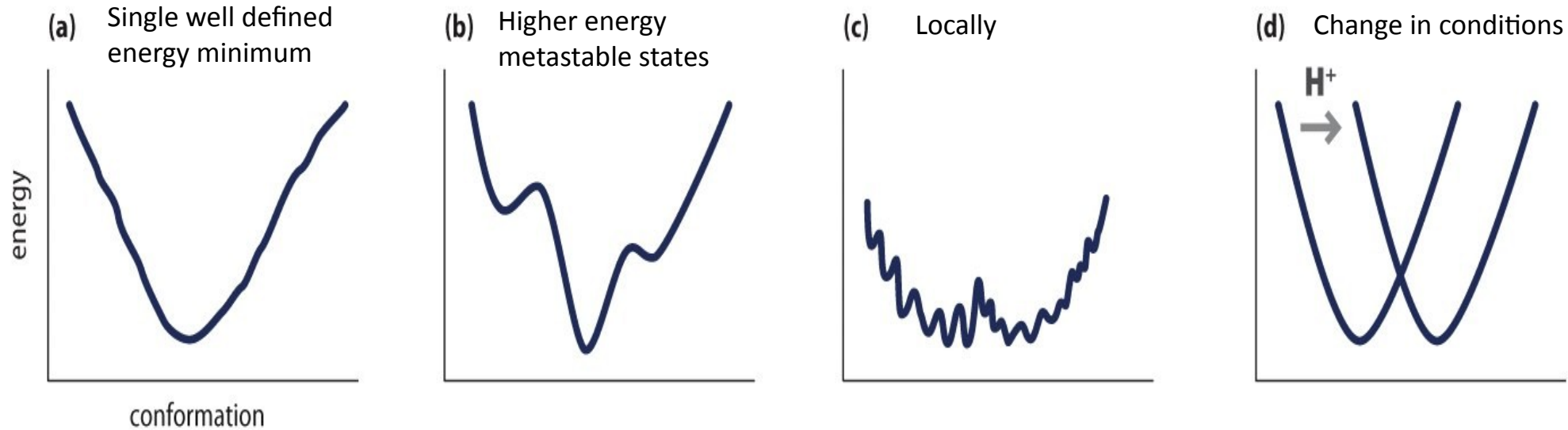
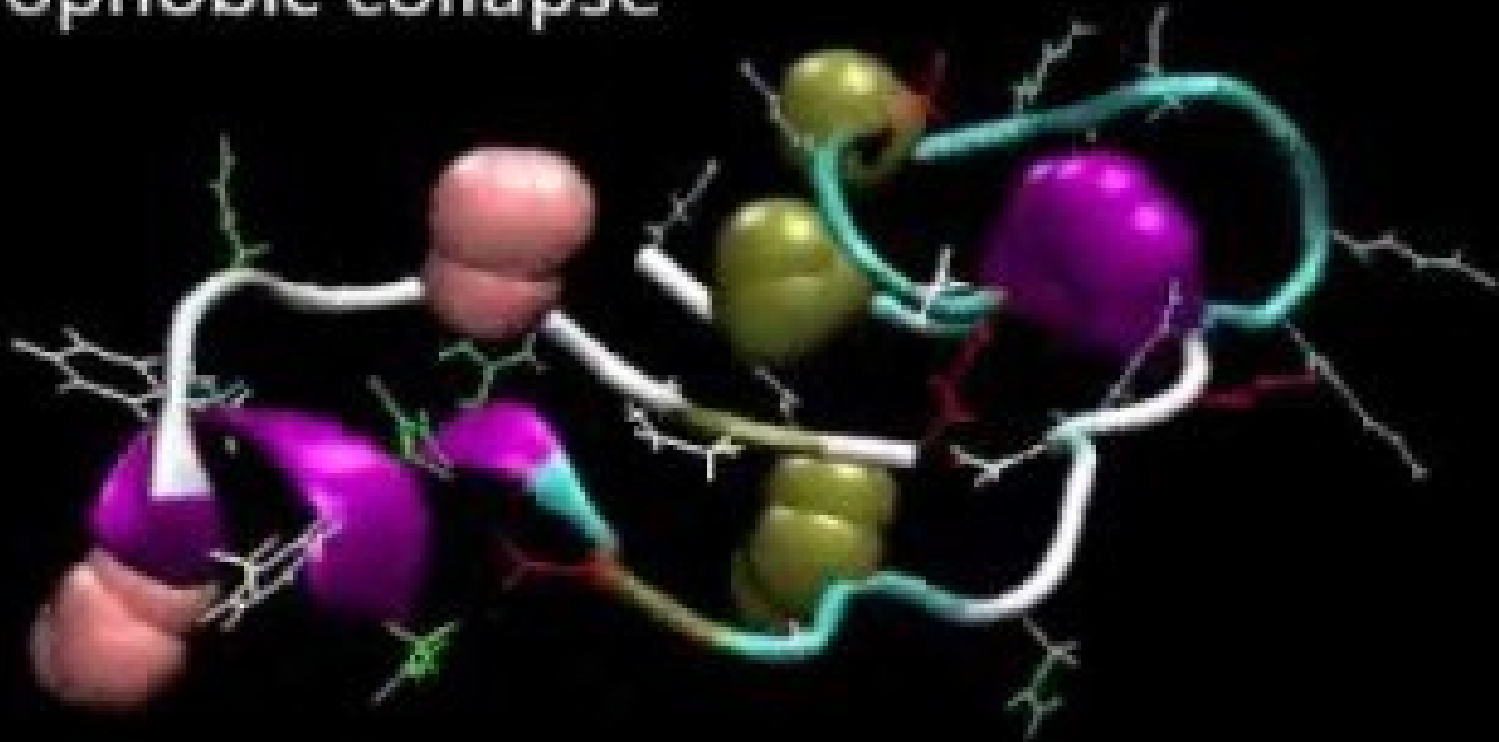


Figure 1.45 How Proteins Work (©2012 Garland Science)

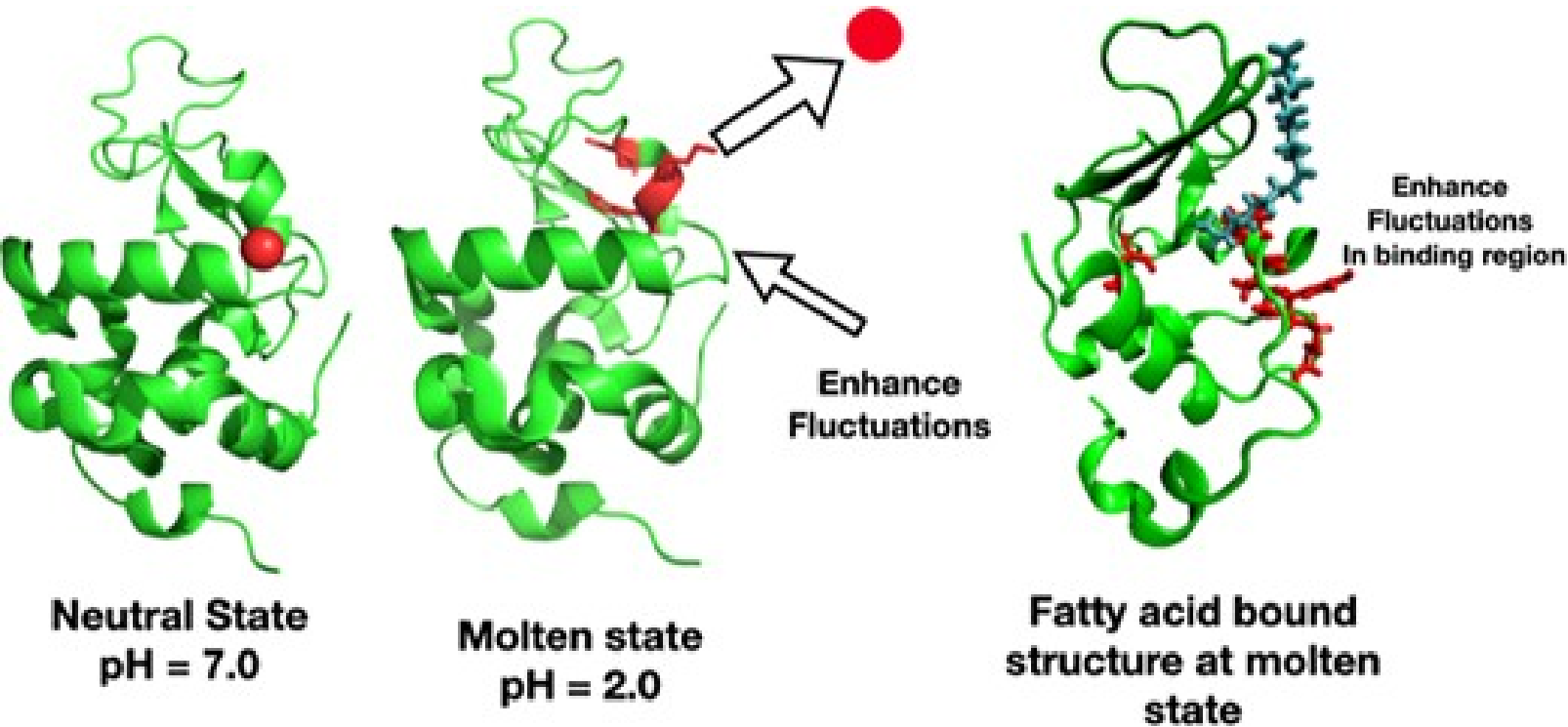
- A. Μια πρωτεΐνη έχει ένα μόνο, καλά καθορισμένο ενεργειακό ελάχιστο, με αποτέλεσμα να αναδιπλώνεται ομαλά προς το συνολικό ελάχιστο.
- B. Ορισμένες (πιθανώς πολλές) πρωτεΐνες παρουσιάζουν μετασταθείς καταστάσεις υψηλότερης ενέργειας, οι οποίες συνήθως έχουν ενεργειακά φράγματα χαμηλής ενέργειας προς το συνολικό ελάχιστο και, ως εκ τούτου, είναι πολύ βραχύβιες.
- C. Τοπικά, η επιφάνεια του τοπίου είναι πιθανώς πολύ ανώμαλη. Ωστόσο, τα περισσότερα ενεργειακά εμπόδια είναι αρκετά χαμηλά ώστε οι πρωτεΐνες σε θερμοκρασία δωματίου να μπορούν να τα ξεπεράσουν γρήγορα.
- D. Μια αλλαγή στις συνθήκες, στην περίπτωση αυτή η πρόσδεση ενός πρωτονίου (δηλαδή, η μείωση του pH), προκαλεί αλλαγή στη δομή του συνολικού ελάχιστου.

hydrophobic collapse



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

Fluctuation-Dominated Ligand Binding in Molten Globule Protein



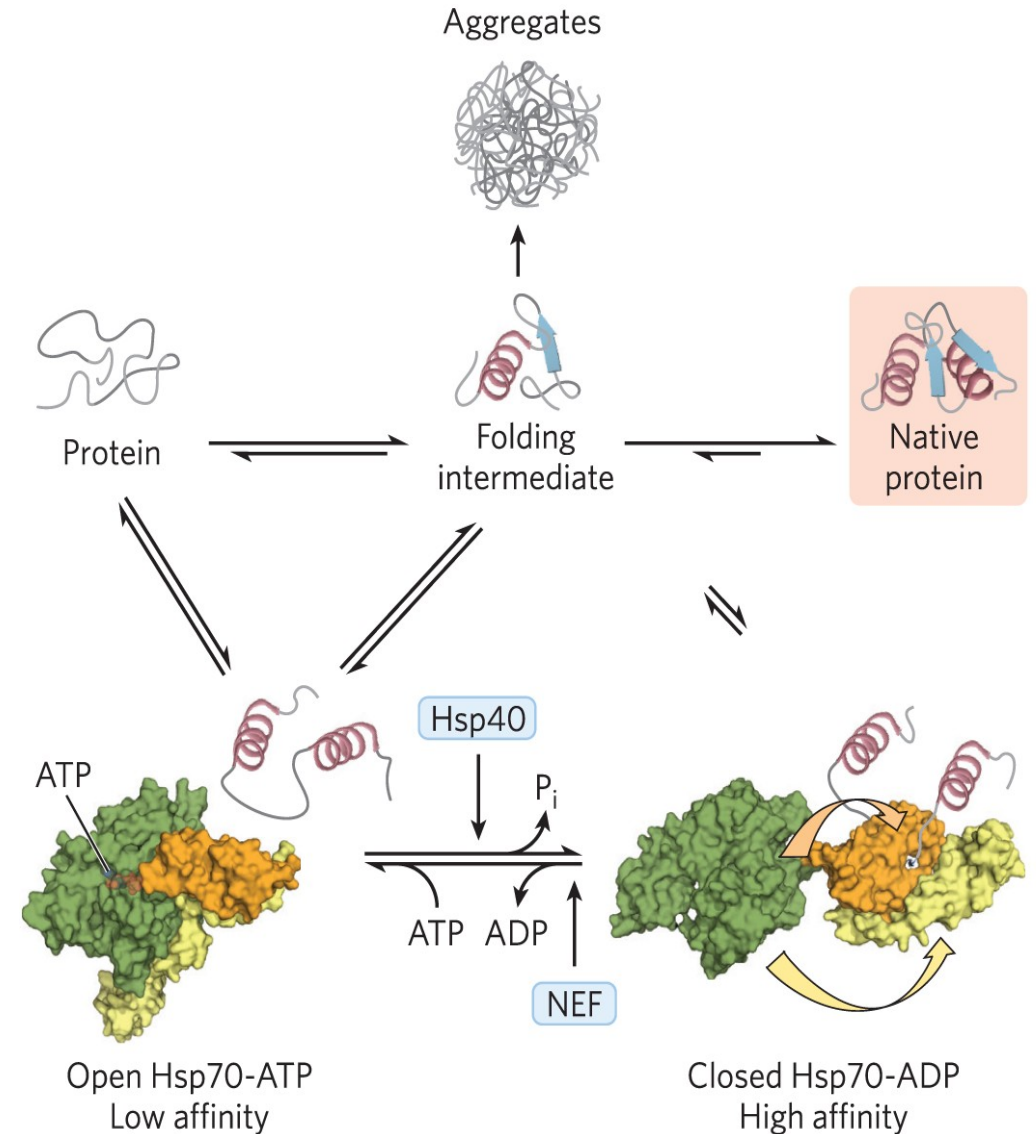
Στις καταστάσεις MG, η α-λακταλβουμίνη (αLA) συνδέεται με το ελαϊκό οξύ (OLA).

Αυτό το σύμπλεγμα, ασκεί κυτταροτοξική δράση έναντι καρκινικών κυτταρικών σειρών.

Η ιδέα των μεταβαλλόμενων θέσεων πρόσδεσης μπορεί να συμβάλει στον ορθολογικό σχεδιασμό φαρμάκων, ο οποίος επιτρέπει τη δημιουργία φαρμάκων που αλληλεπιδρούν με τη δυναμική θέση της πρωτεΐνης στόχου με πιο αποτελεσματικό τρόπο.

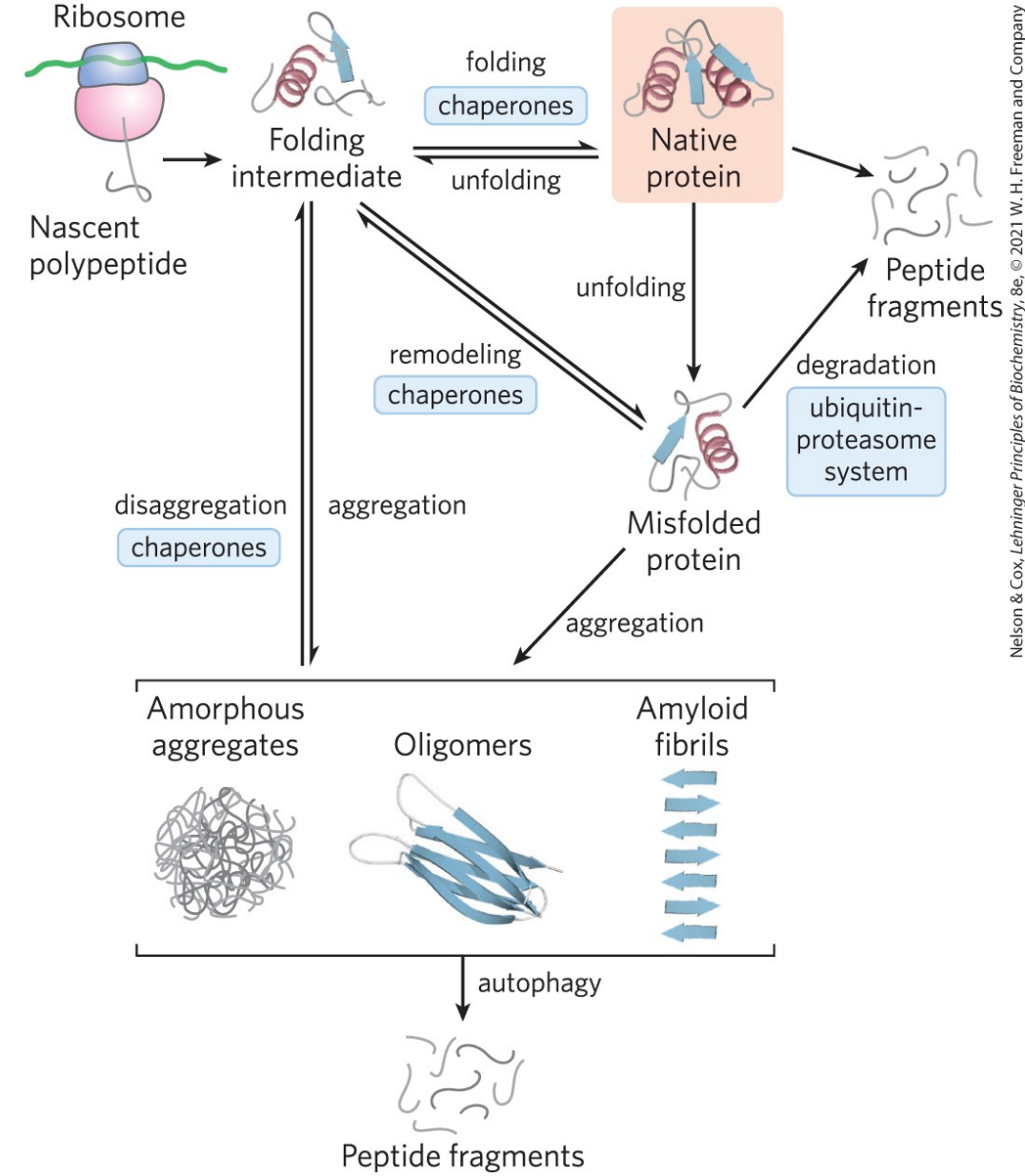
Some Proteins Undergo Assisted Folding

- **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

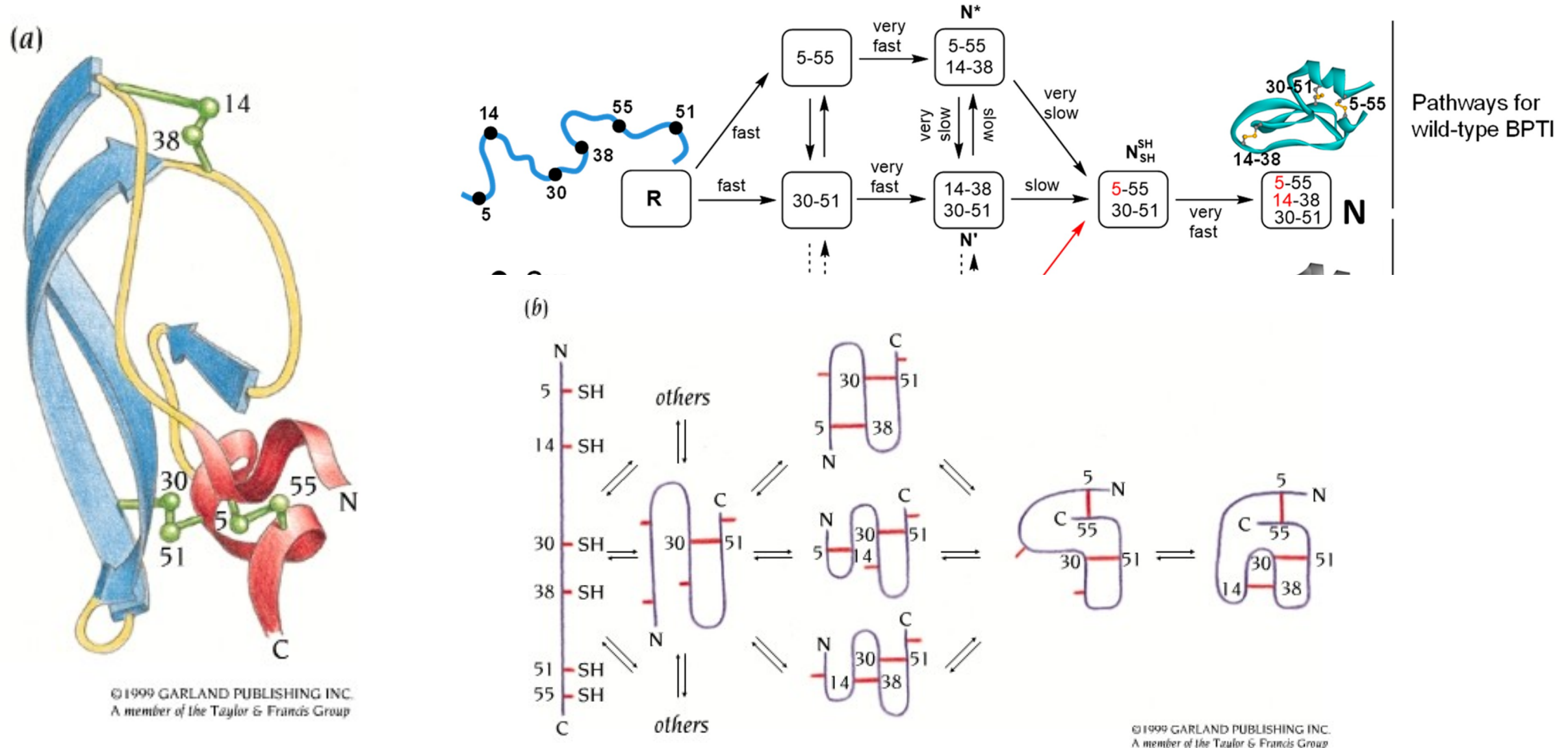


Pathways Involved in Proteostasis

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



Bovine pancreatic trypsin inhibitor, BPTI.



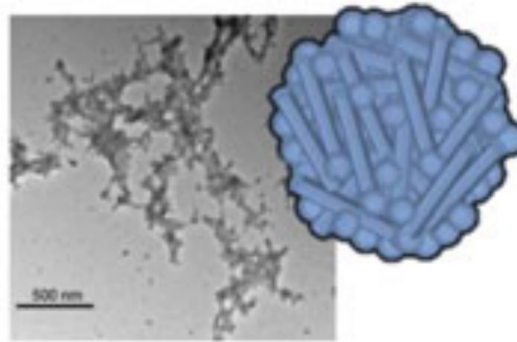
Physical and structural characteristics of misfolded proteins

Destabilized protein



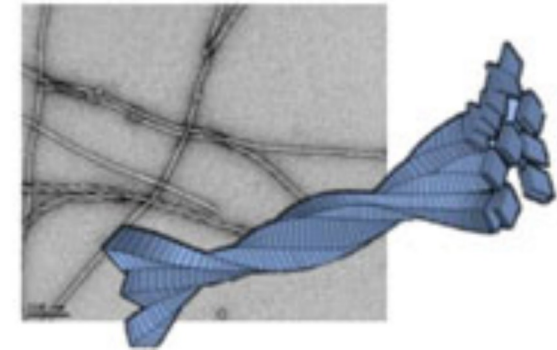
- Low stability conformational state
- May have locally altered secondary structure or poor tertiary interactions.
- It usually retains some biological function
- More susceptible to proteolysis than native

Protein Aggregate



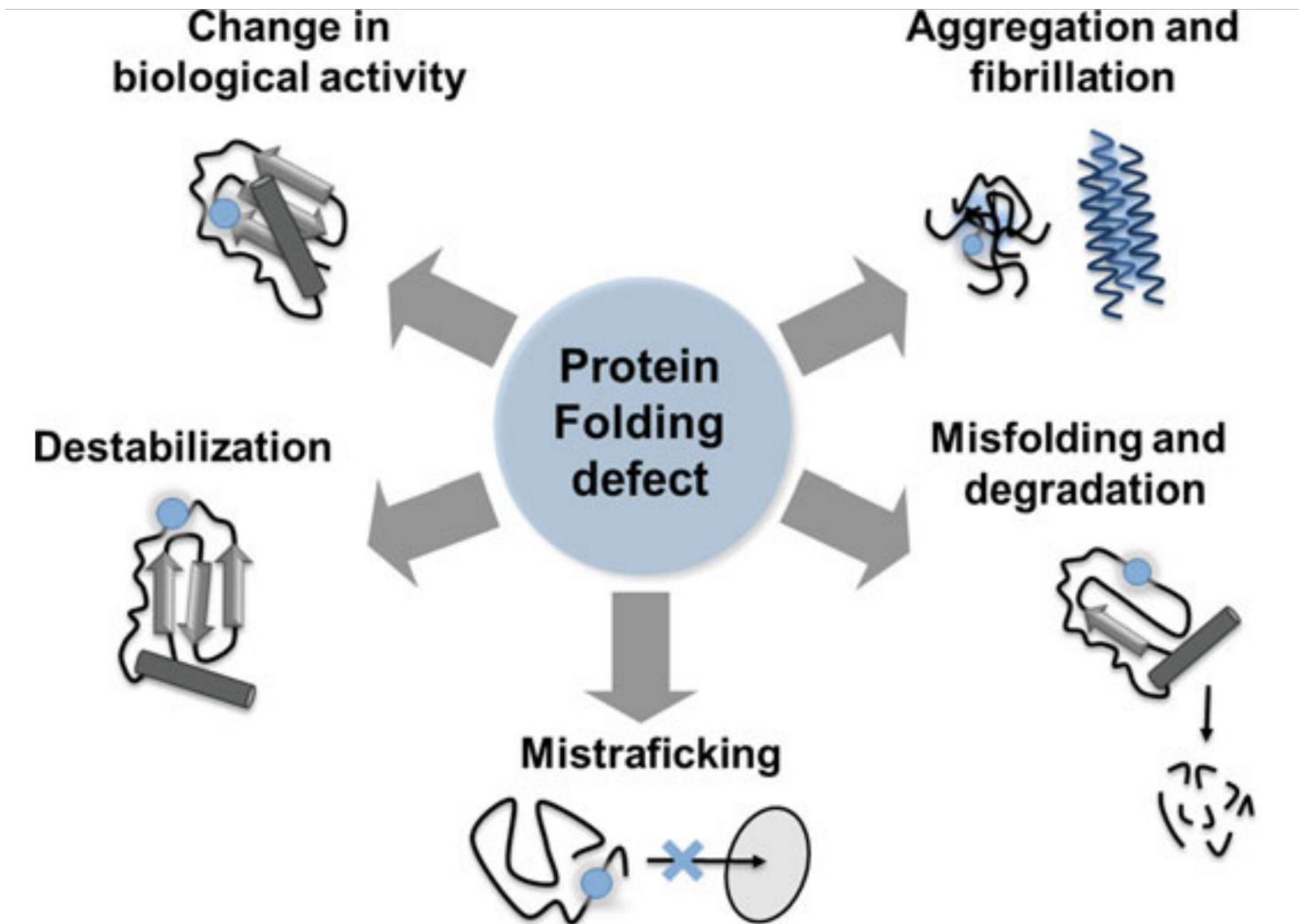
- Amorphous
- insoluble protein conglomerate
- Results from intermolecular hydrophobic interactions between misfolded proteins
- Readily resolubilized in buffer in native like conditions

Amyloid fibril

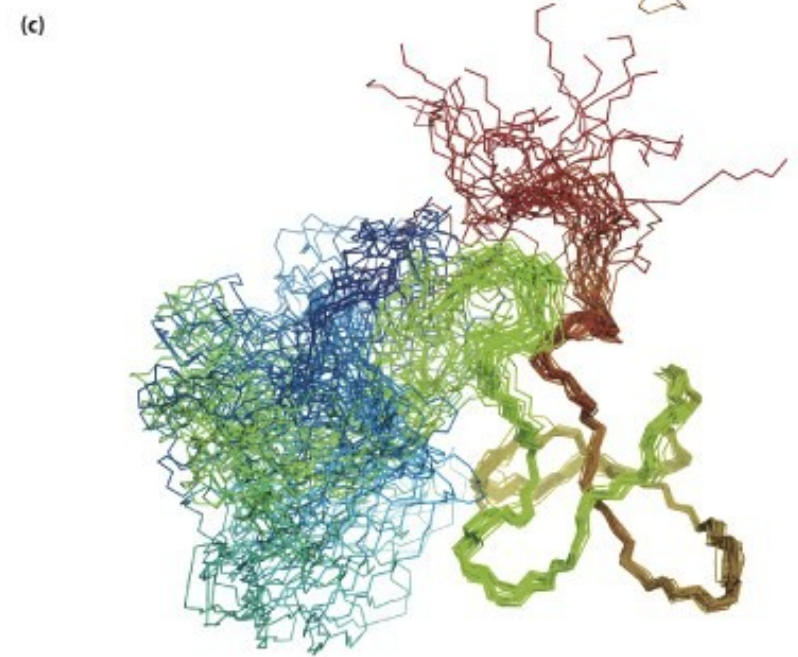
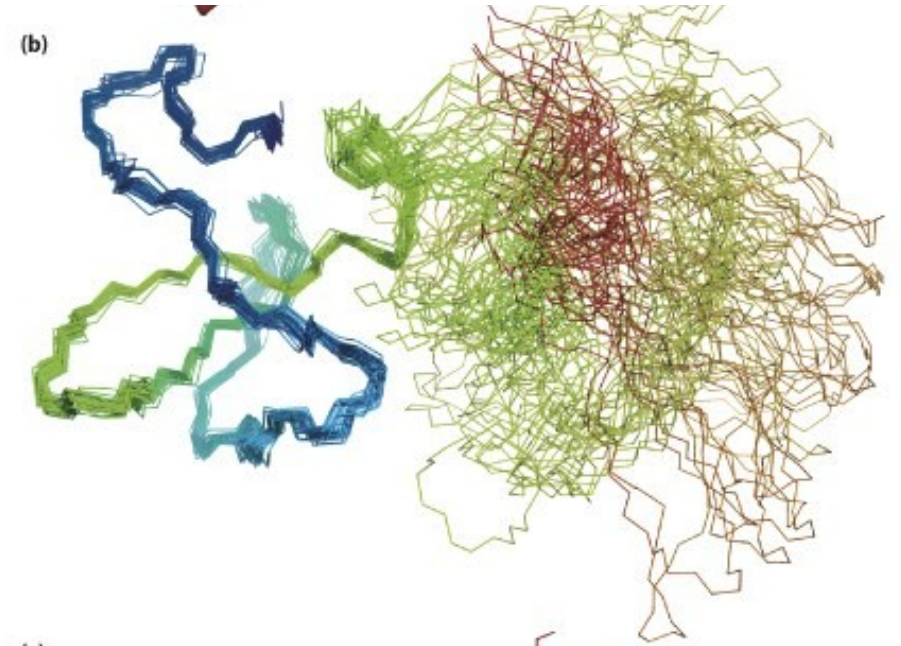
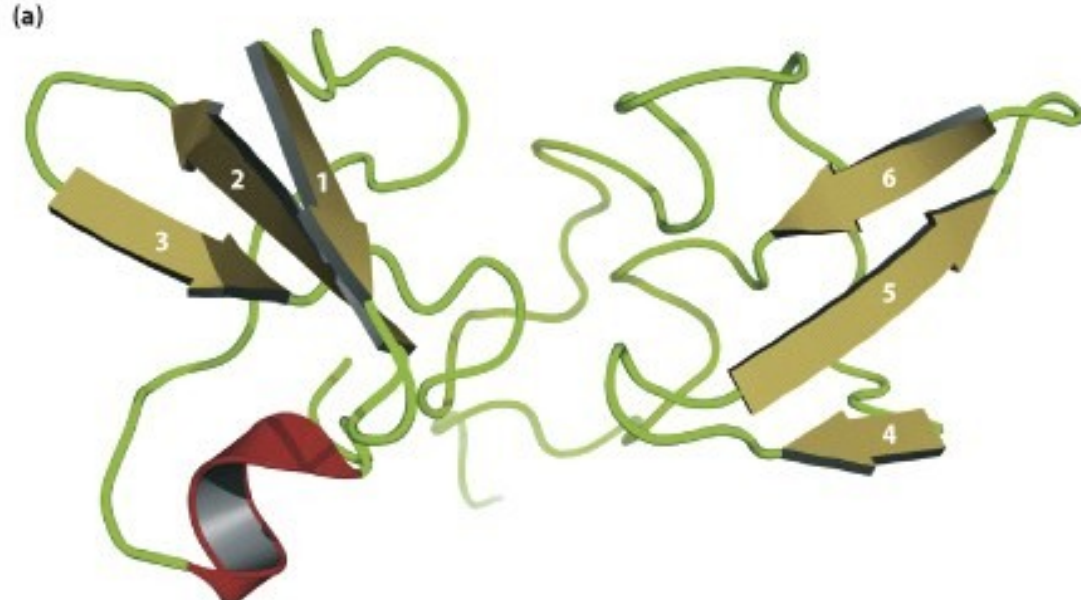


- Highly ordered
- Insoluble fibril-shaped protein aggregates
- formed from β -sheet stacking in a cross- β motif
- Highly resistant to proteolysis
- Requires high concentrations of denaturant or detergent to resolubilize

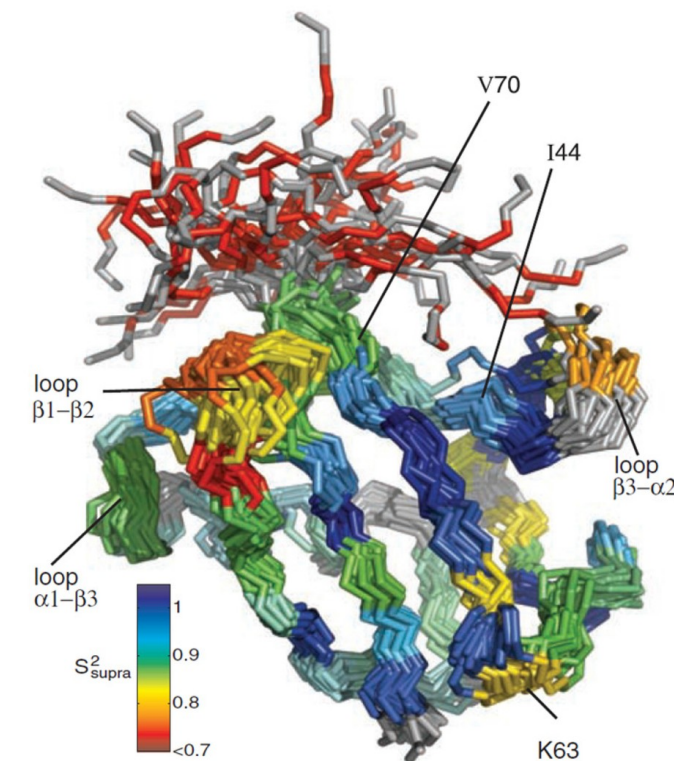
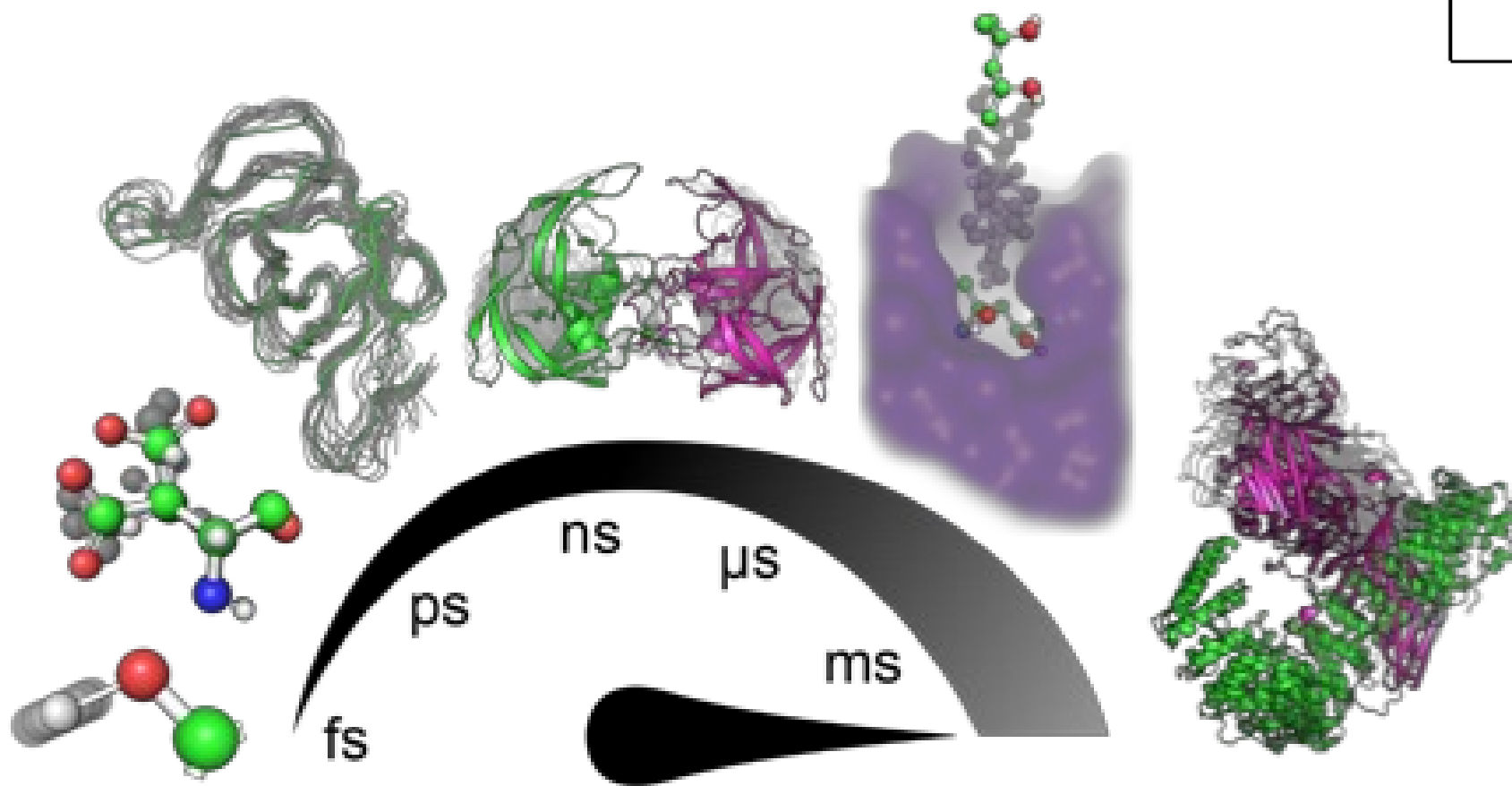
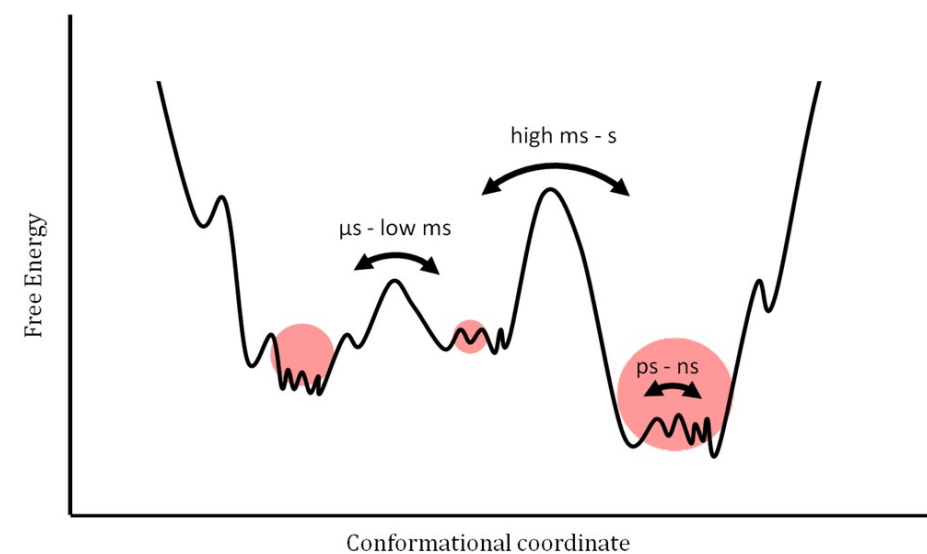
Misfolded proteins: multiple pathways to disease



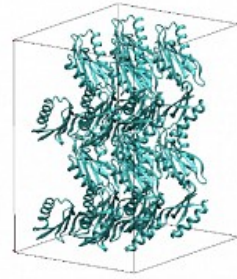
dynamics of a protein



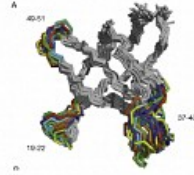
Motion in protein dynamics



Exploring the role of dynamics in protein function using NMR



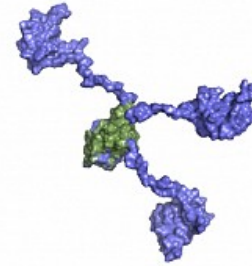
Dynamics in
microcrystalline
proteins



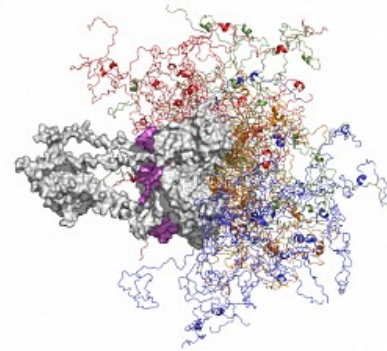
Local dynamic
modes on multiple
timescales....



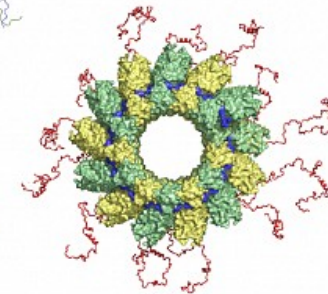
...and their role
in functional complexes



Multidomain proteins
with flexible linkers



Multidomain proteins
with highly disordered
functional domains



Flexible domains
in highly ordered
assemblies



Intrinsically
disordered
proteins

The order parameter

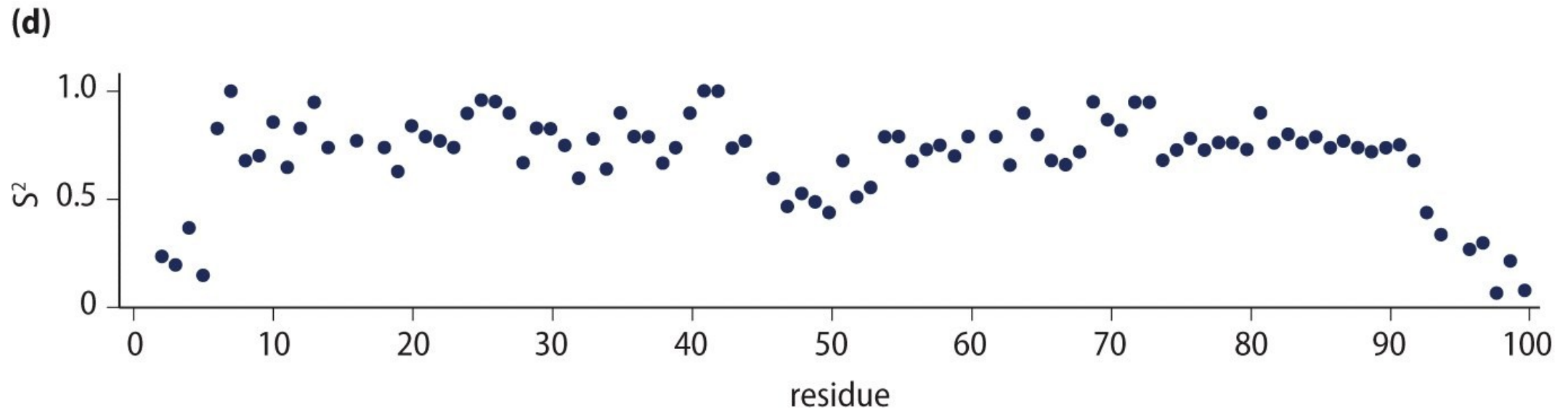
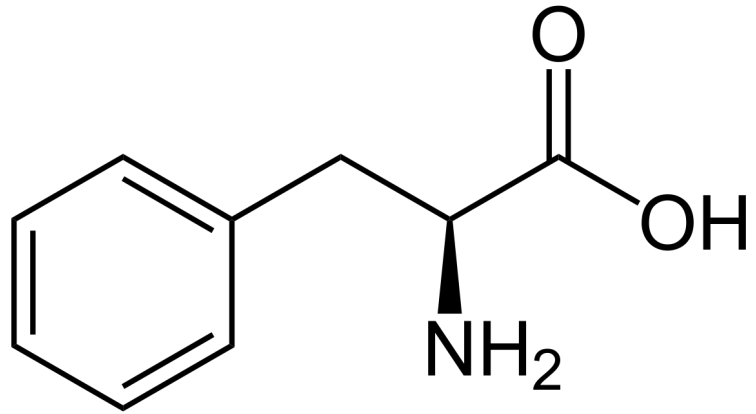


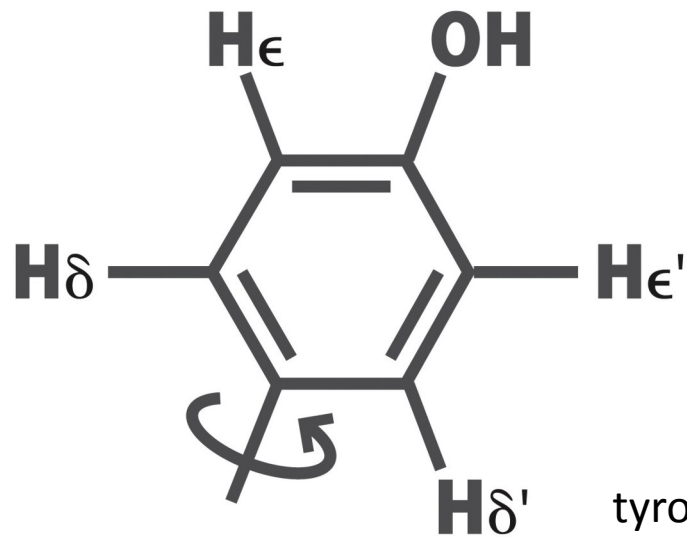
Figure 6.3 part 2 of 2 How Proteins Work (©2012 Garland Science)

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

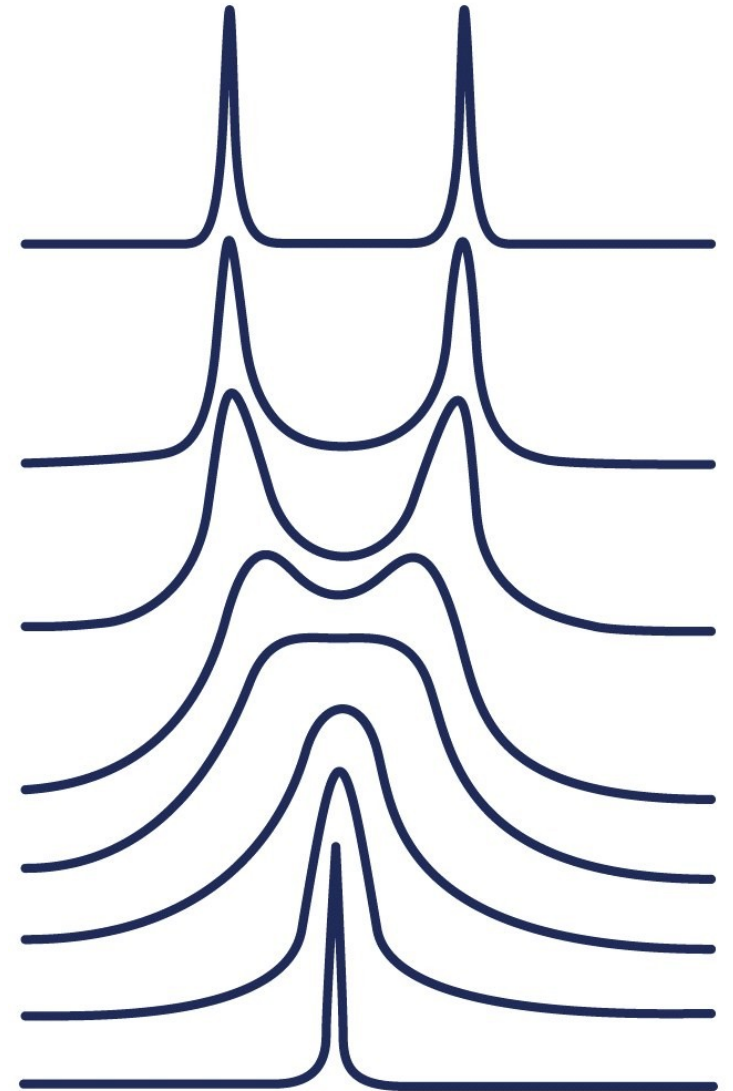
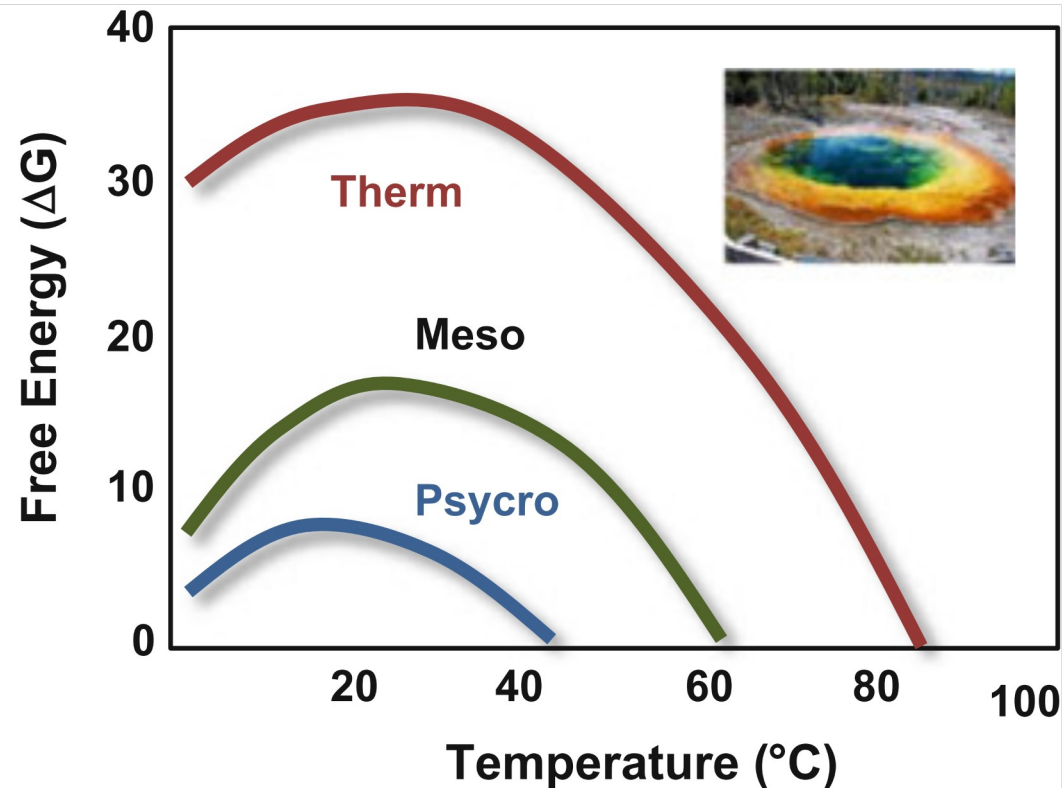


Figure 6.7 How Proteins Work (©2012 Garland Science)

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

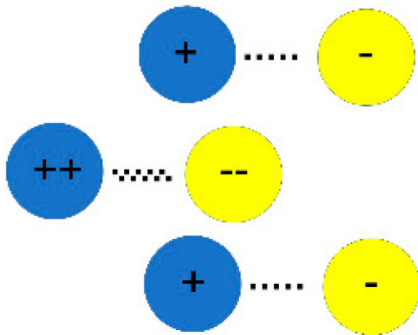
Sequence adaptations

Thermostable Proteins-Structural adaptations

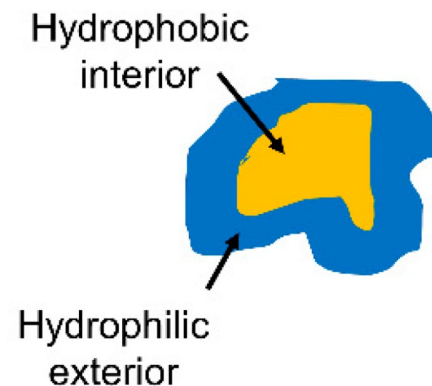
η προσαρμογή γενικά έχει ως αποτέλεσμα την αύξηση της δομικής ακαμψίας των πρωτεϊνών, διατηρώντας παράλληλα την τοπική ευκαμψία των λειτουργικά σημαντικών περιοχών

Characteristics of thermophilic proteins compared to mesophilic proteins

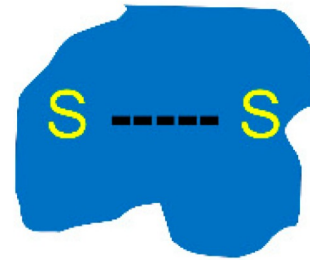
More ion pairs



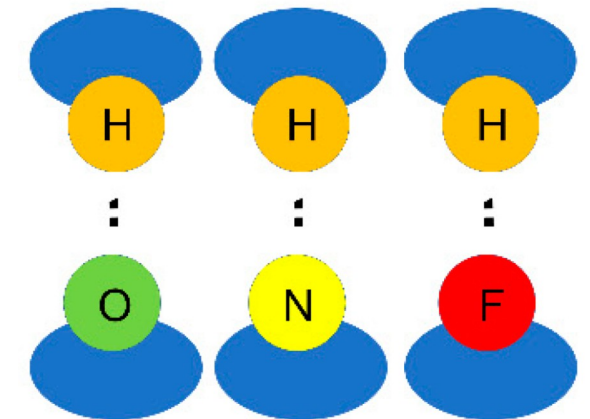
Greater average hydrophobicity of interior residues



More compact core containing disulfide bonds



More hydrogen bonds



Thermostable Proteins-Sequence adaptations

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

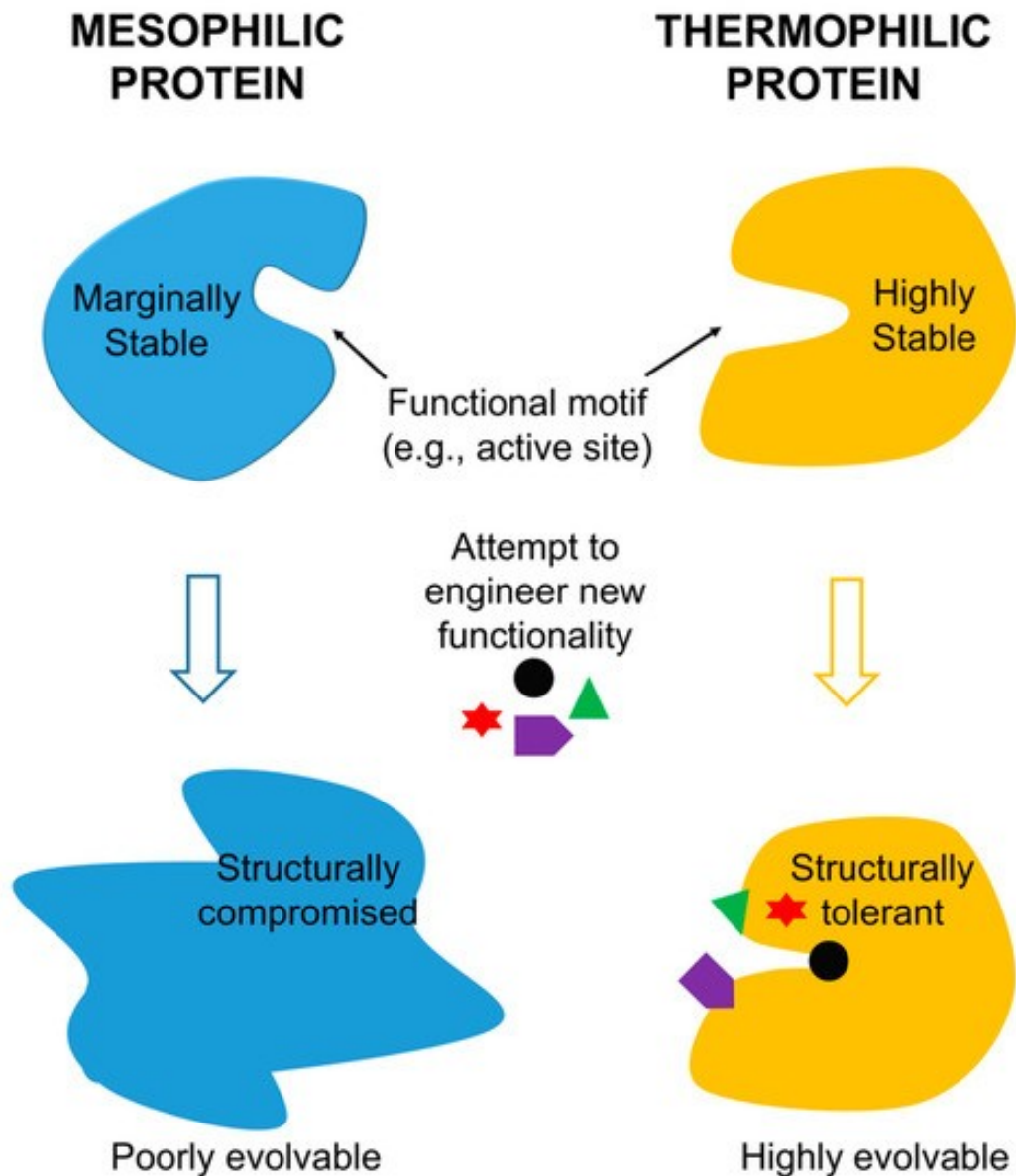
αύξηση των φορτισμένων αμινοξέων, ειδικά Arg και Glu που συμβάλλουν στις ιοντικές αλληλεπιδράσεις·

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

μείωση Met και των μη φορτισμένων πολικών αμινοξέων, 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



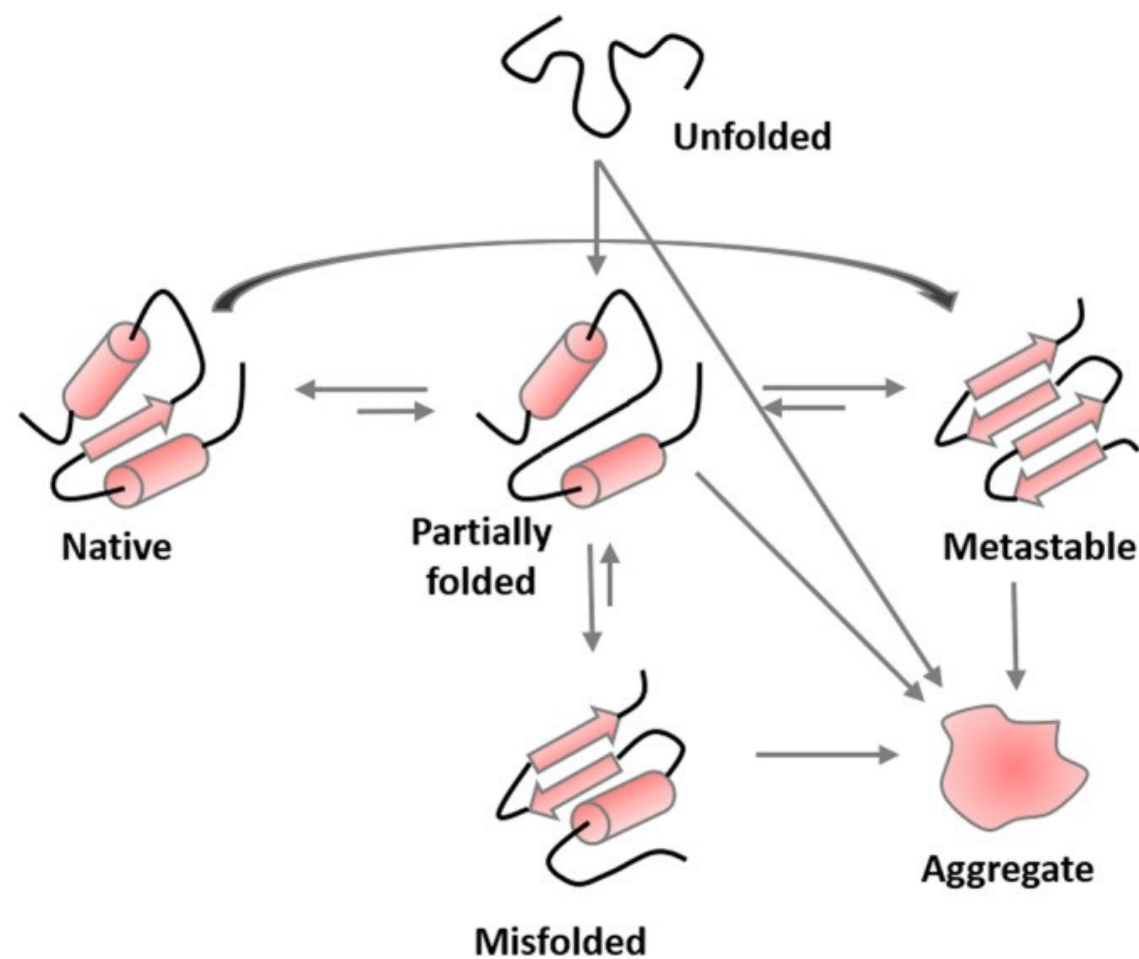
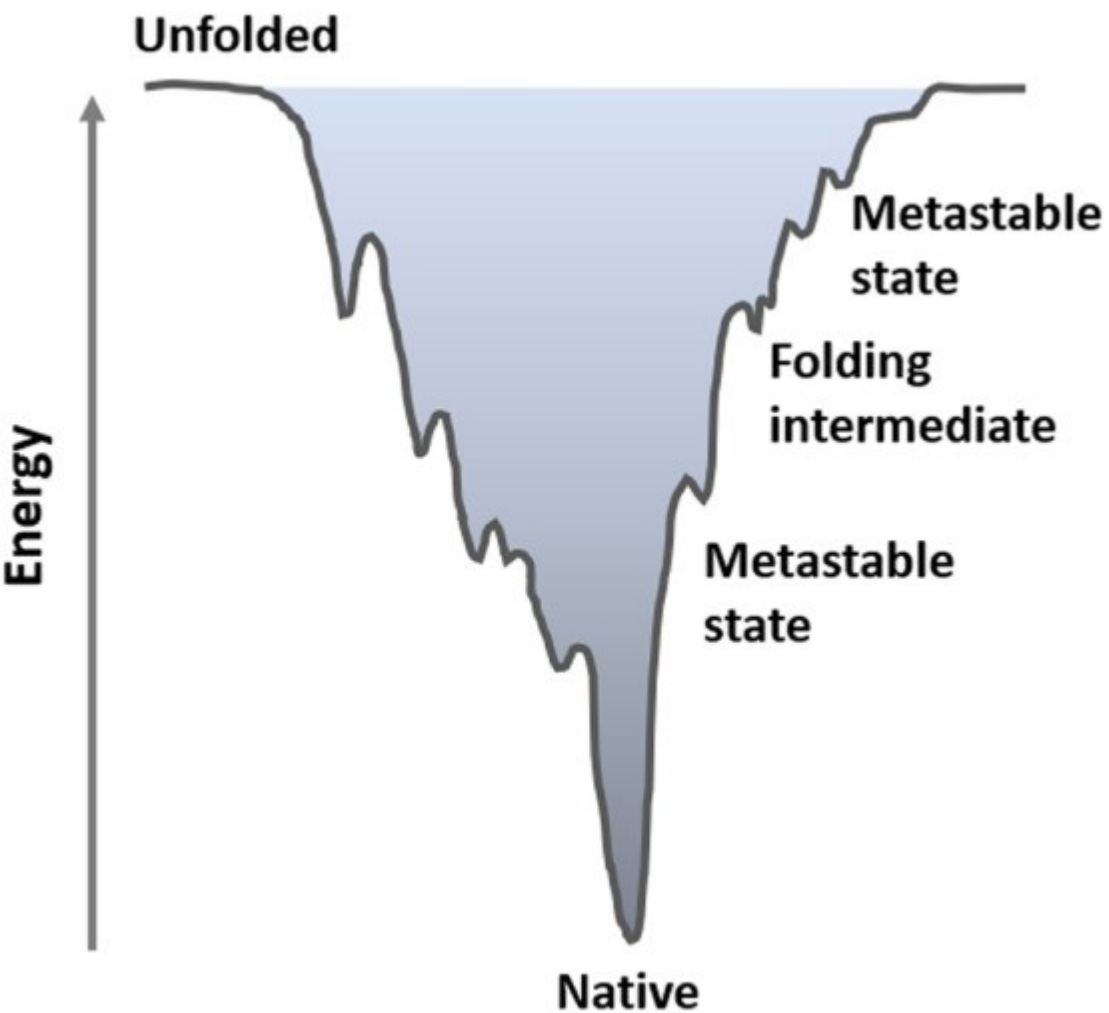
Οι θερμοφιλικές πρωτεΐνες αποτελούν μια αποτελεσματική και αποδοτική λύση στο πρόβλημα που θέτει η ταυτόχρονη διαχείριση της λειτουργίας των πρωτεϊνών και η διατήρηση της σταθερότητάς τους.

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

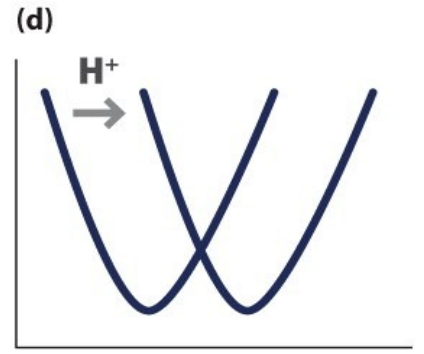
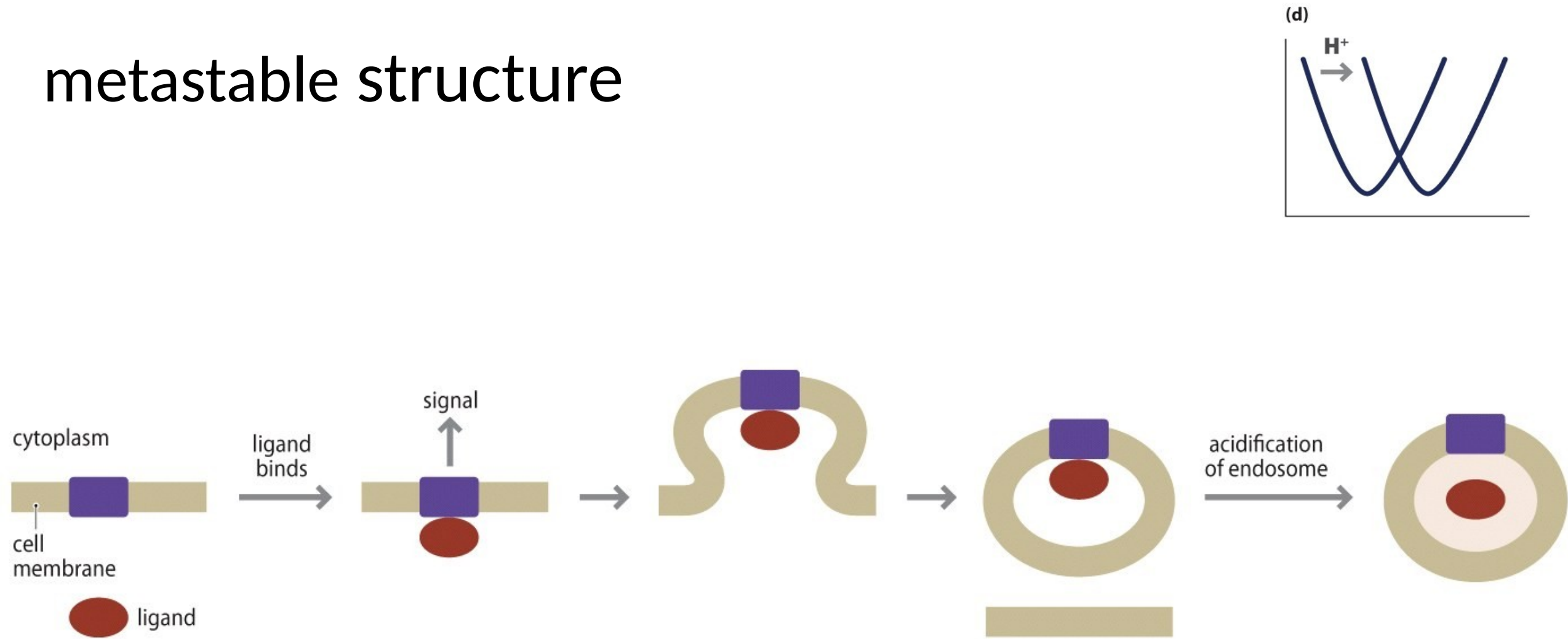


Figure 1.46 How Proteins Work (©2012 Garland Science)

metastable structure

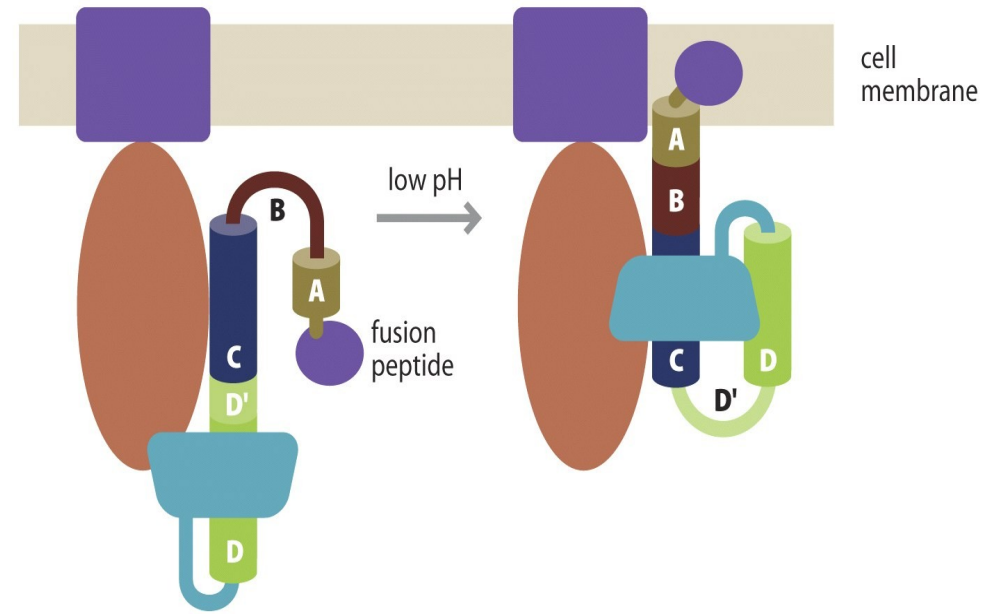
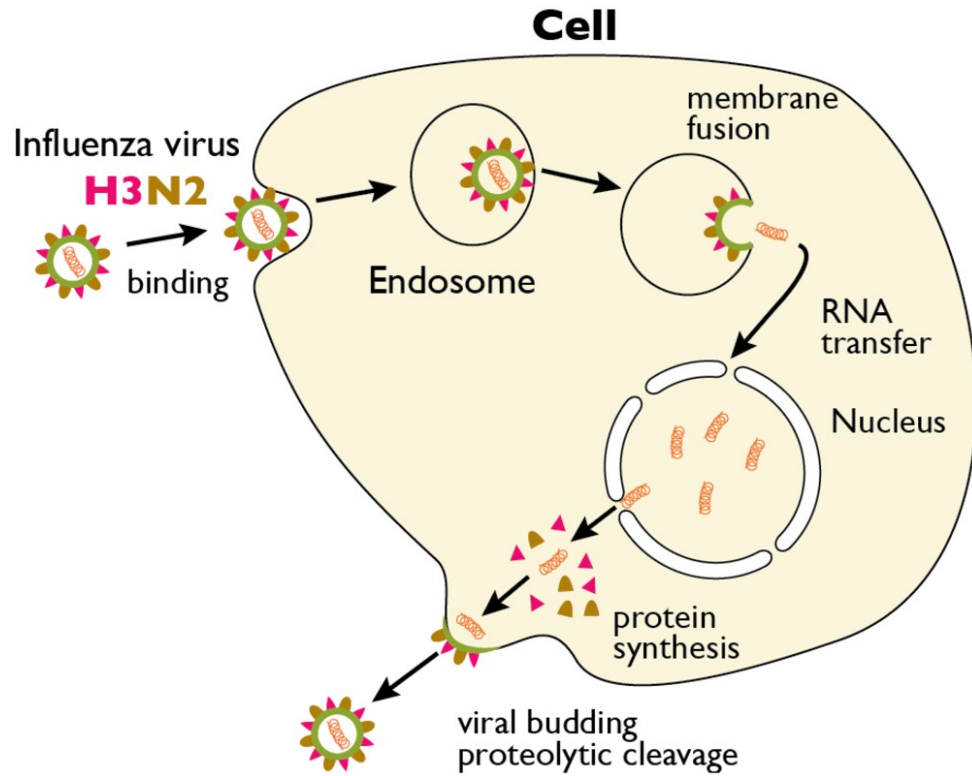
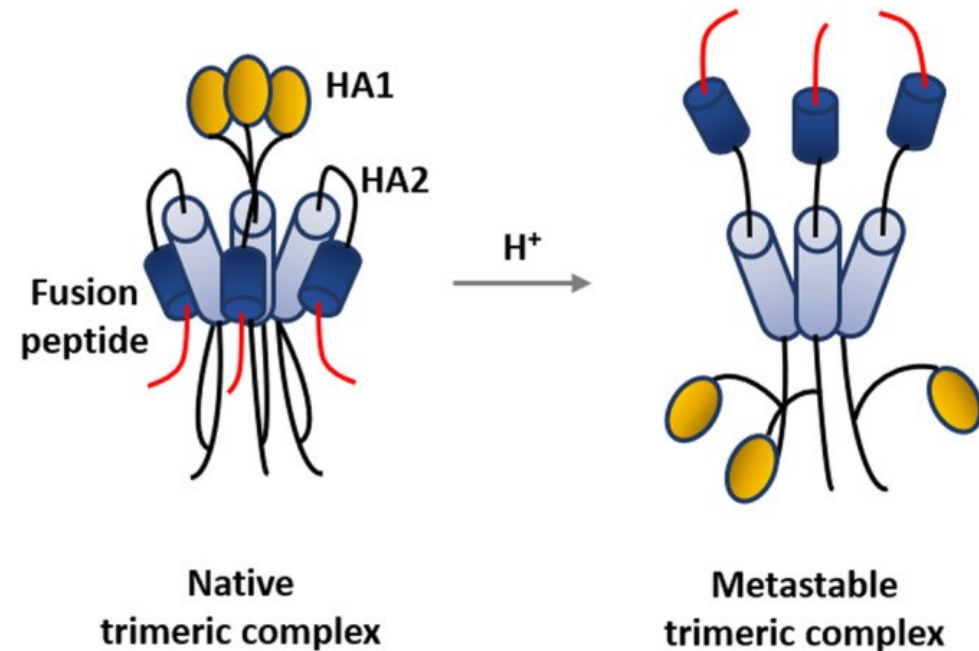


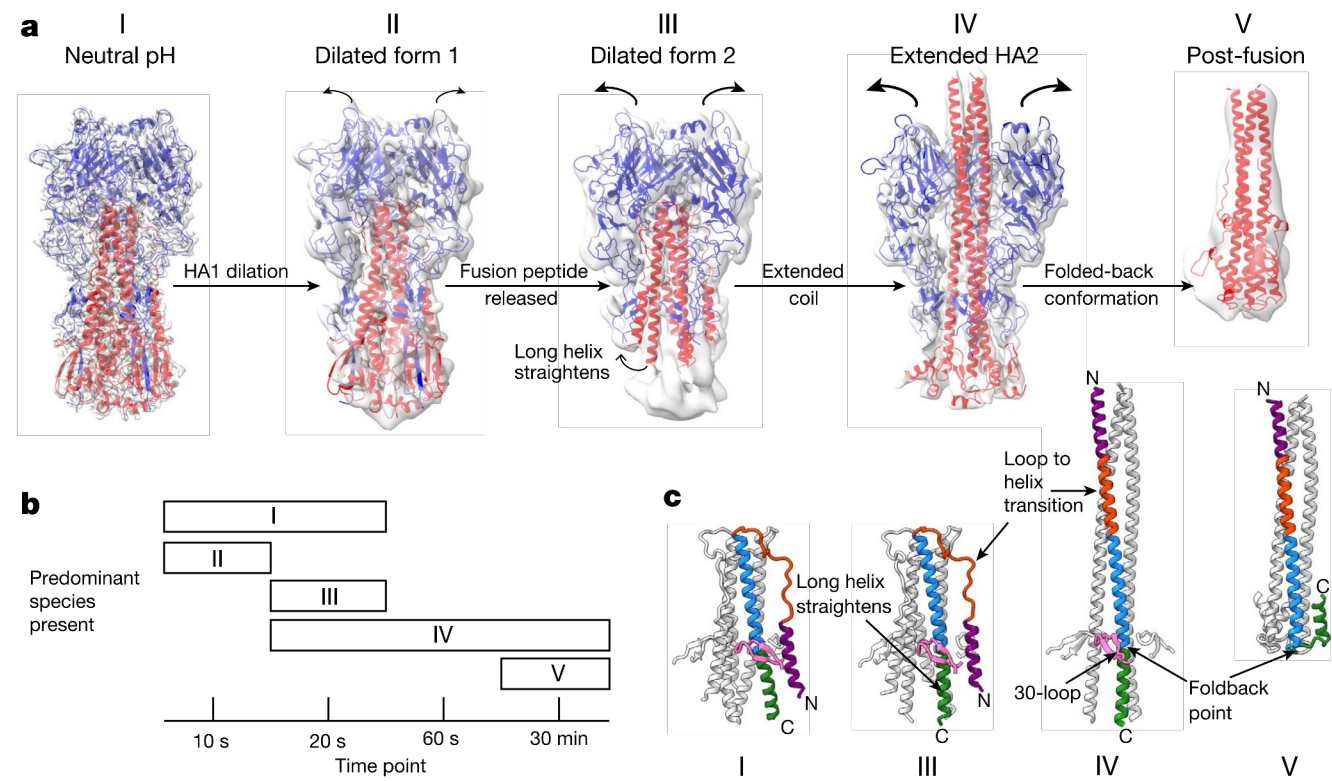
Figure 1.47 How Proteins Work (©2012 Garland Science)

Hemagglutinin, part of viral coat

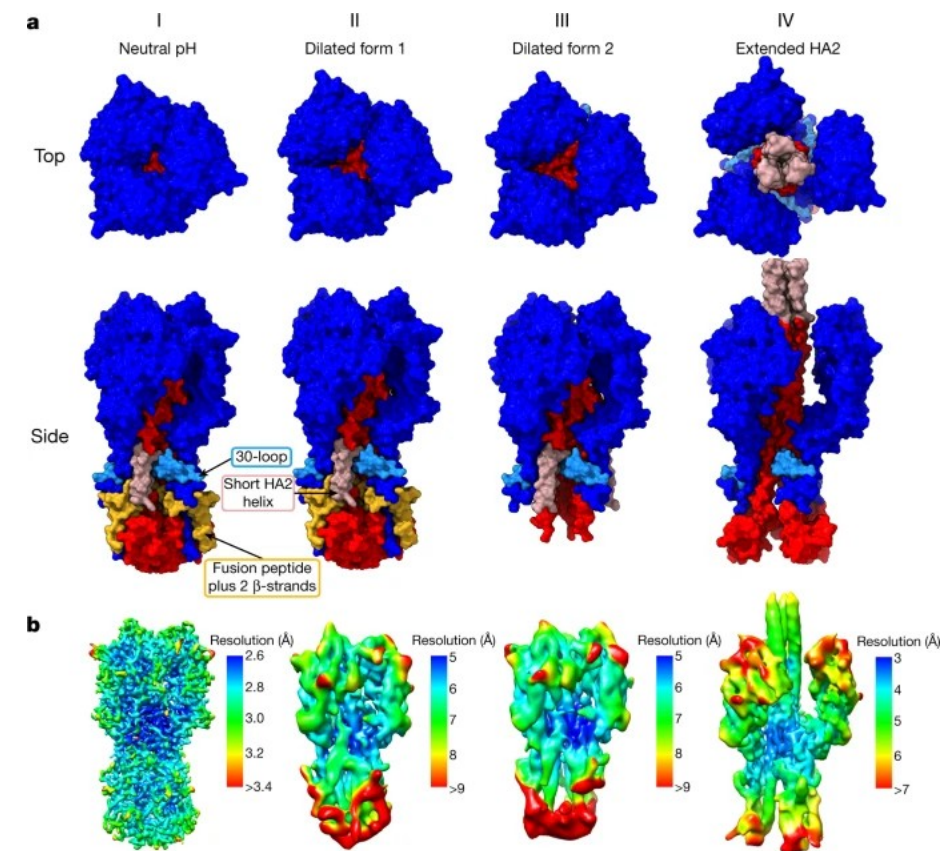


Structural transitions in influenza haemagglutinin at membrane fusion pH

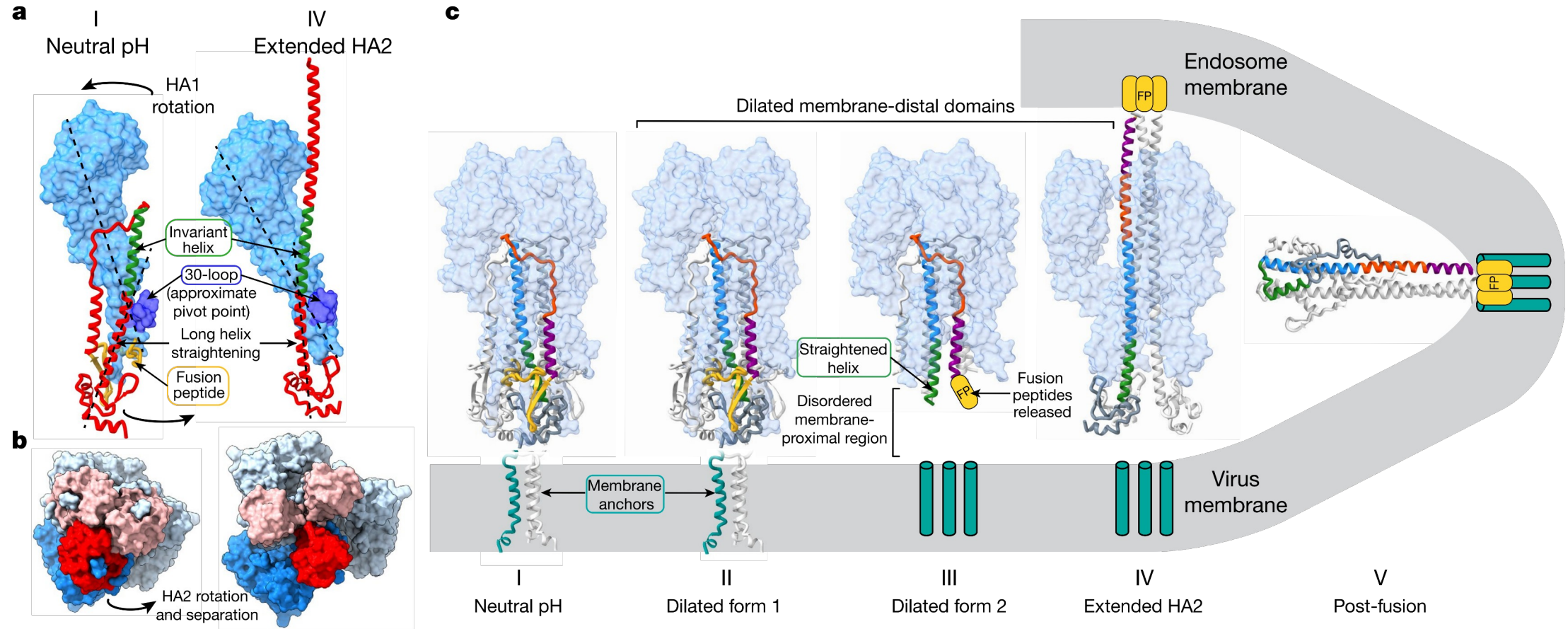
HA fusion intermediates.



Surface representations of HA fusion intermediates

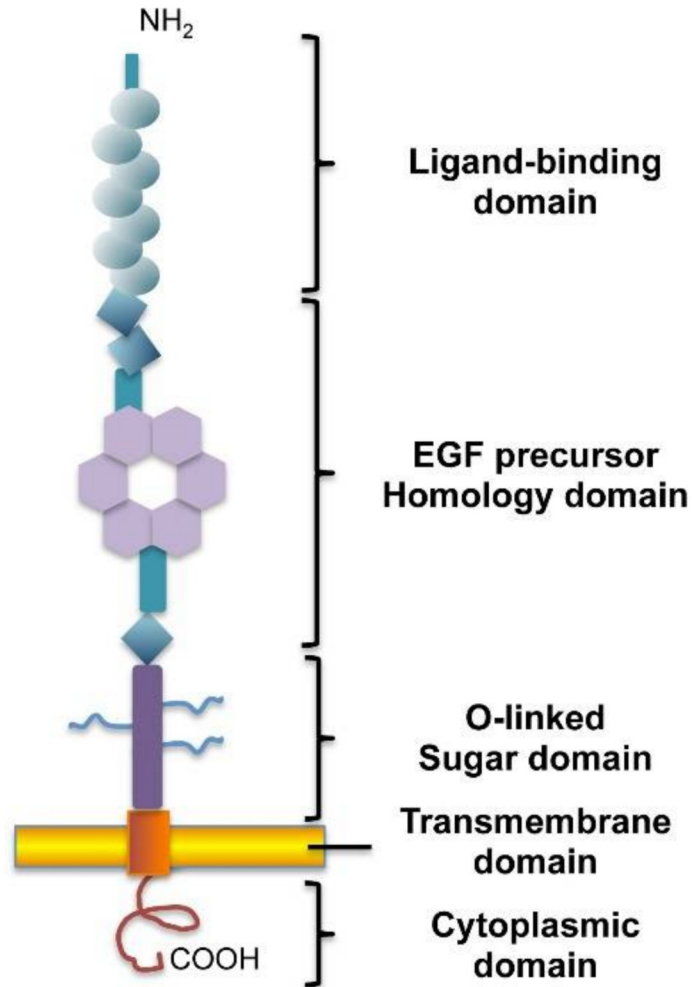


Structural rearrangements of HA fusion intermediates

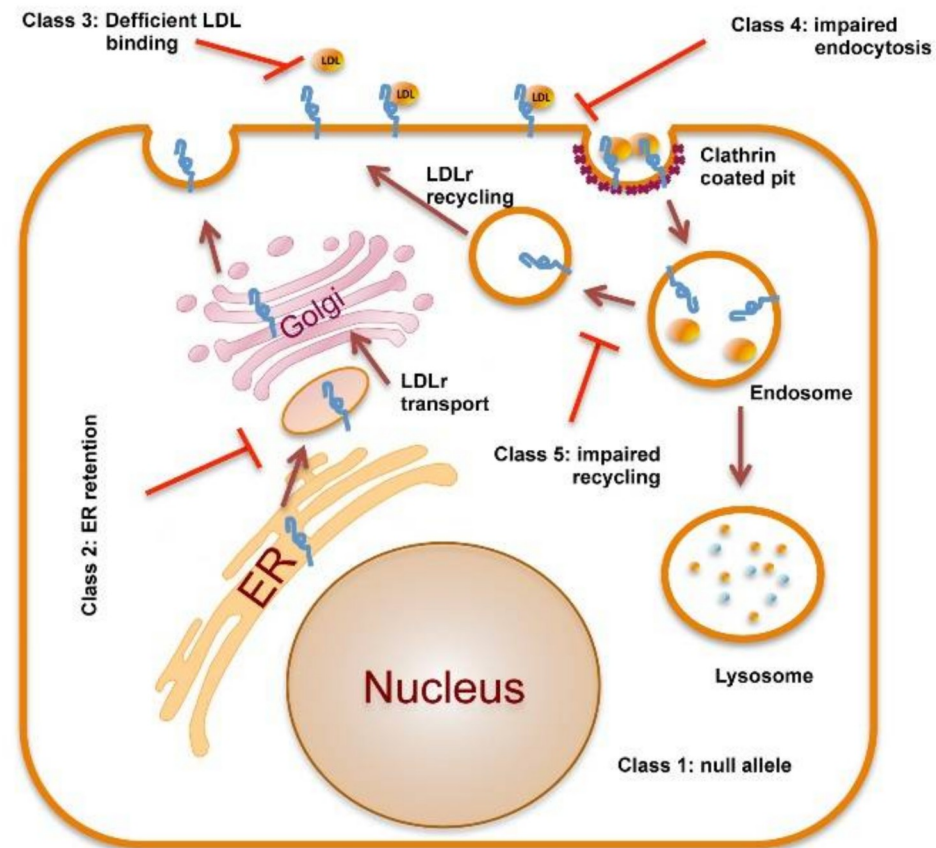


metastable structure

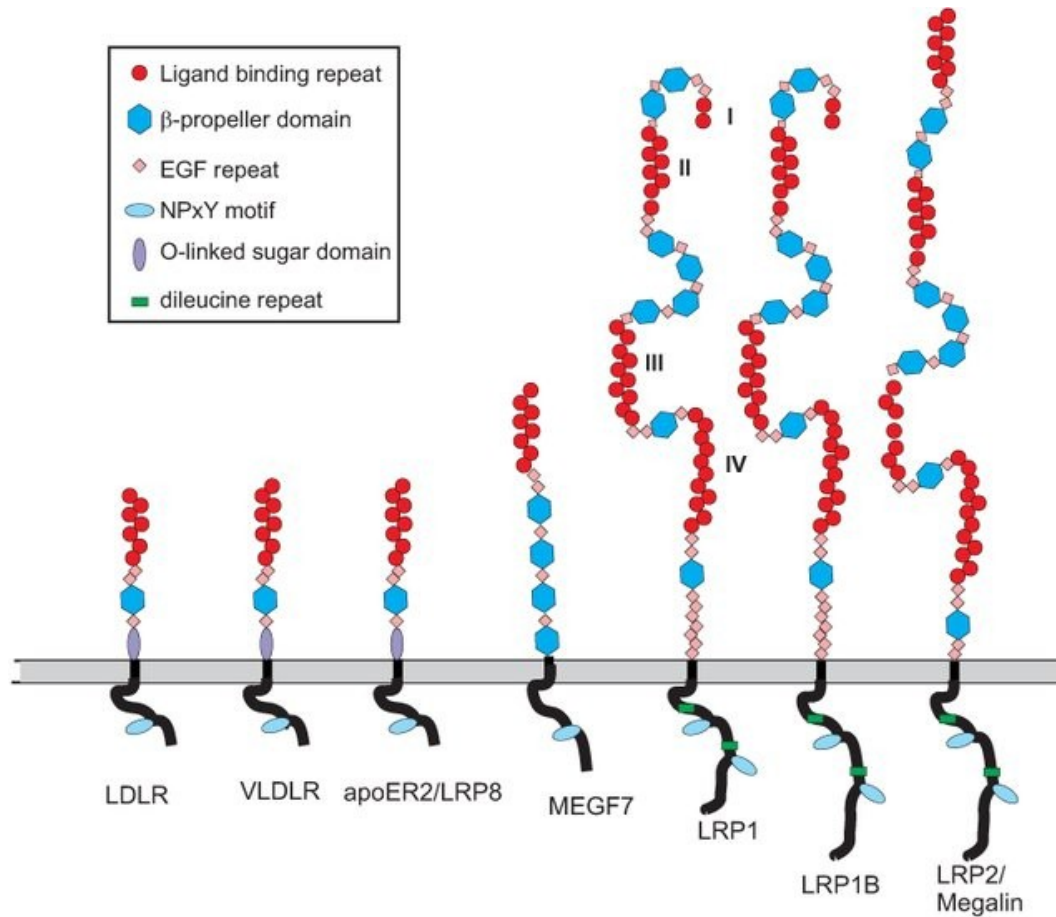
A) LDL receptor



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.

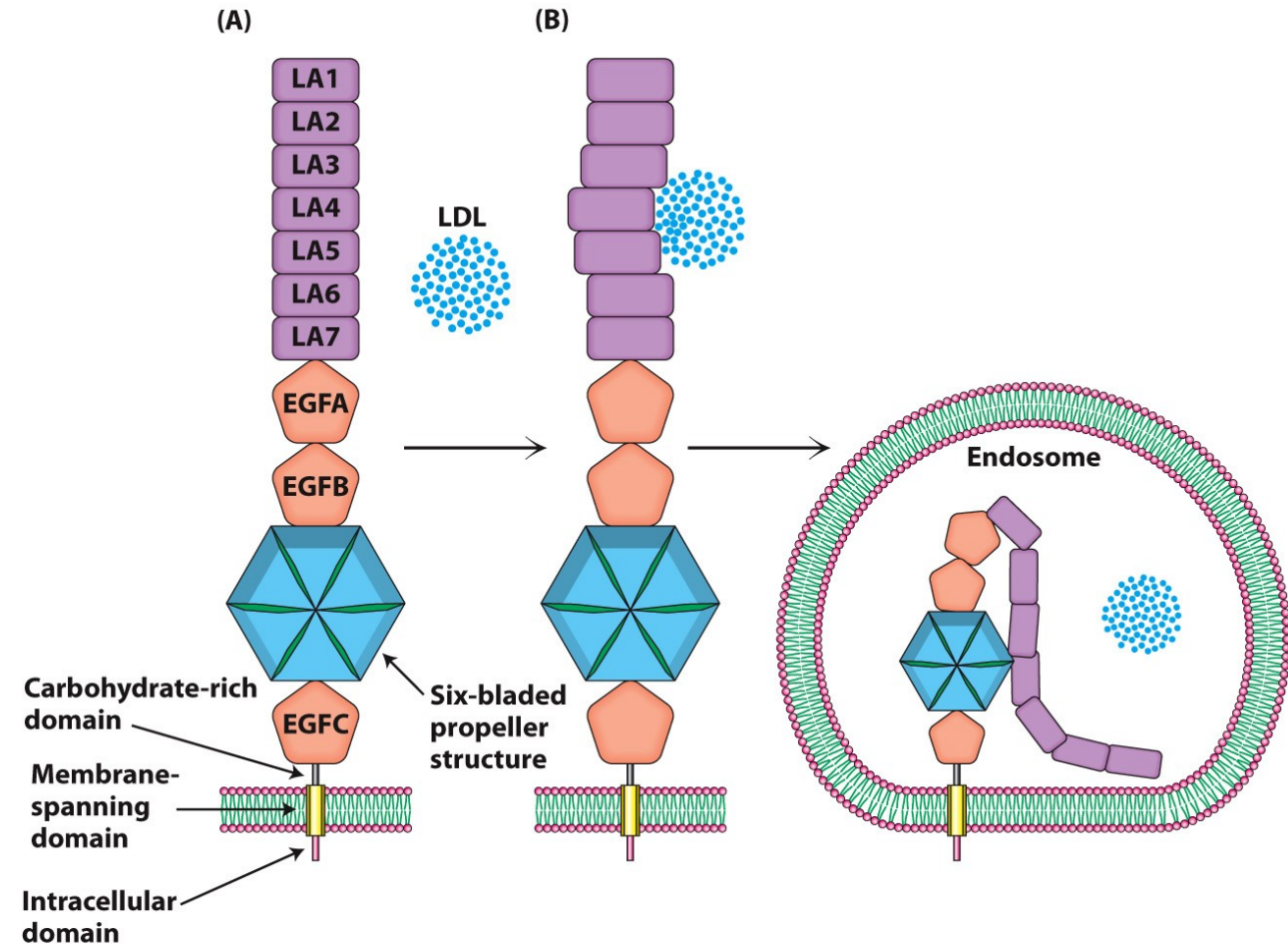
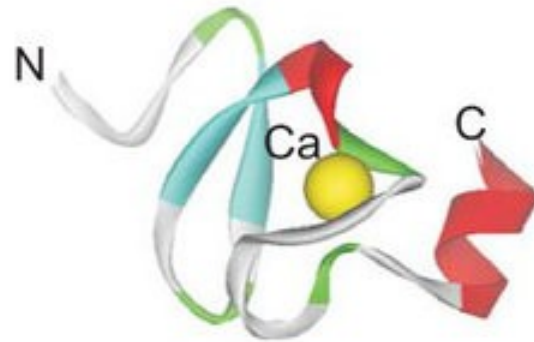


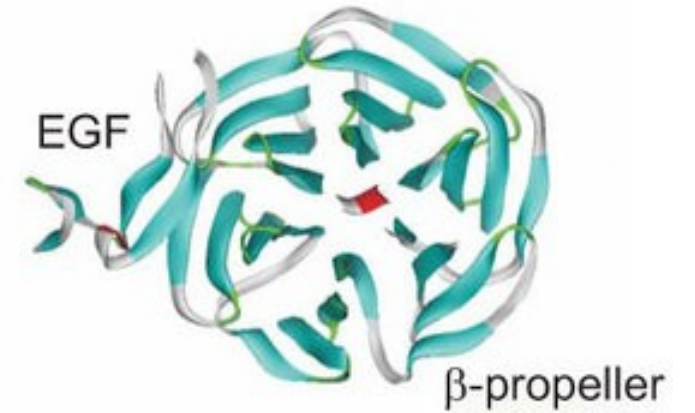
Figure 26.22
Biochemistry, Eighth Edition
 © 2015 Macmillan Education

metastable structure

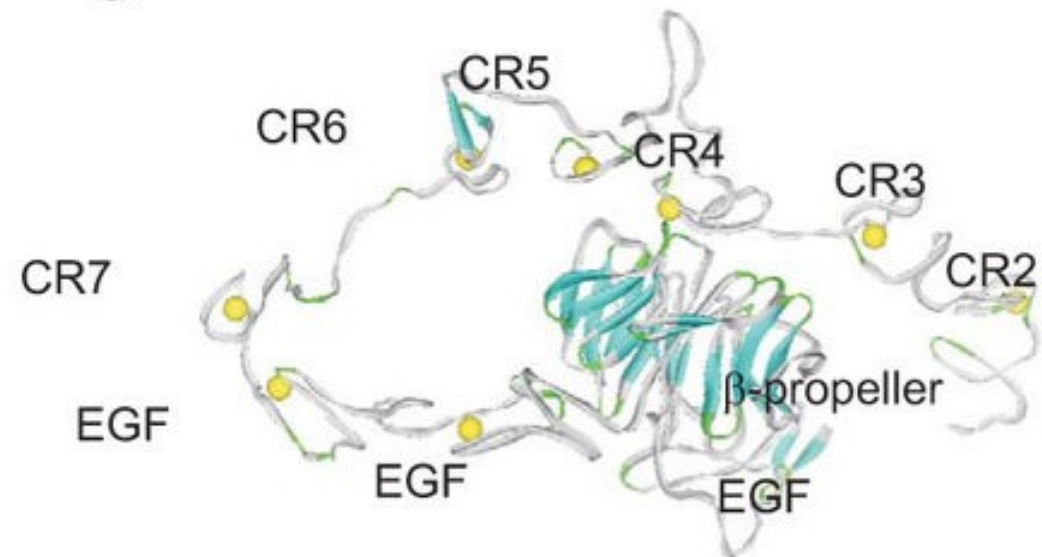
A



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

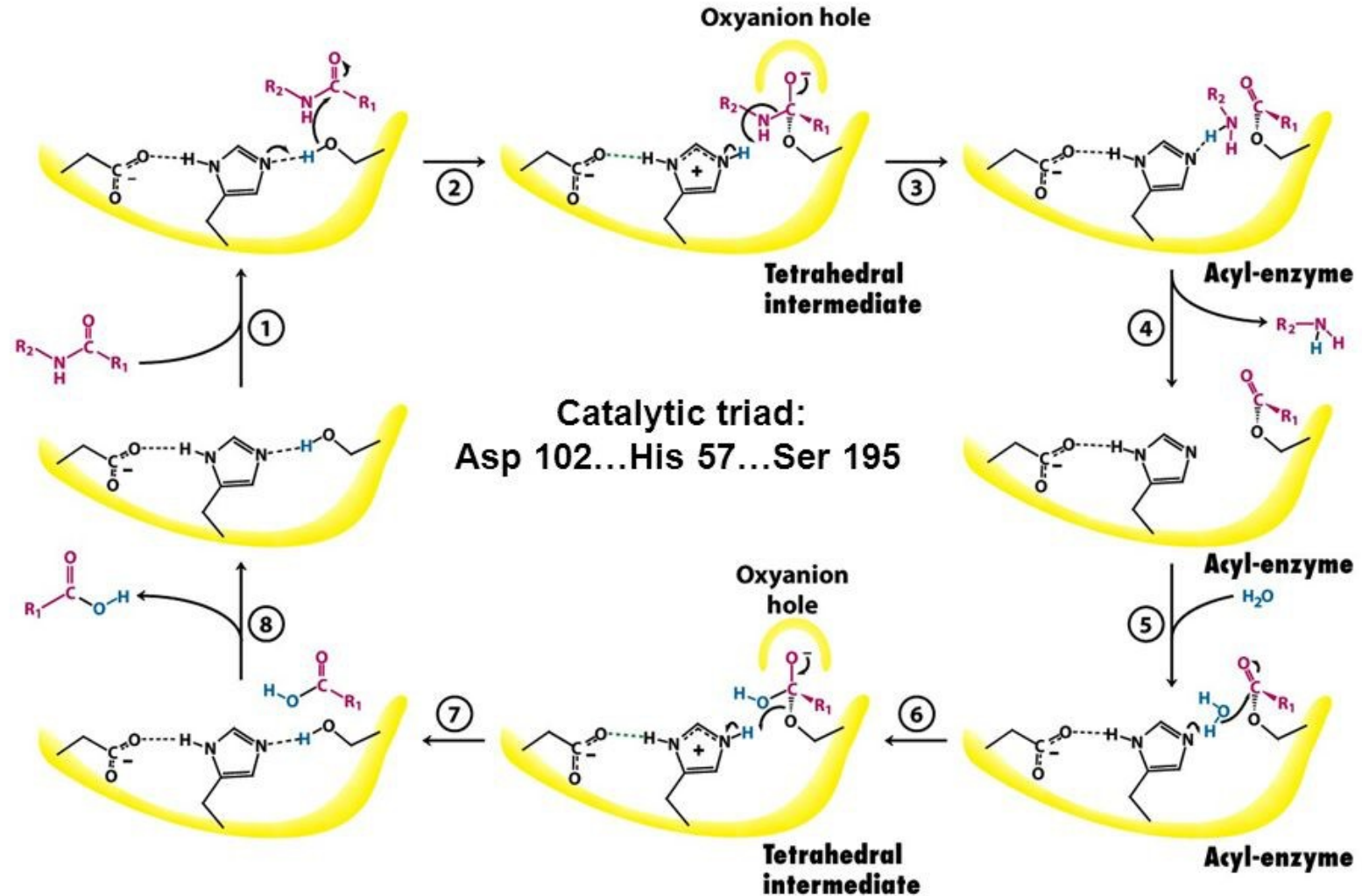
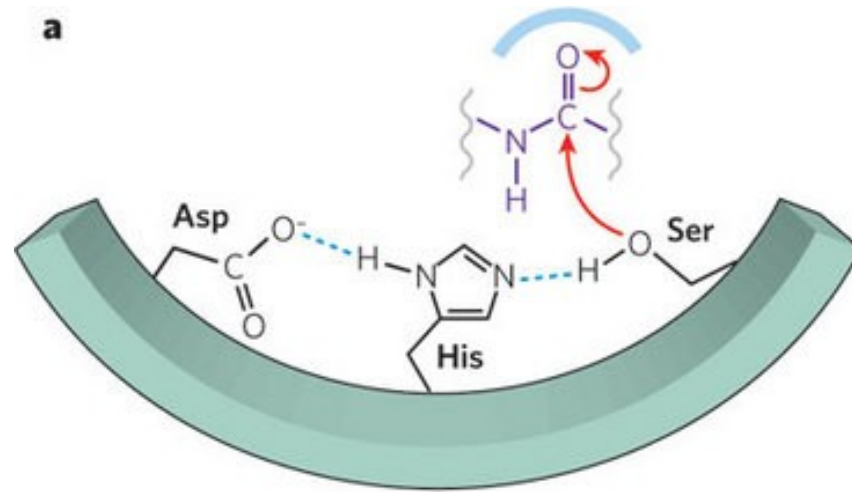


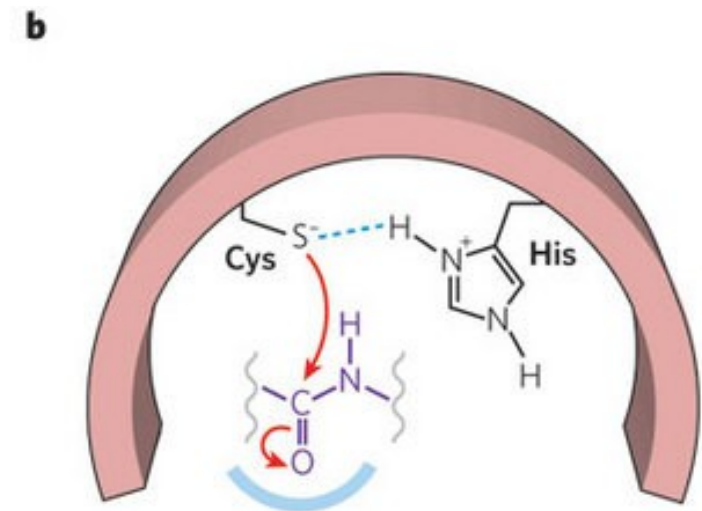
Figure 9-8
Biochemistry, Sixth Edition
© 2007 W. H. Freeman and Company

Protease

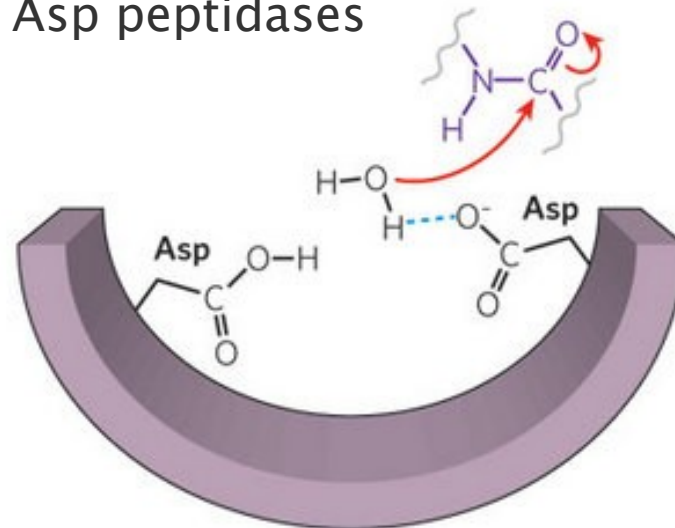
serin peptidases



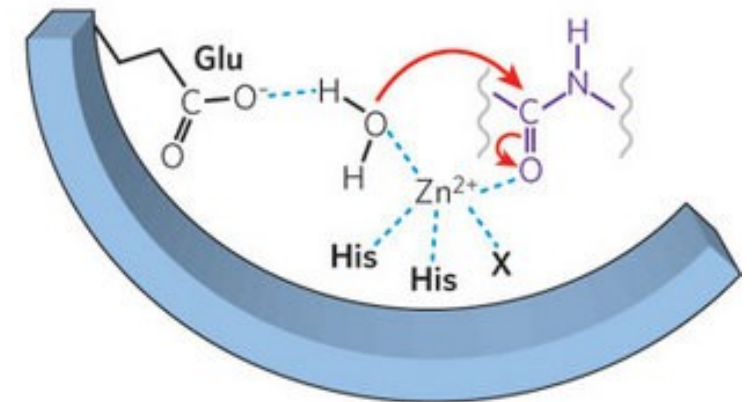
cysteine peptidases



c Asp peptidases



d Metall ion peptidases



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%)

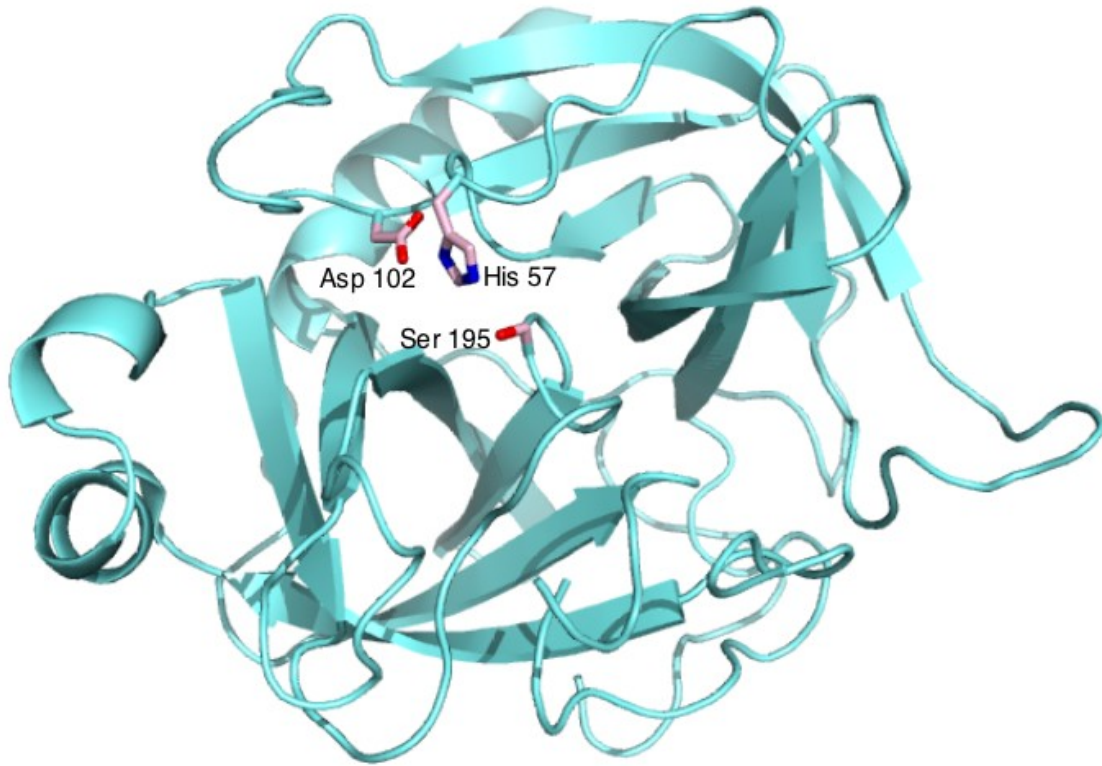
Bovine chymotrypsin

Human neutrophil elastase

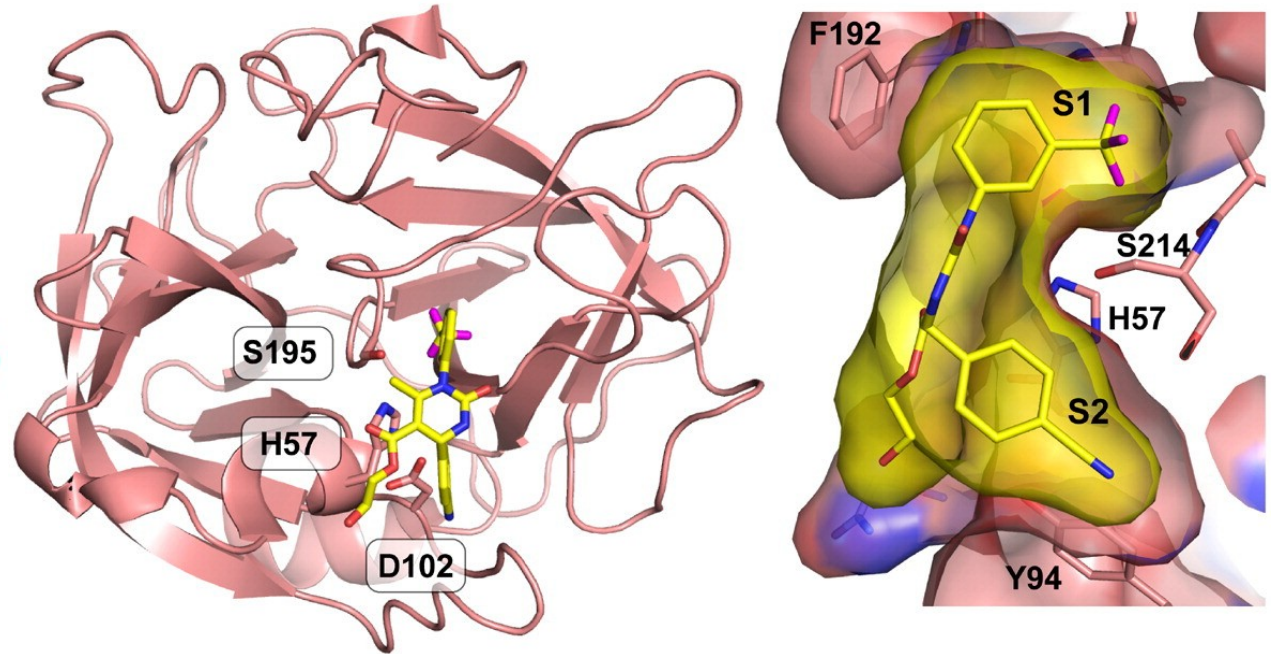
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		VGG A PH+WP+ +SLQ LR H CG TLI PN V++AA	HC++N	V LG	
Sbjct	1	VGGRRARPHAWPFMVSLQ-LRGG---HFCGATLIAPNFVMSAA	HC	VANVNVRAVRVVLGA	56
Query	59	NNLEVEDEAGSLYVGVDITFVHEKWNSFLVRN	D	I ALIKLAETVELSDTIQVACLPEEGSL	118
		+NL + ++ V IF ++ + N	D	I +++L + ++ +QVA LP +G	
Sbjct	57	HNLSRREPTRQVFA-VQRIF-ENGYDPVNLLN	D	I VILQLNGSATINANVQVAQLPAQGRR	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	S	GGPLNCQAENGNDVRGIVSFGSGLSCNTFKKPTVFTRVSAYIDWINQKLQ	237
		C GD	S	SG PL C N + GI SF G C + P F V+ +++WI+ +Q	
Sbjct	168	---CFGD	S	GSPLVC-----NGLIHGIASFVRG-GCASGLYPDAFAPVAQFVNWIDSIIQ	217

Figure 1.48 How Proteins Work (©2012 Garland Science)

sequence alignment



Human neutrophil elastase inhibitor complex

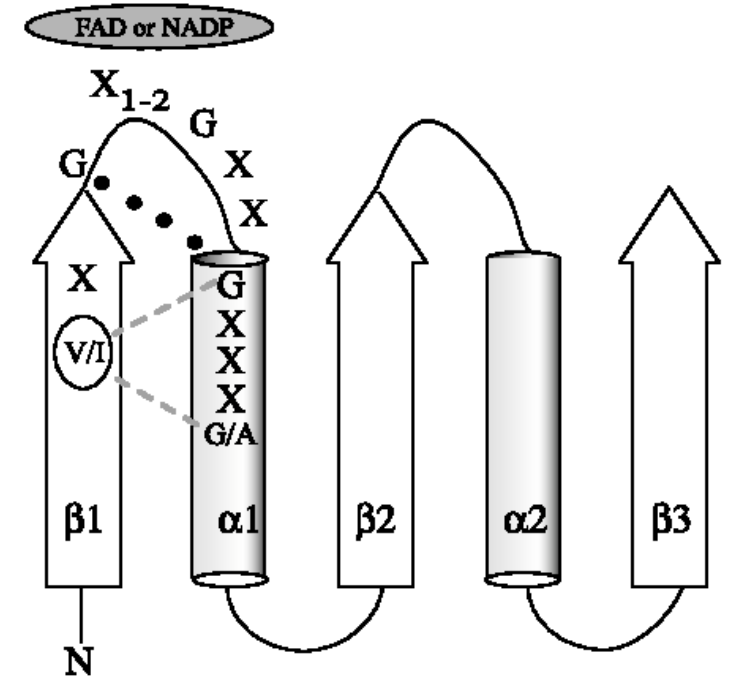
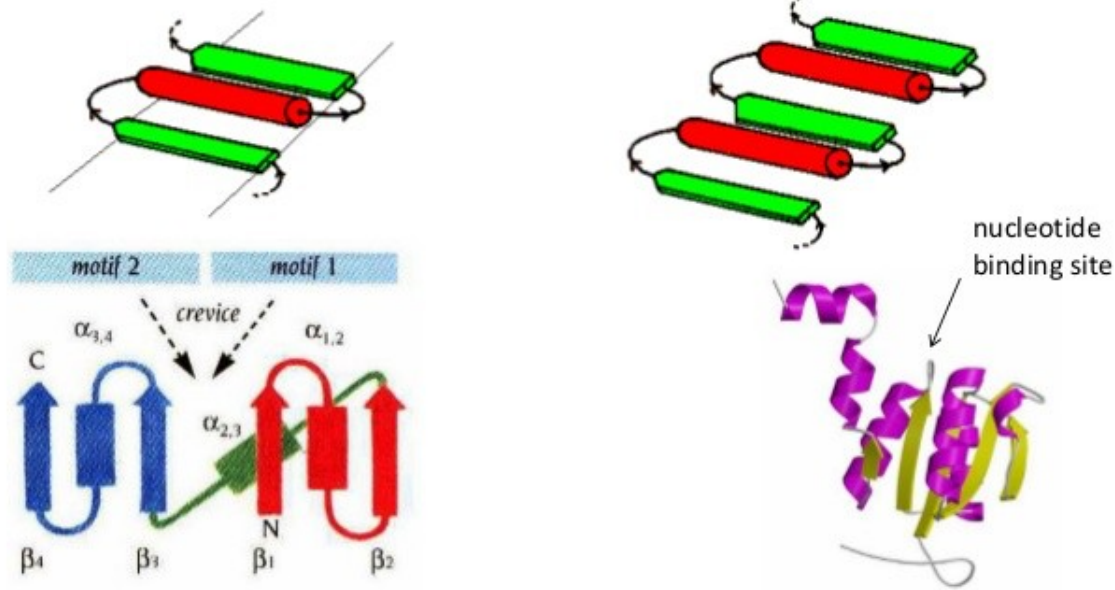


dihydropyrimidone inhibitor

sequence motif

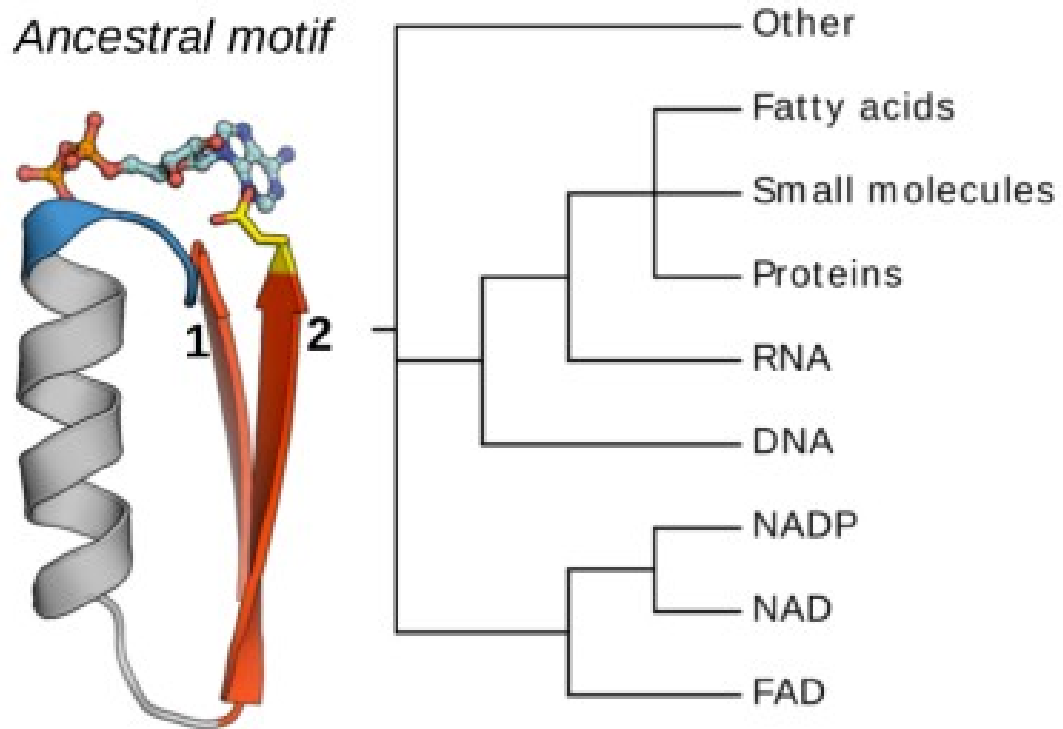
Rossmann Fold

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.

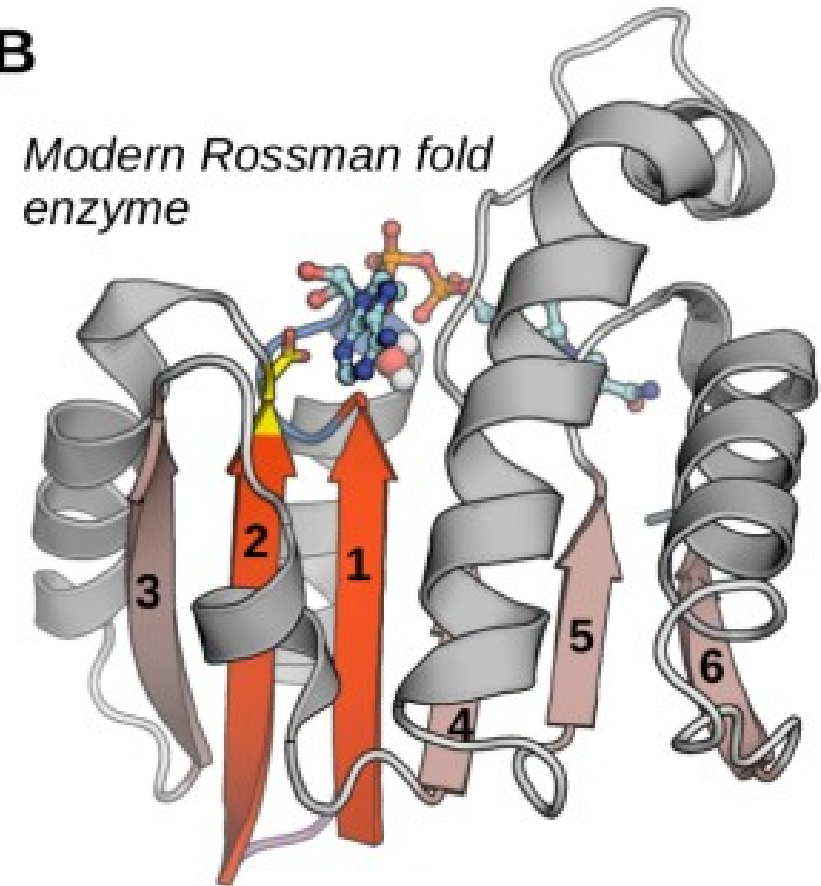


sequence motif

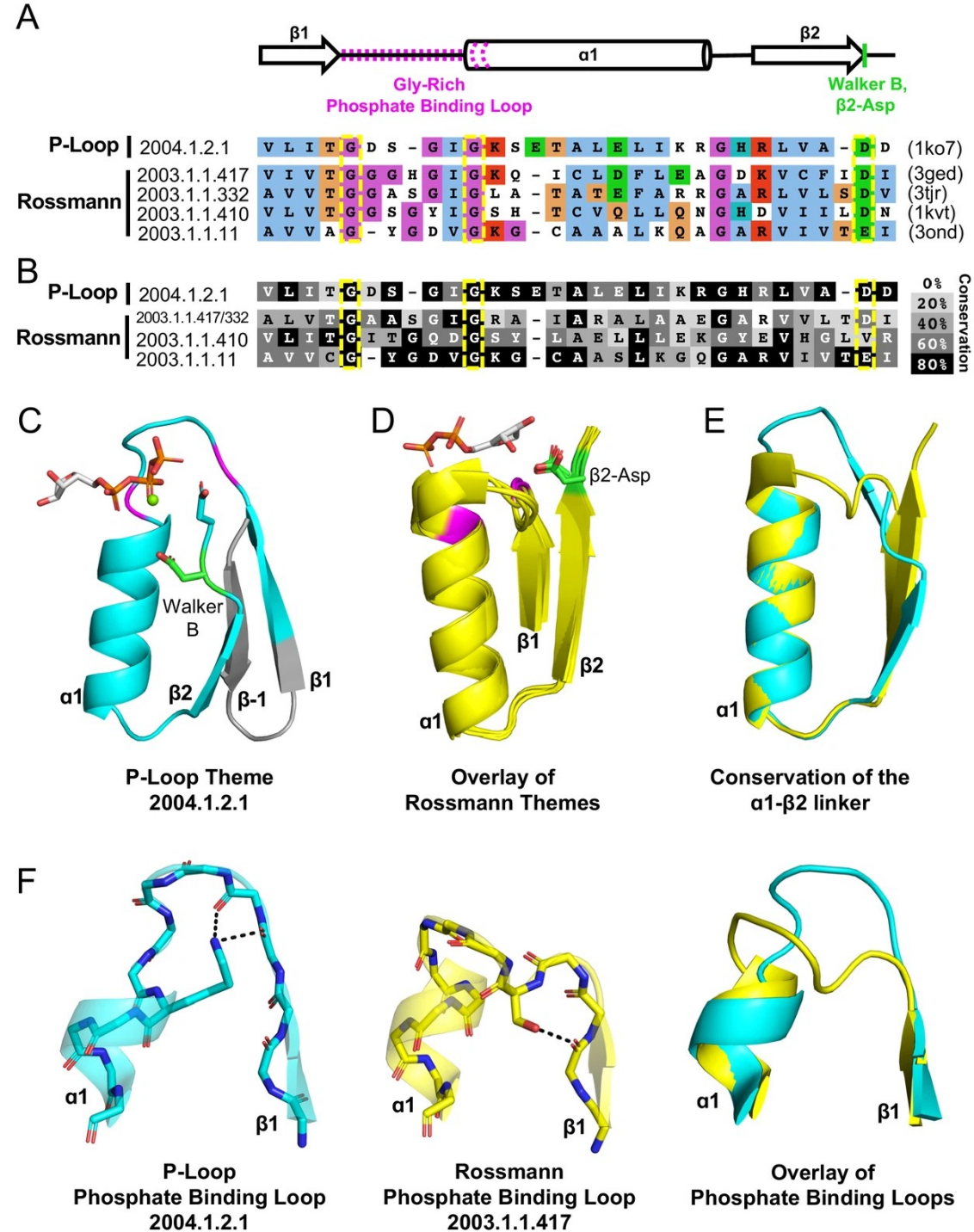
A



B



sequence motif



evolution of proteins

Evolution of cyt c

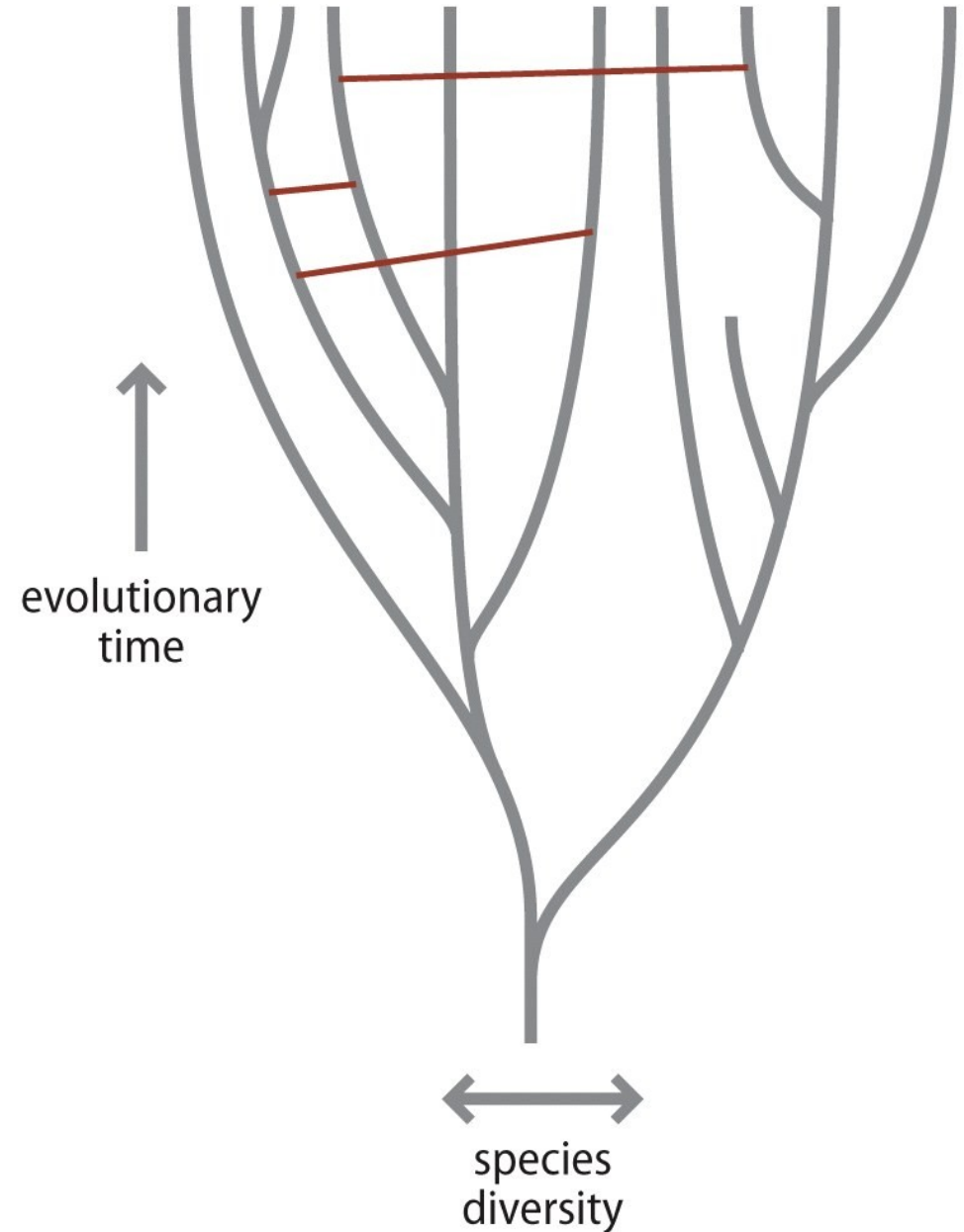
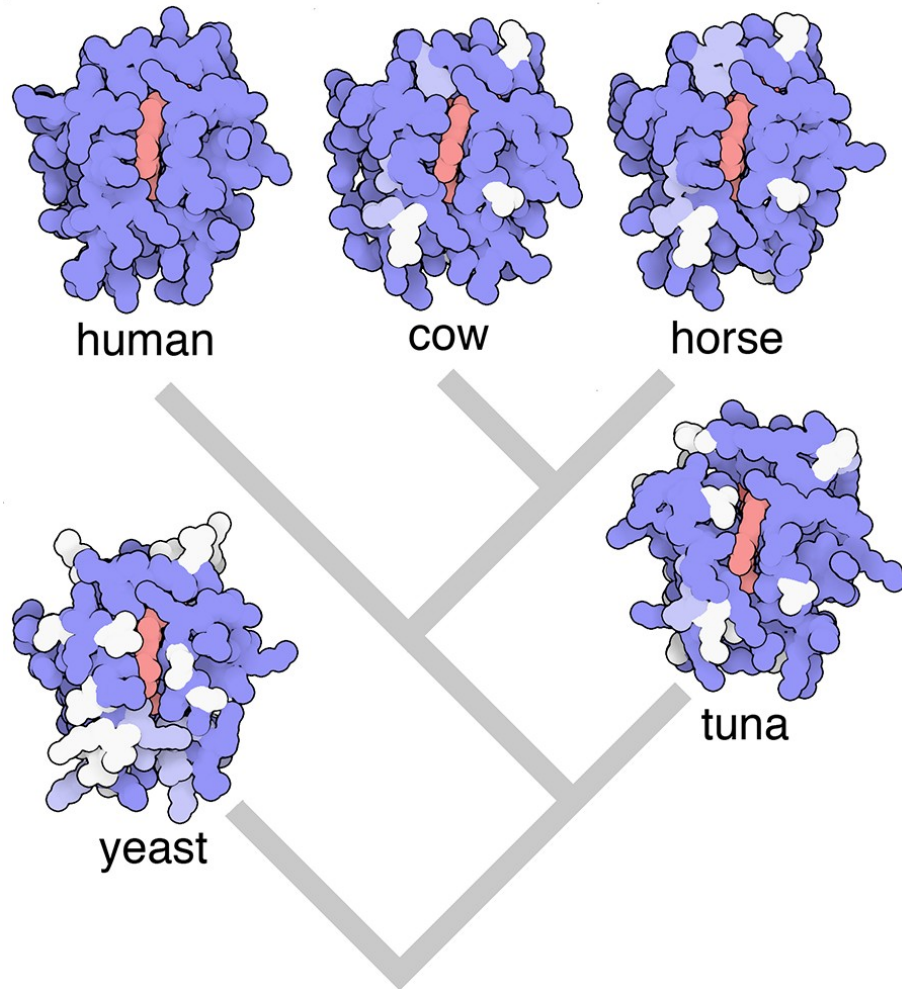


Figure 1.52 How Proteins Work (©2012 Garland Science)

structure conservation

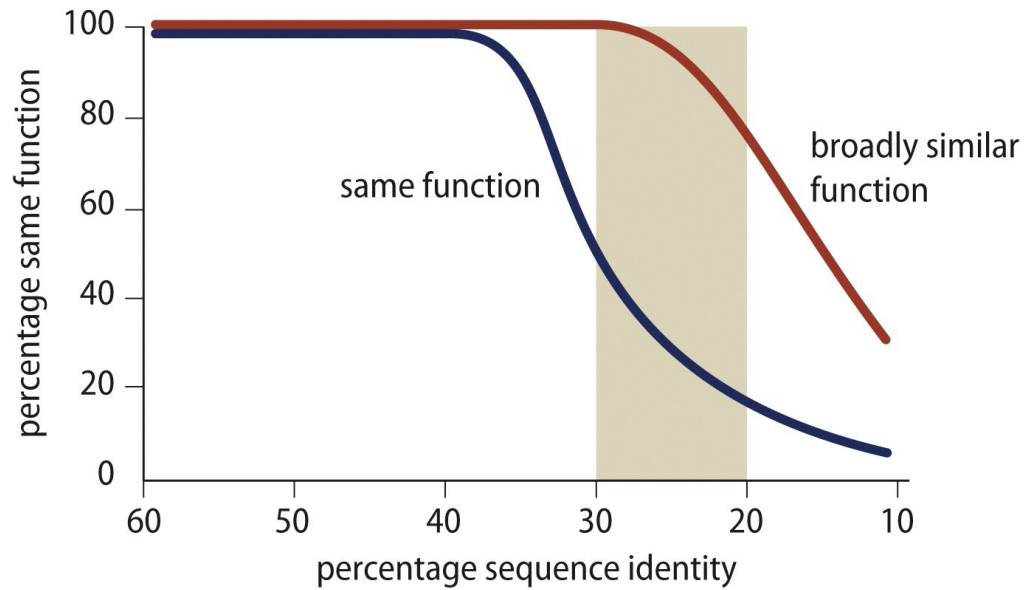


Figure 1.50 How Proteins Work (©2012 Garland Science)

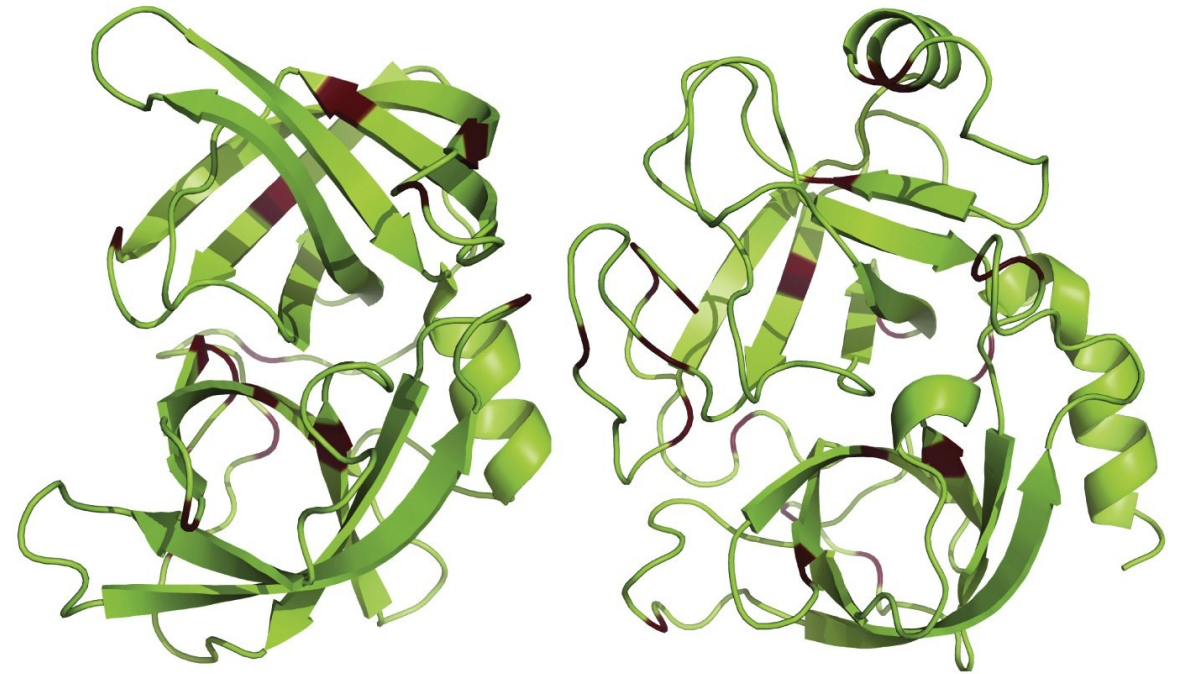


Figure 1.49 How Proteins Work (©2012 Garland Science)

Protease B
Streptomyces griseus

β -trypsin
Bovine

homologous recombination

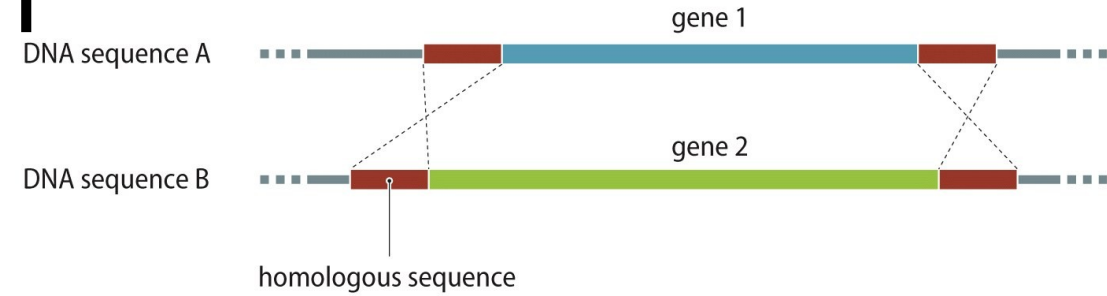
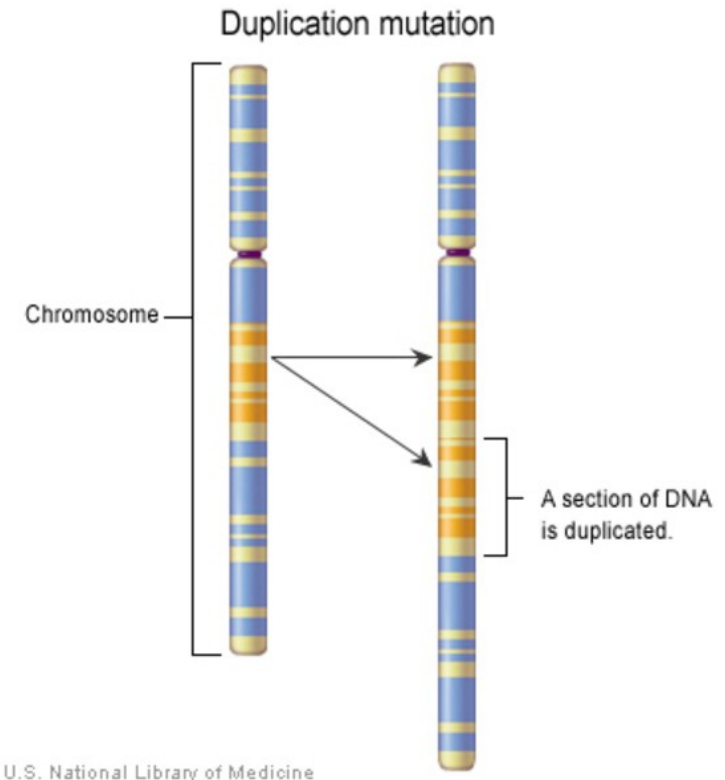
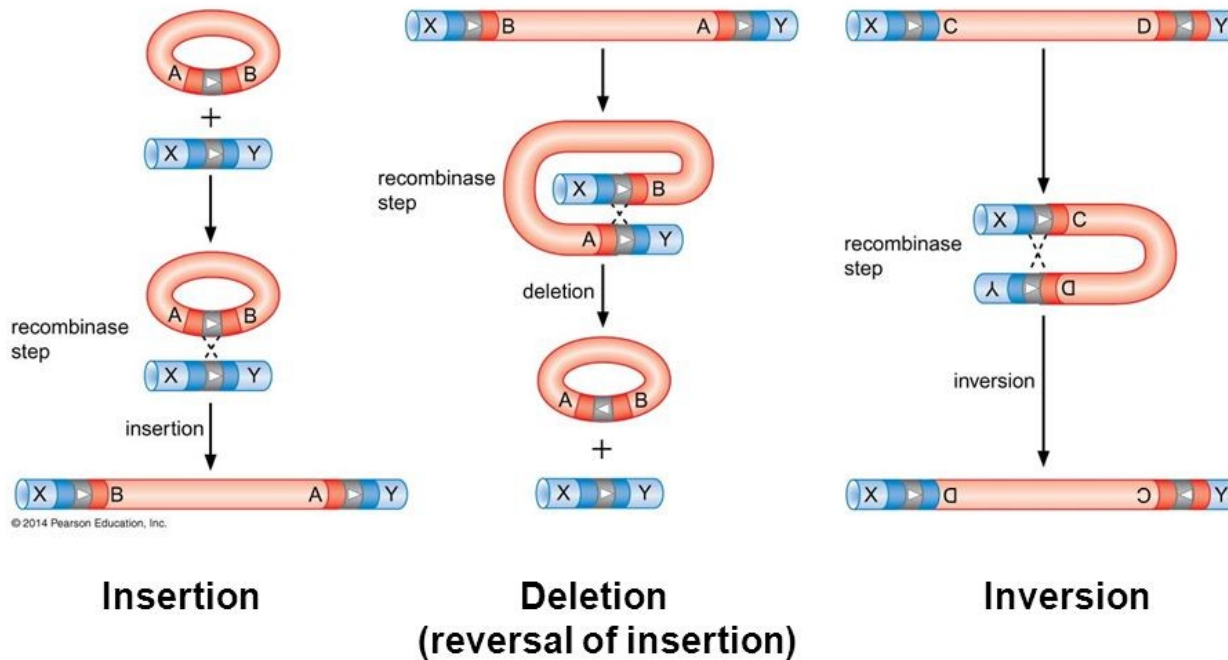


Figure 1.17.1 How Proteins Work (©2012 Garland Science)

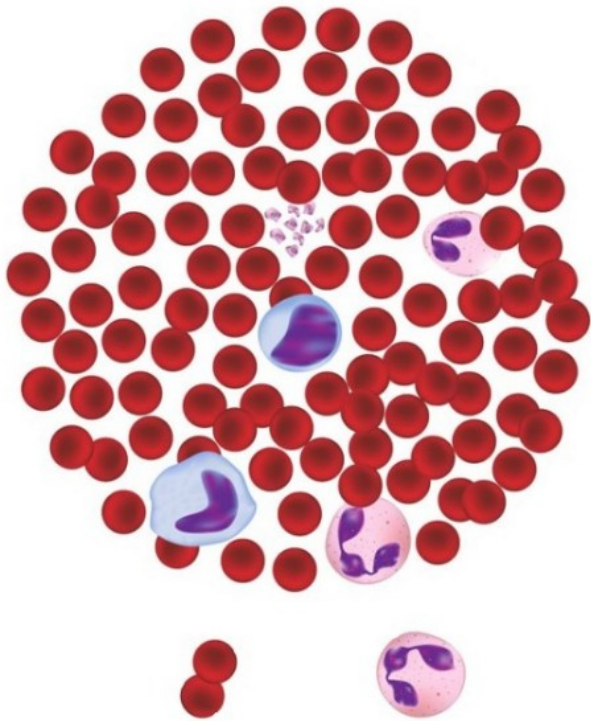
Site-specific recombination either integrates, deletes, or reverses a DNA sequence



homologous recombination

Chronic Myeloid Leukemia

Normal Blood



Erythrocytes

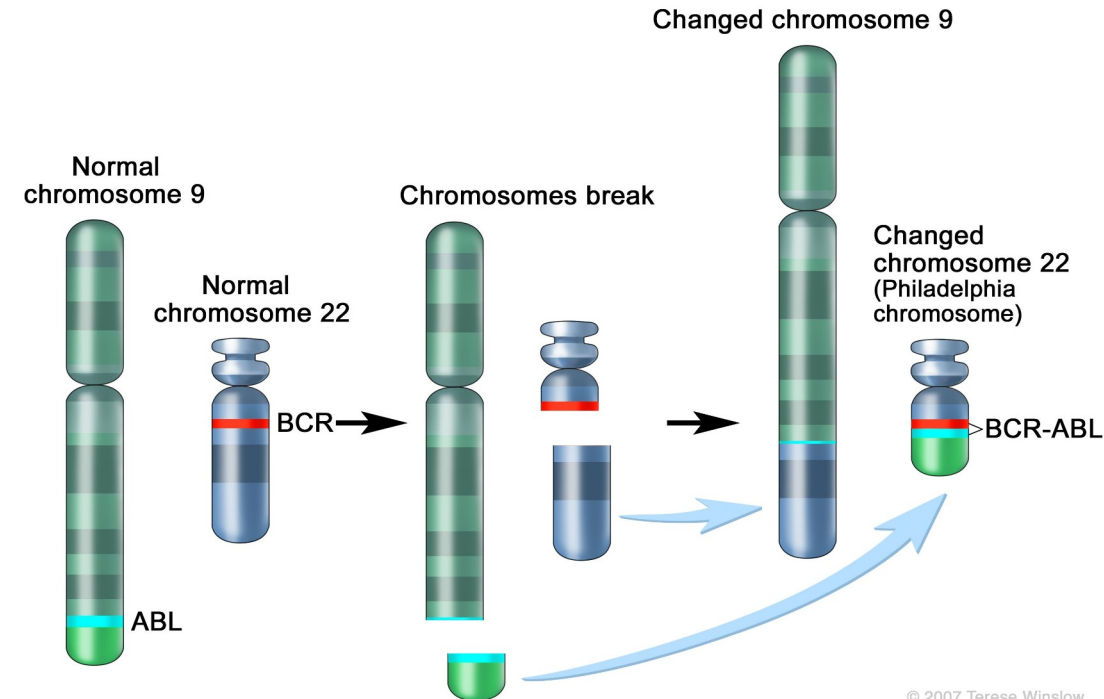
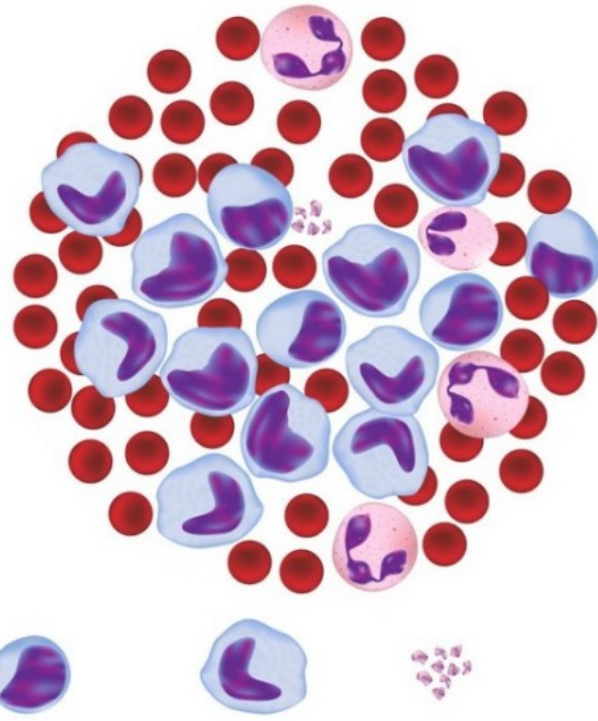
Neutrophil

Lymphocyte

Monocyte

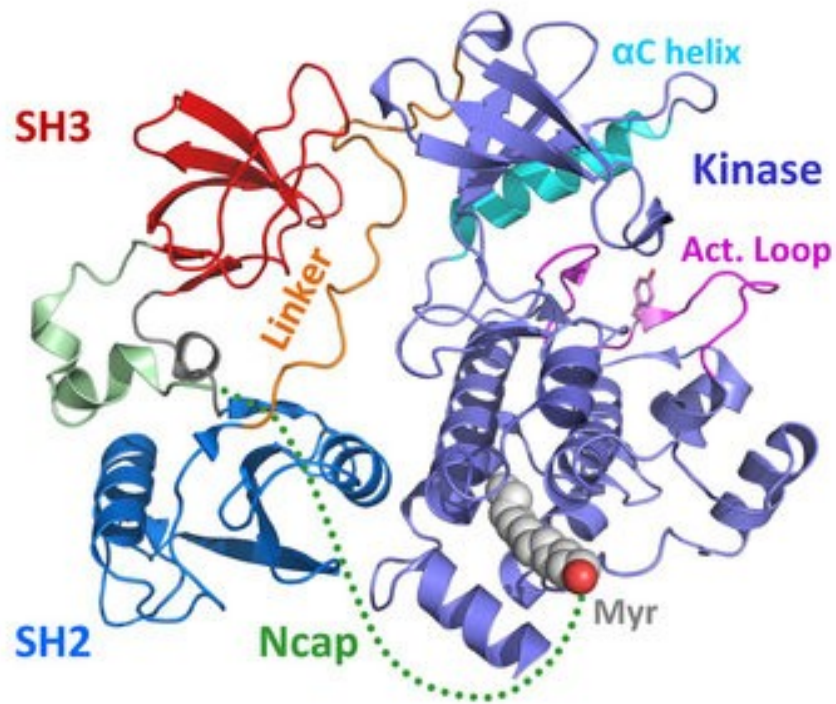
Platelets

Leukemia

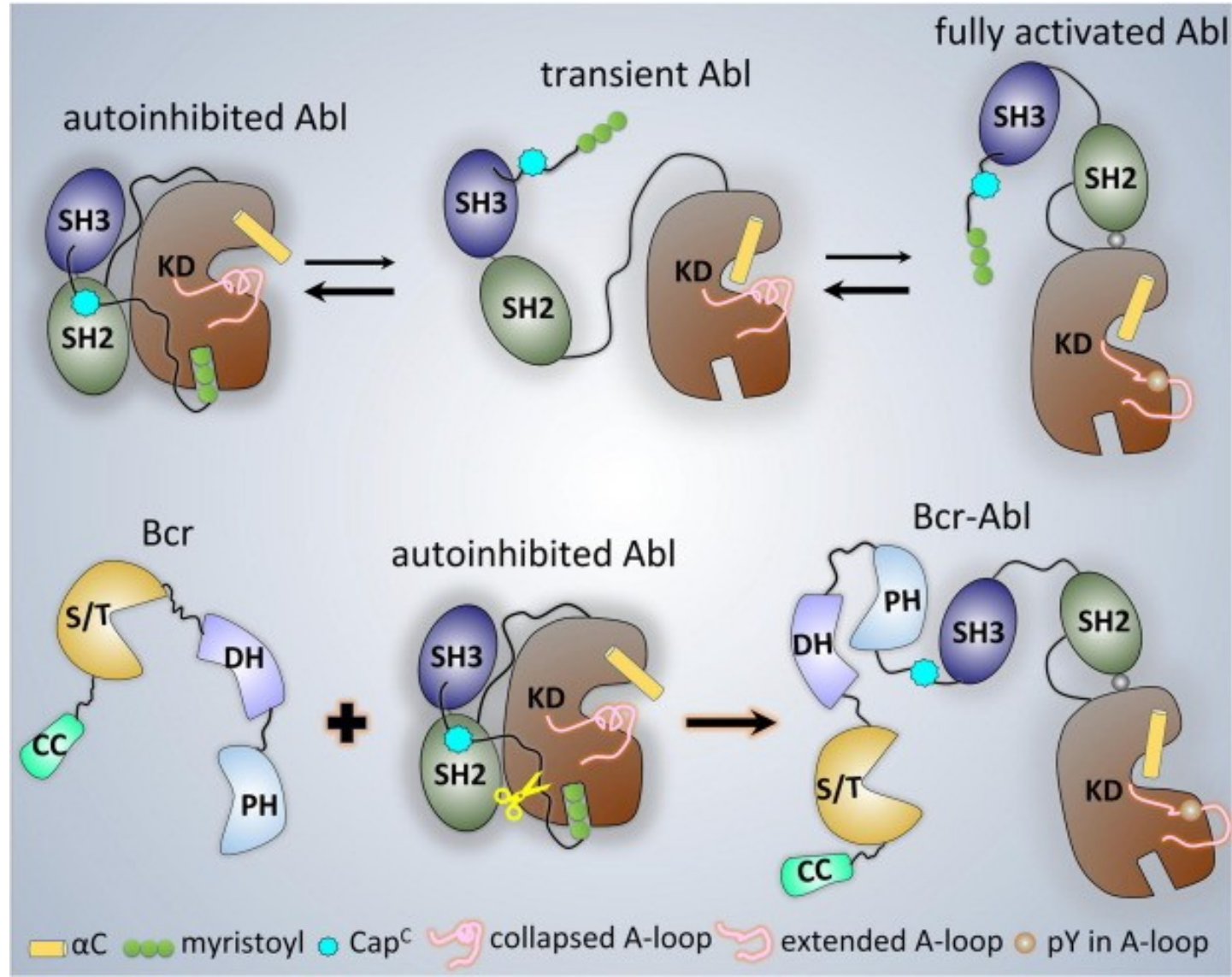


homologous recombination

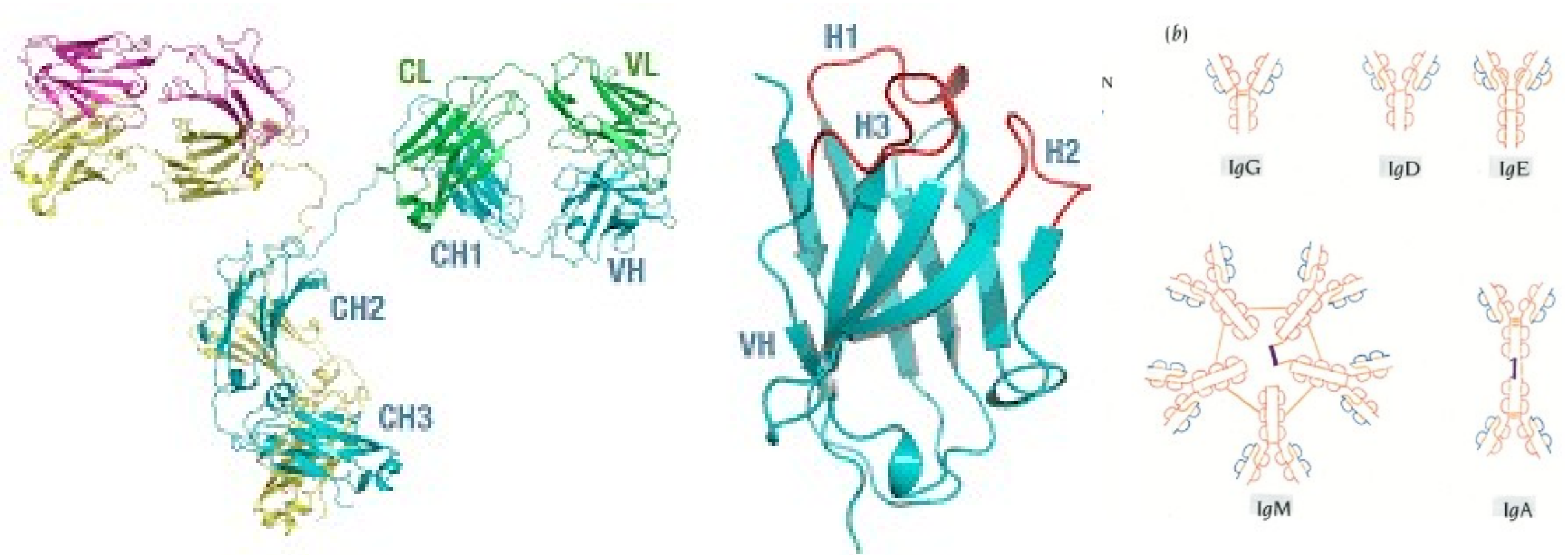
Chronic Myeloid Leukemia



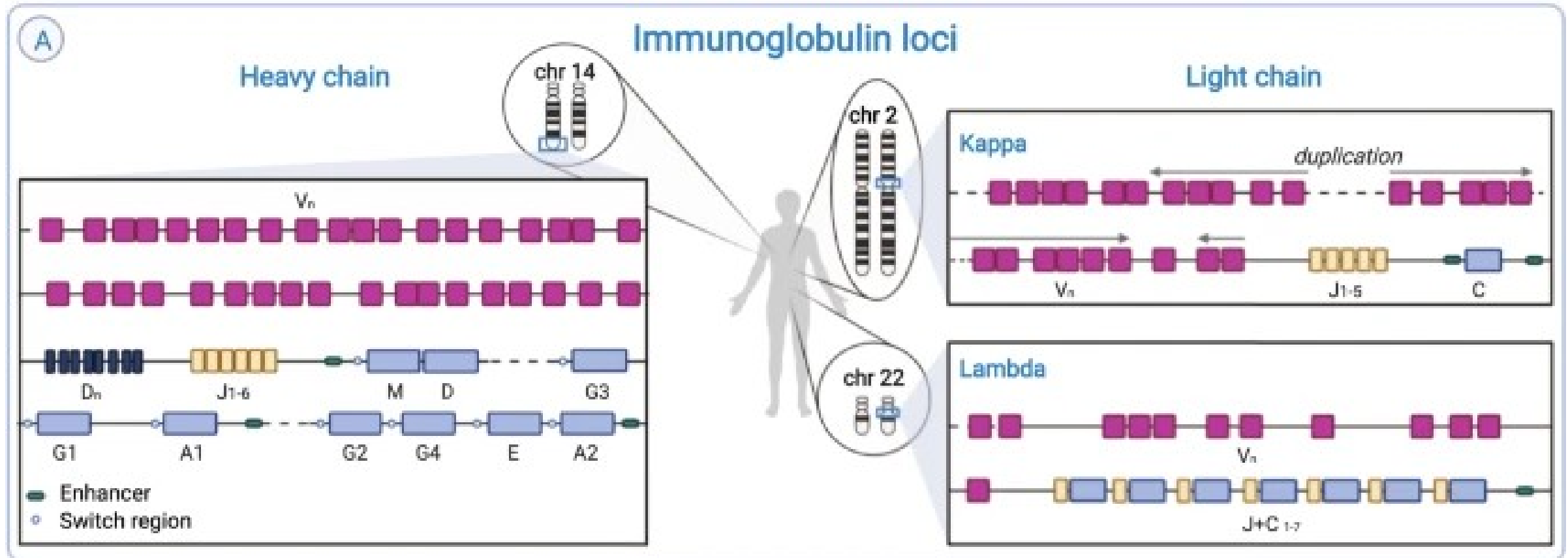
Chronic Myeloid Leukemia



insertion and deletions-antibodies



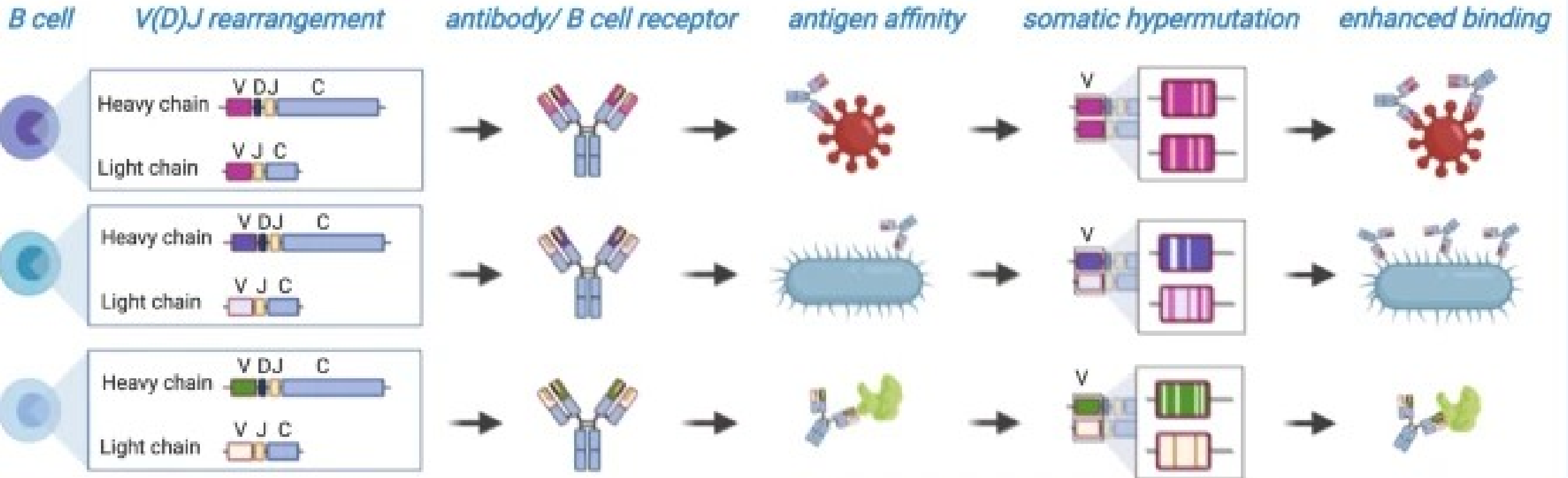
Antibodies



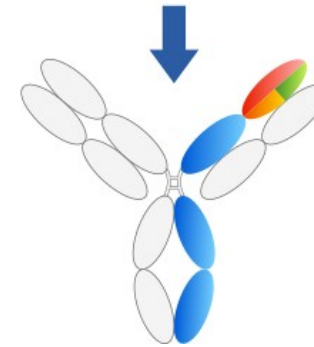
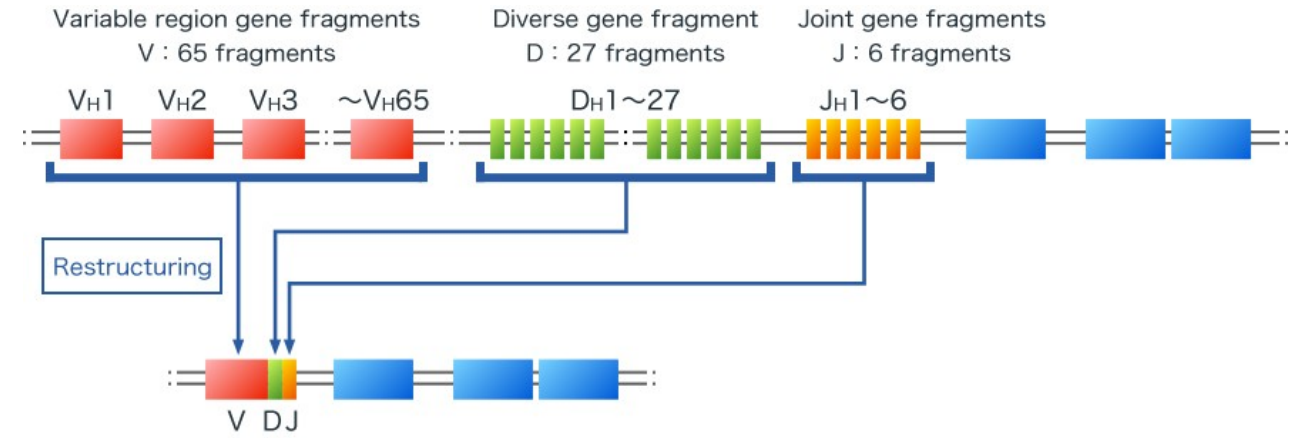
Antibodies

B

Immunoglobulin diversity enables broad recognition breadth



Diversity of antibodies

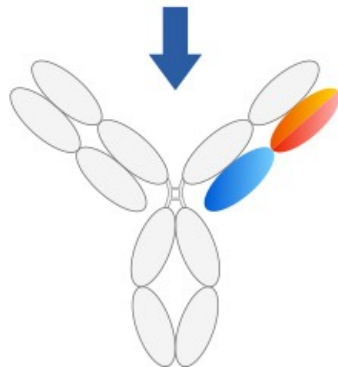
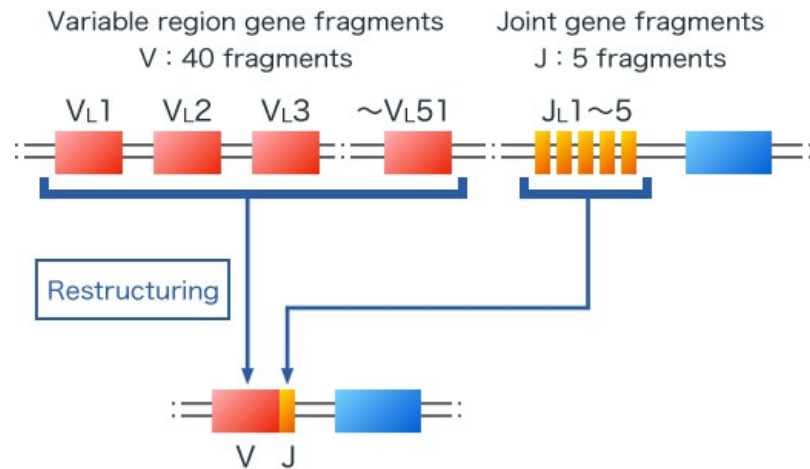


Types of antibodies produced by genes in restructured H chain variable regions

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

fragments fragments fragments

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



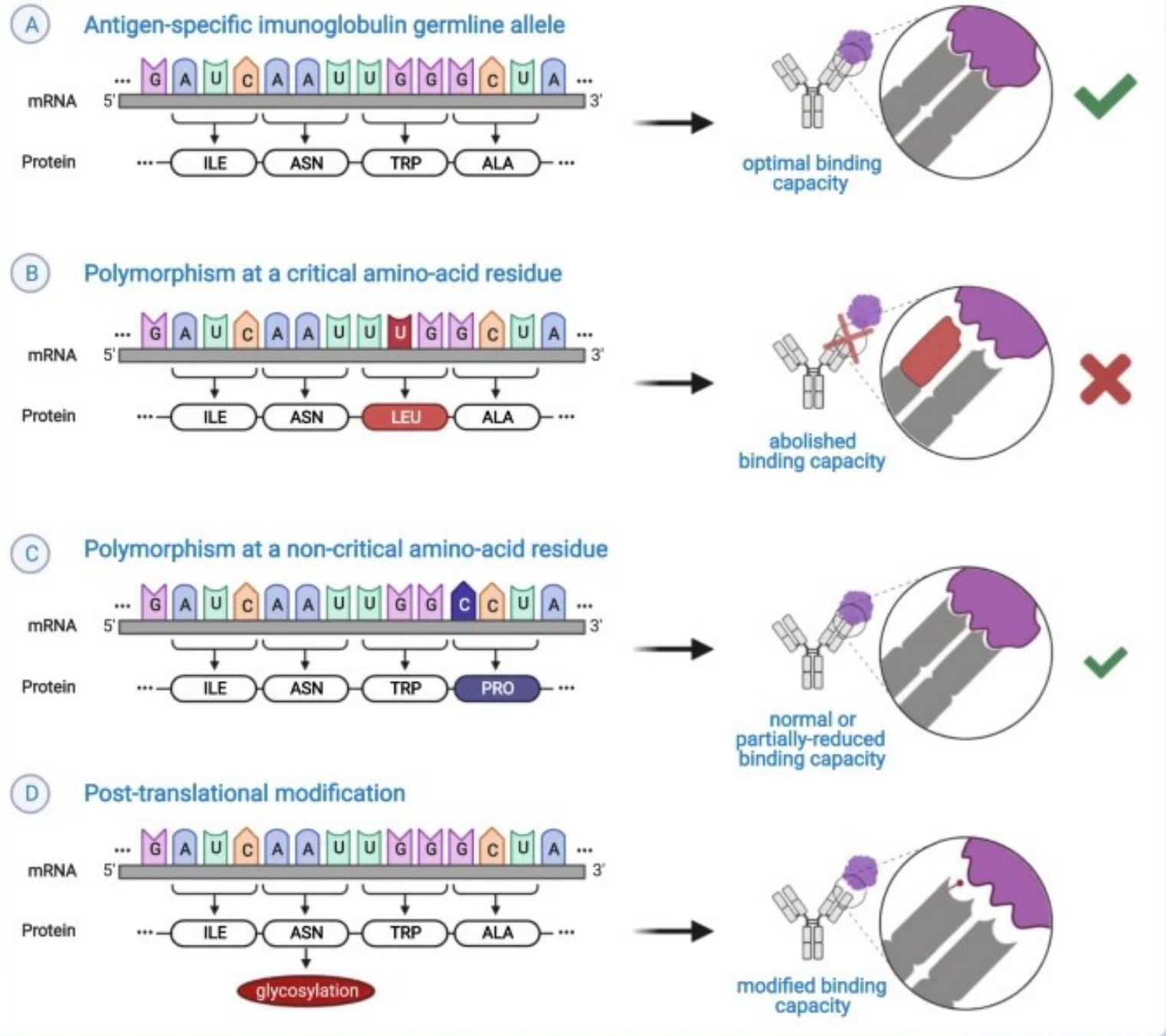
Types of antibodies produced by genes in restructured L chain variable regions

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

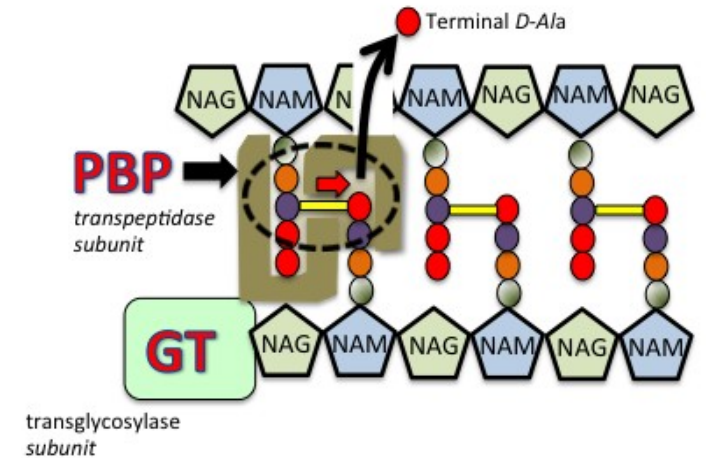
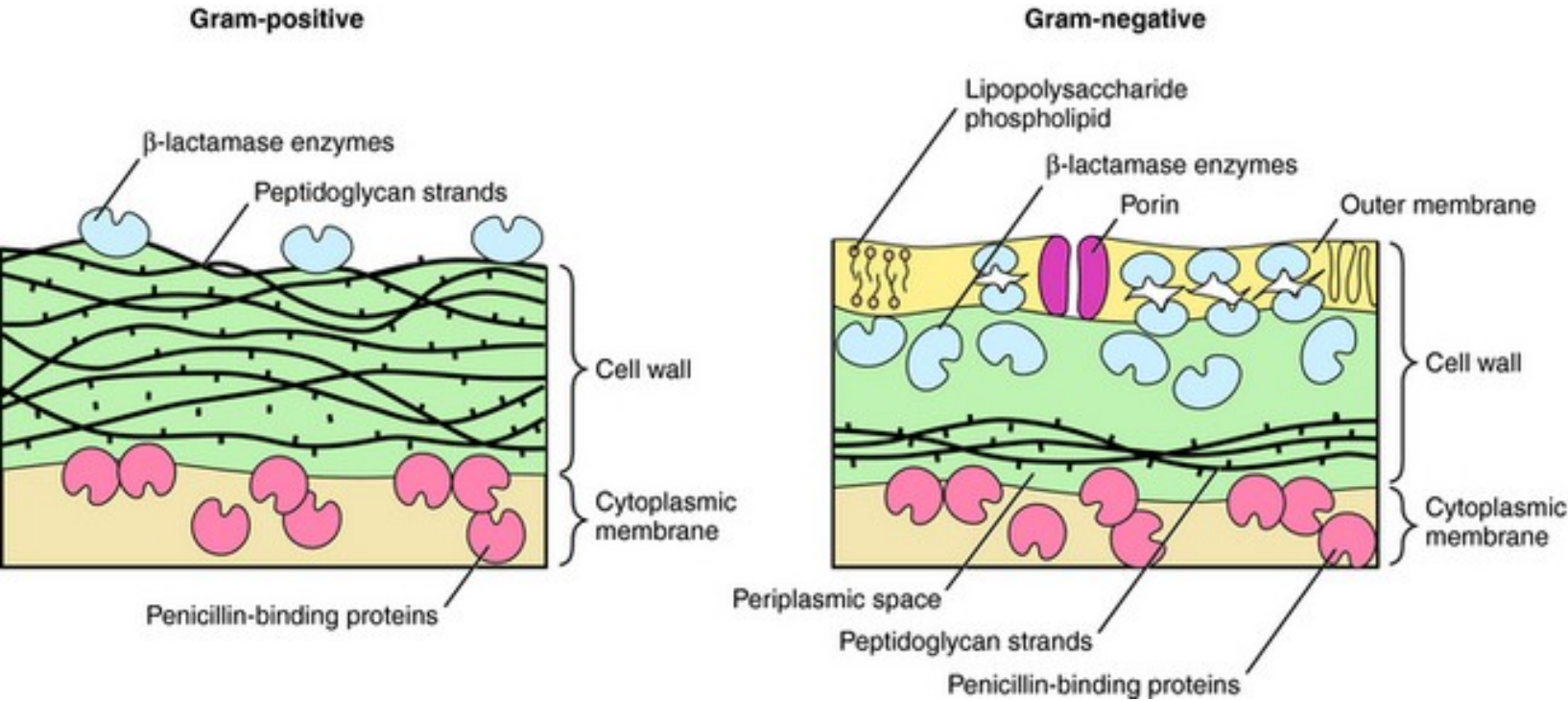
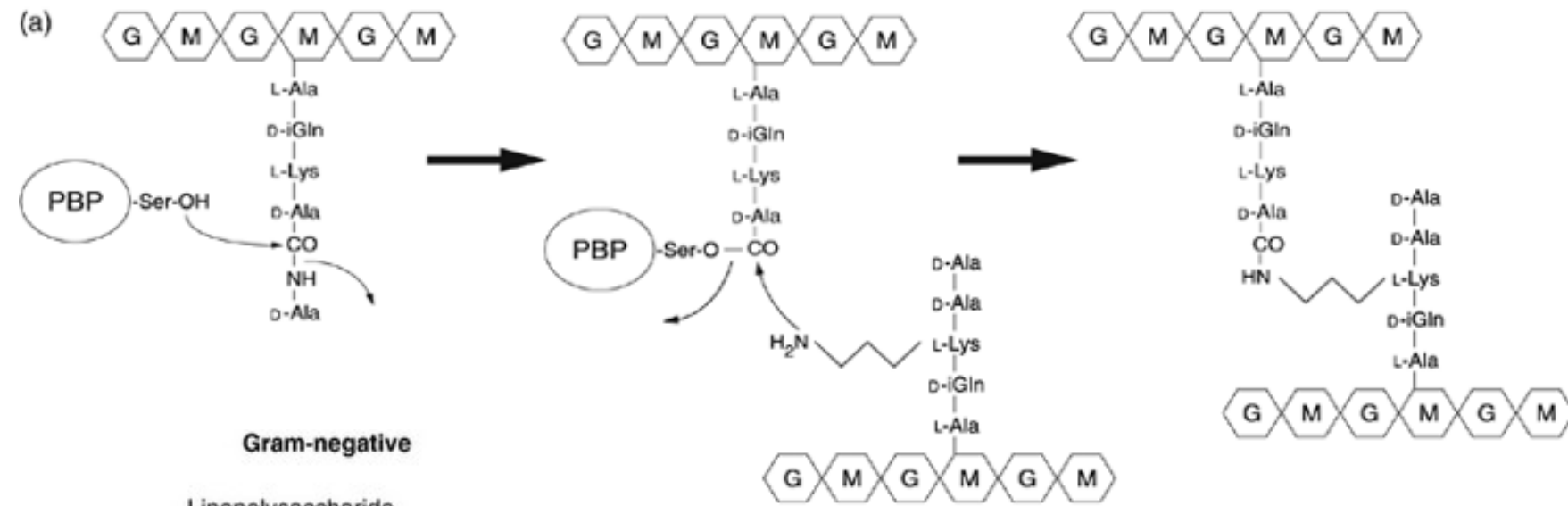
fragments fragments

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

Antibody specificity

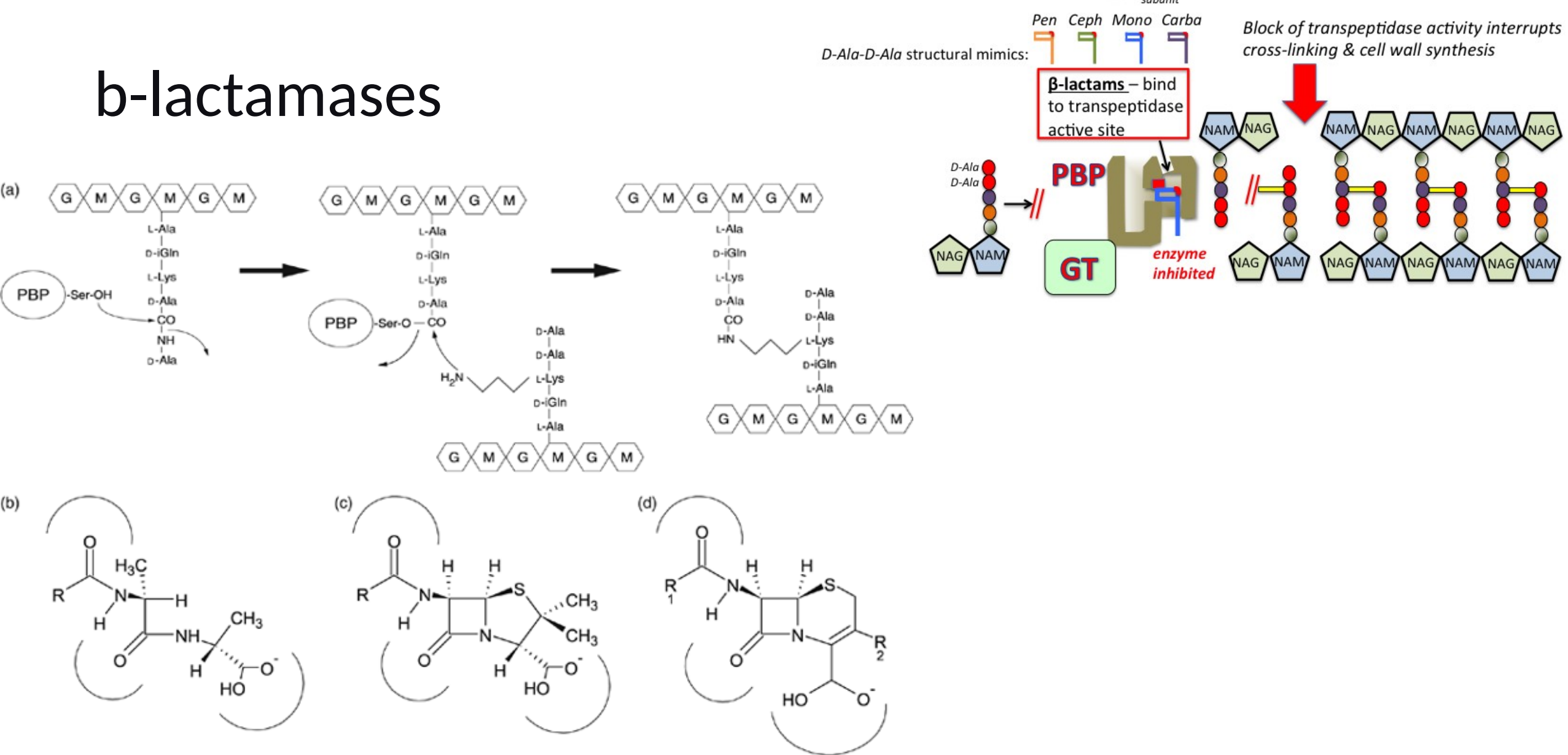


b-lactamases



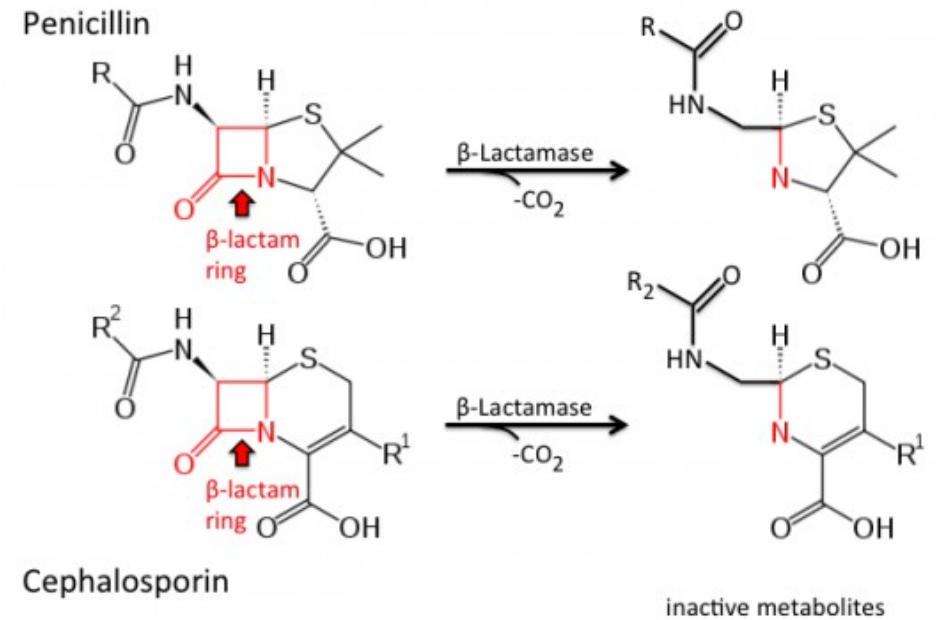
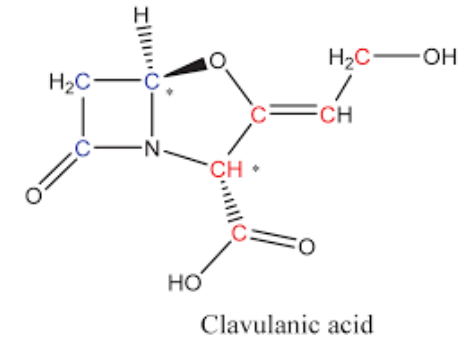
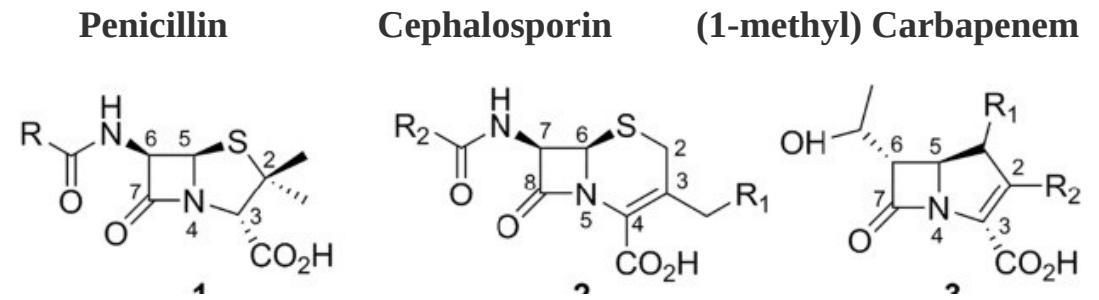
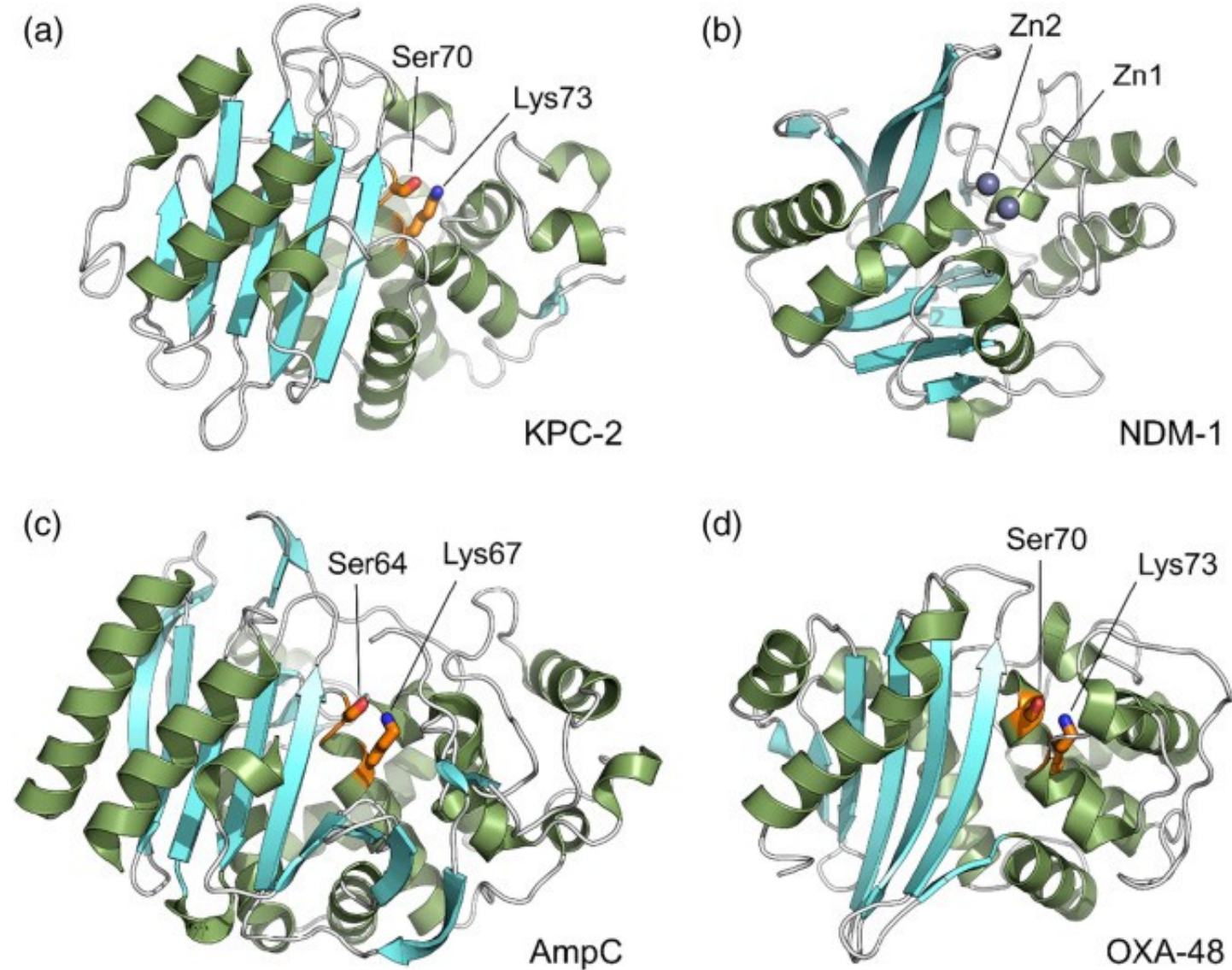
transpeptidase enzymes (Penicillin Binding Proteins; PBP)
 Glycosyltransferases (GT), which exist as either separate subunits, or tightly associated with transpeptidases (PBP-2) create covalent bonds between adjacent sugar molecules NAM & NAG

b-lactamases

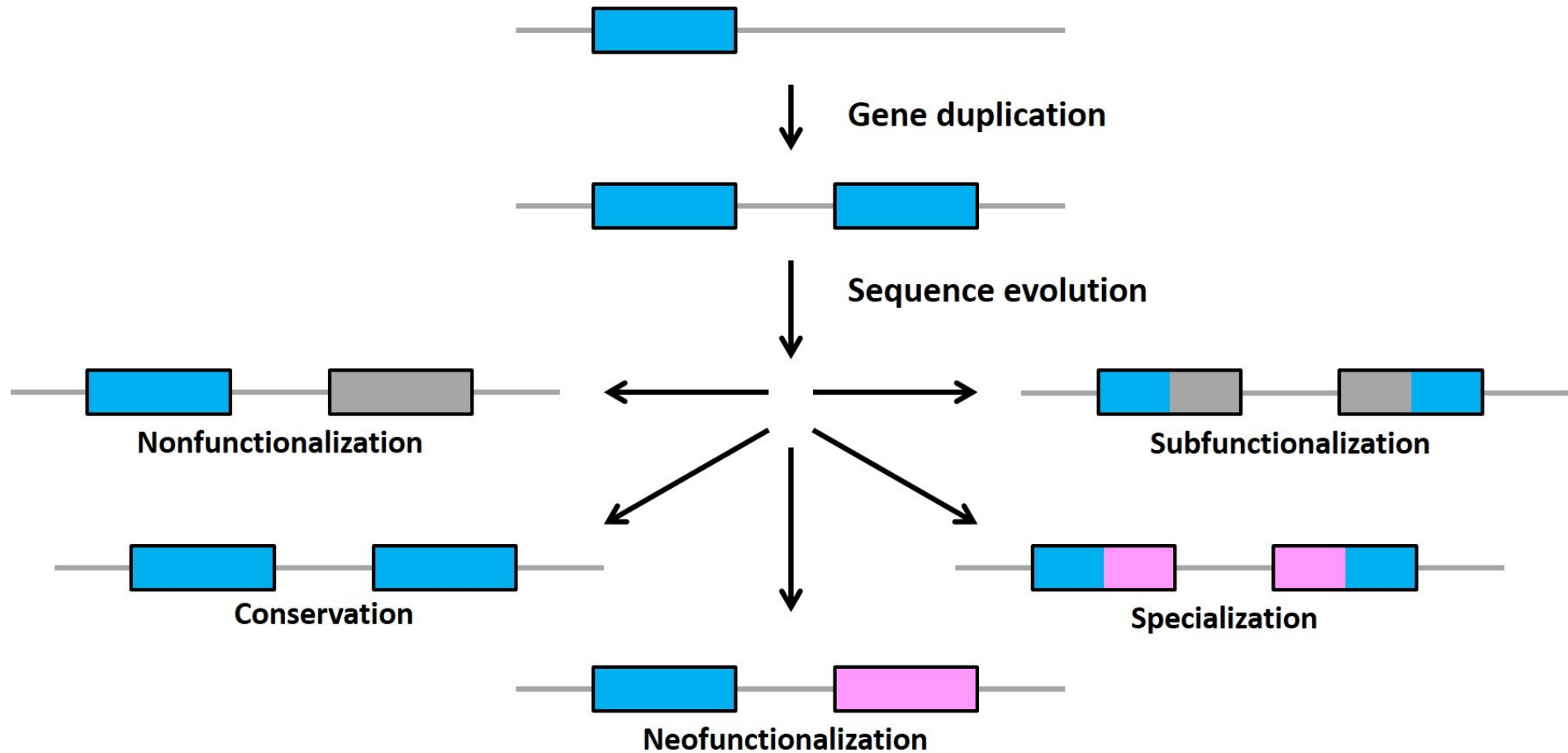


transpeptidase enzymes (Penicillin Binding Proteins; PBP Glycosyltransferases (GT), which exist as either separate subunits, or tightly associated with transpeptidases (e.g. as is the case for PBP-2) create covalent bonds between adjacent sugar molecules NAM & NAG

β -lactamases



gene duplication

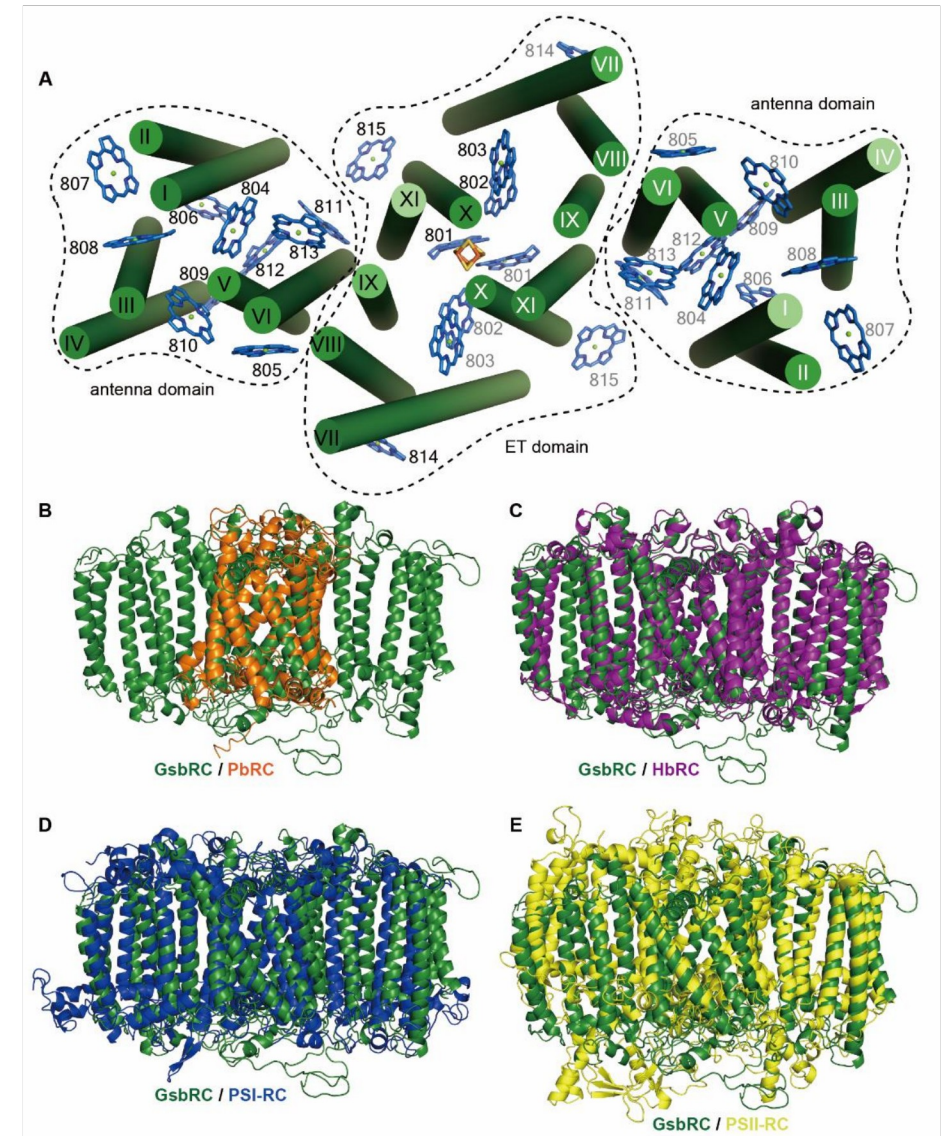
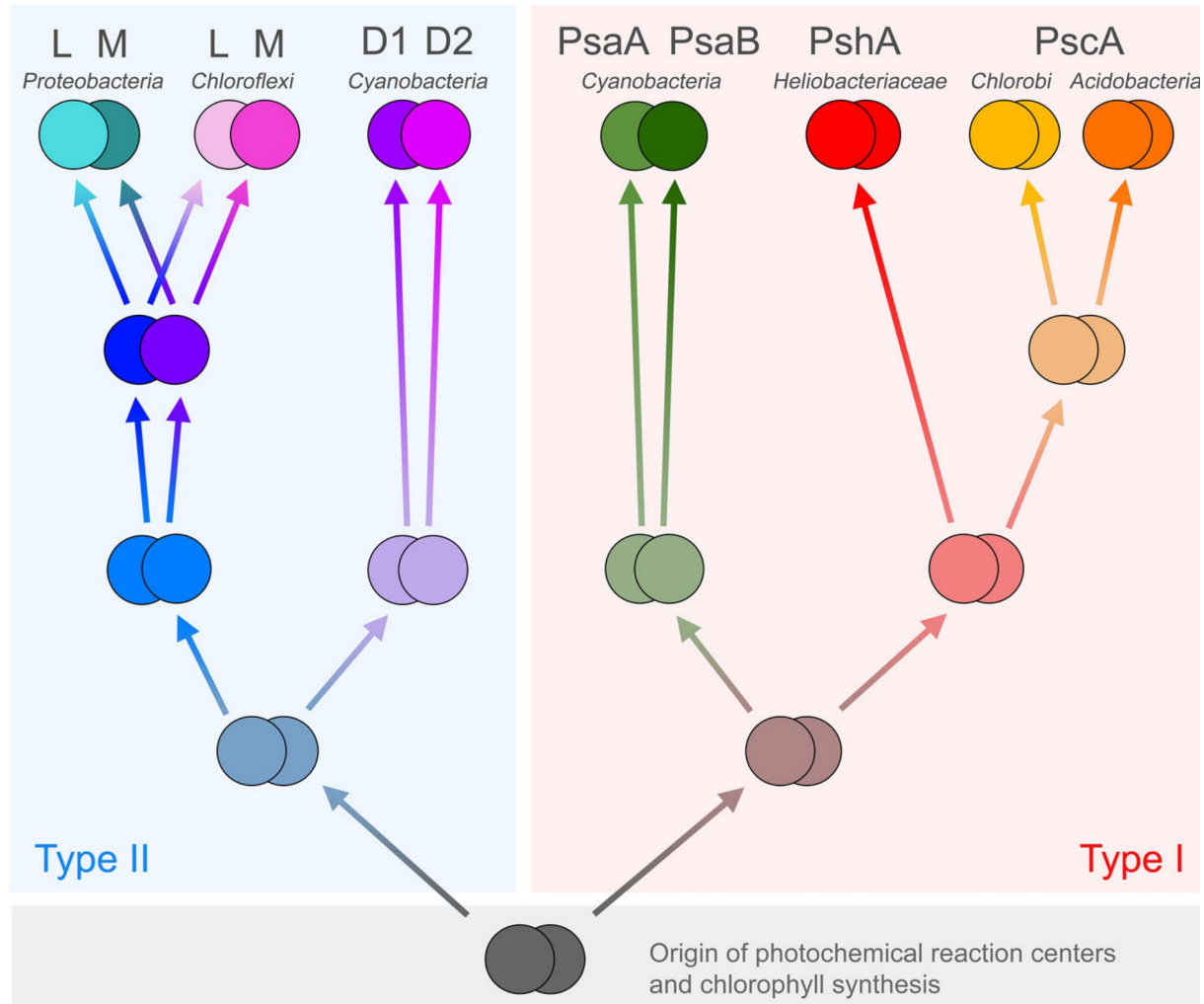


33% of the genes in *Haemophilus influenzae* have arisen from gene duplications

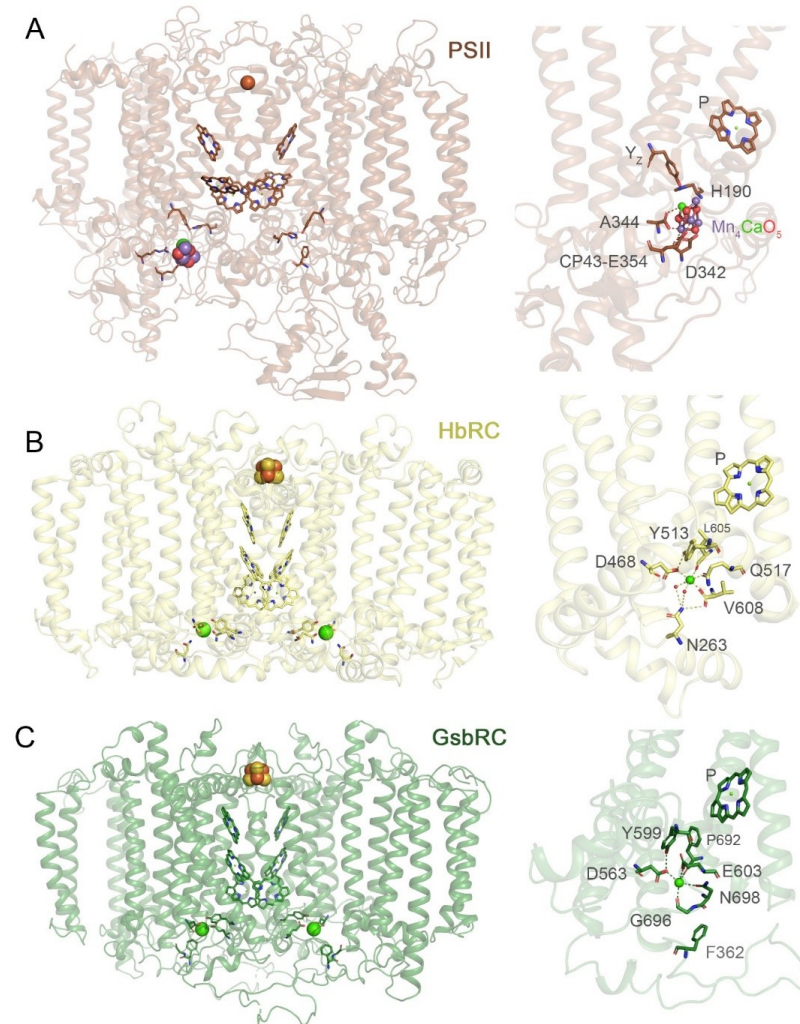
88% of the *Saccharomyces cerevisiae* genome

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

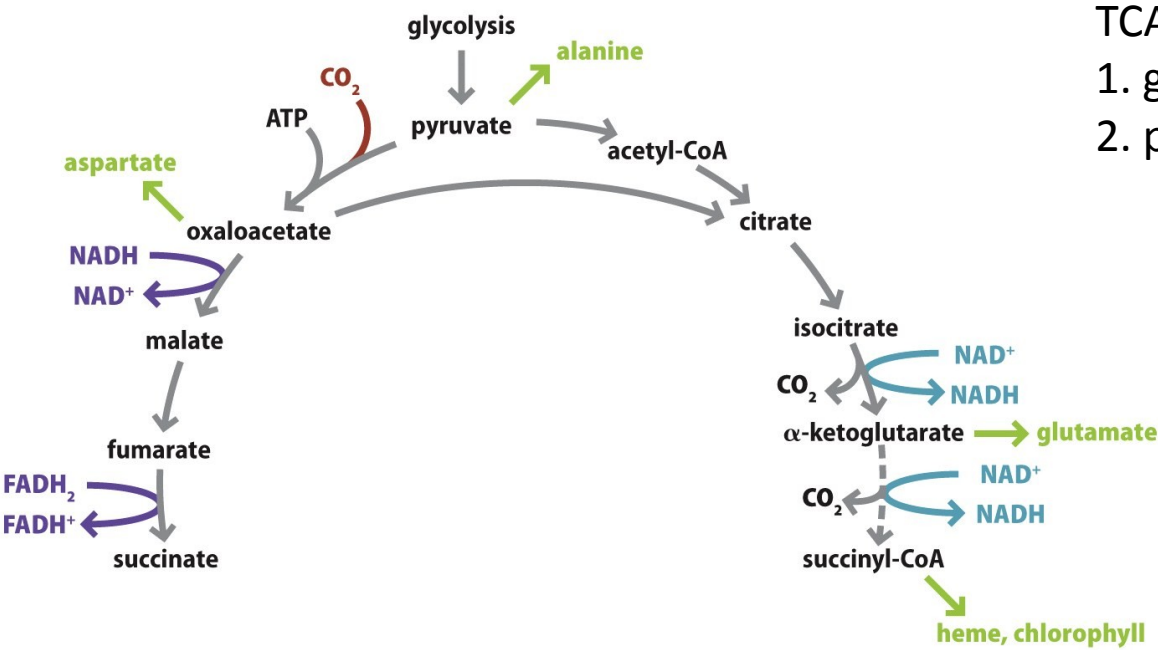


Figure 1.54 How Proteins Work (©2012 Garland Science)

TCA
 1. generate metabolic intermediates
 2. produce energy

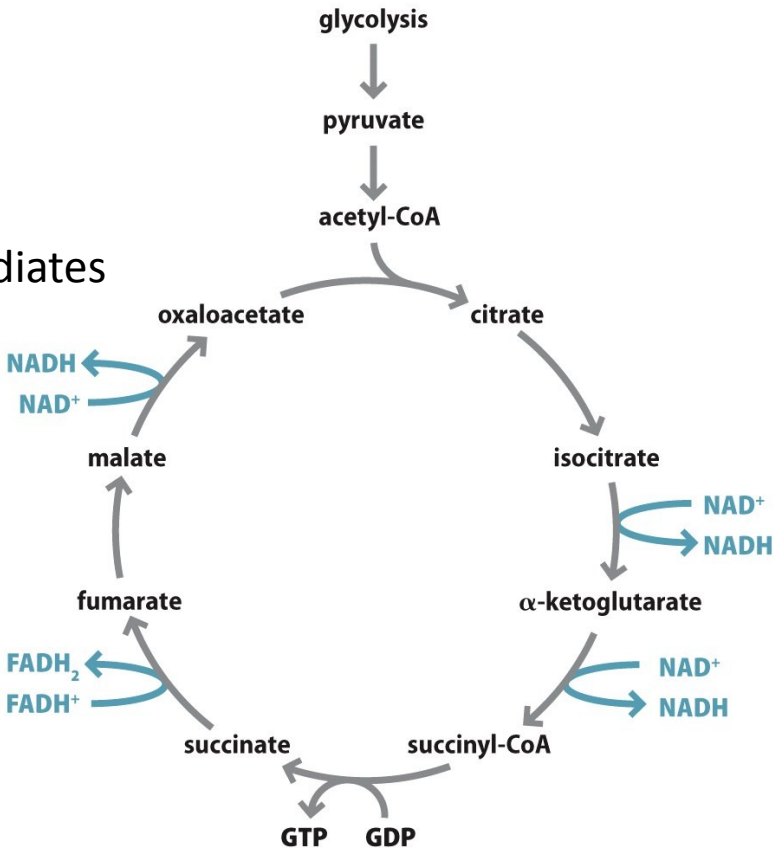
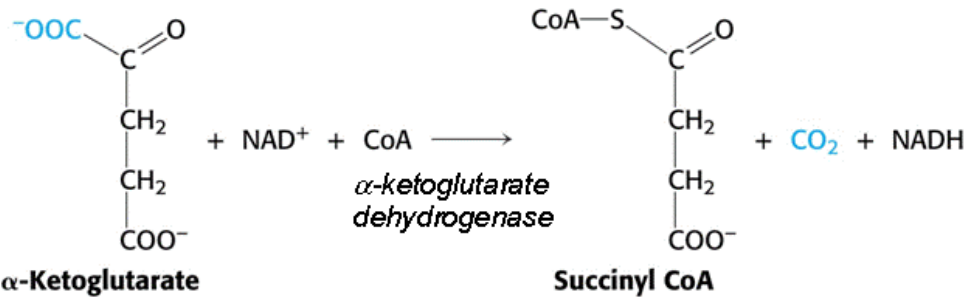
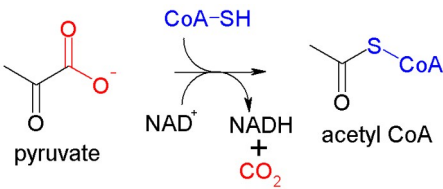


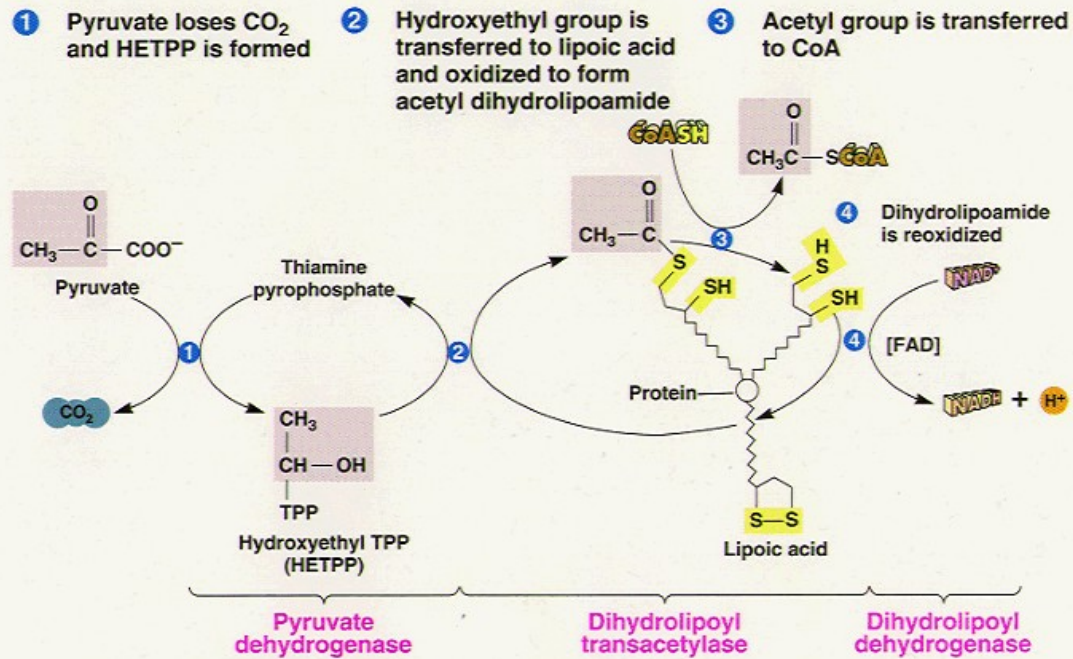
Figure 1.55 How Proteins Work (©2012 Garland Science)

pyruvate dehydrogenase



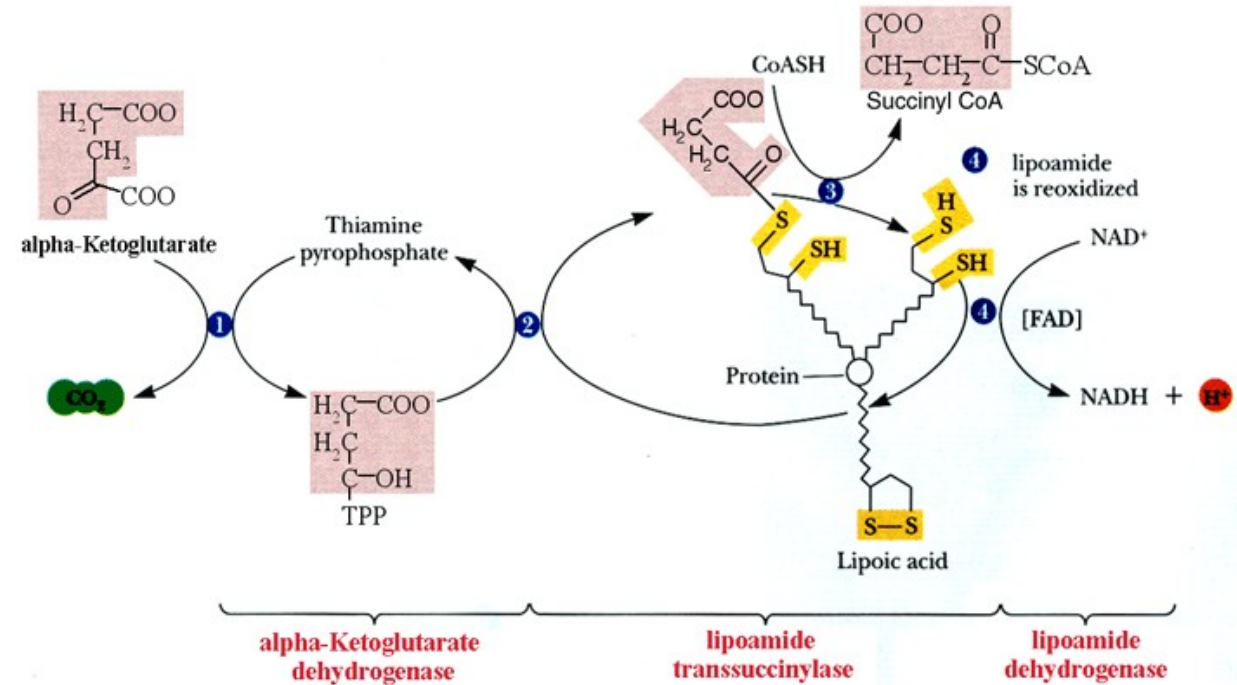
succinyl-CoA synthetase

Mechanisms

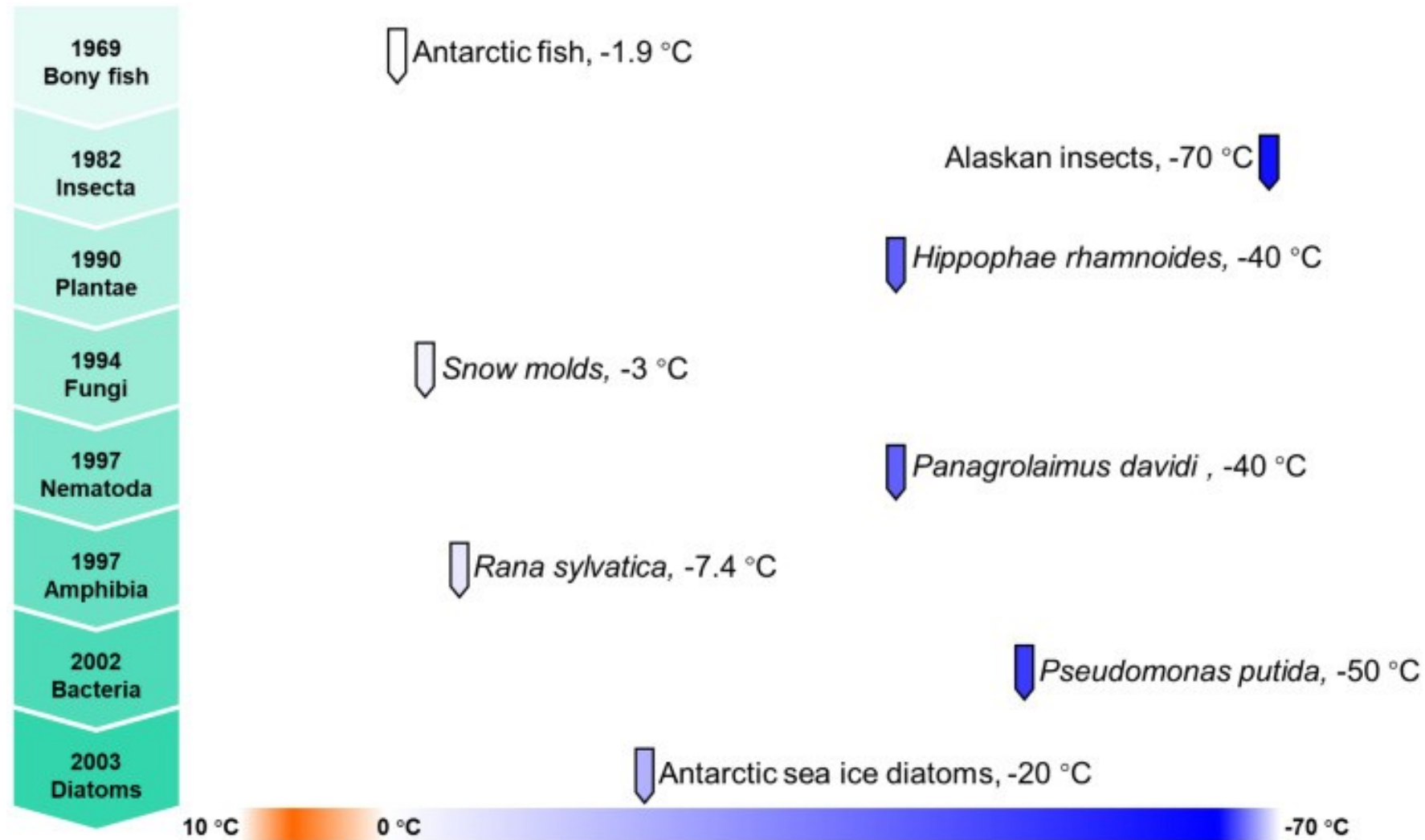


Overhead transparencies to accompany Garrett/Grisham: *Biochemistry*
Transparency 59 Figure 14.41

page 497
©1995 Saunders College Publishing



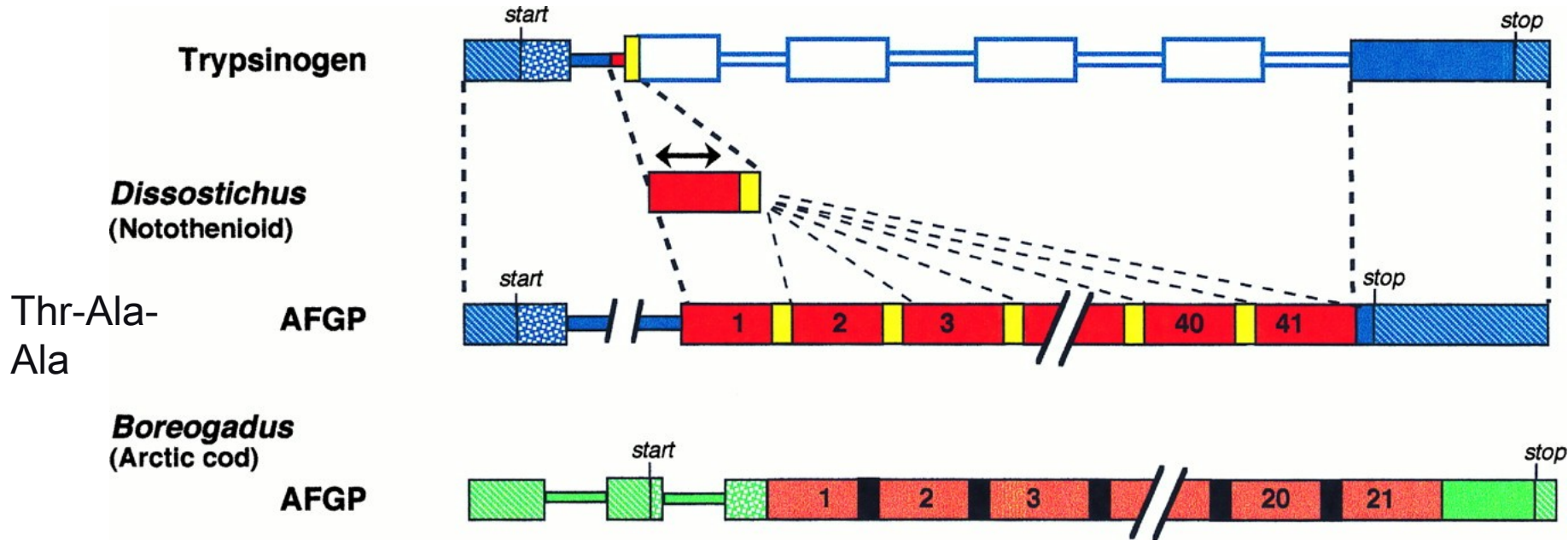
survive in extremely cold weather



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



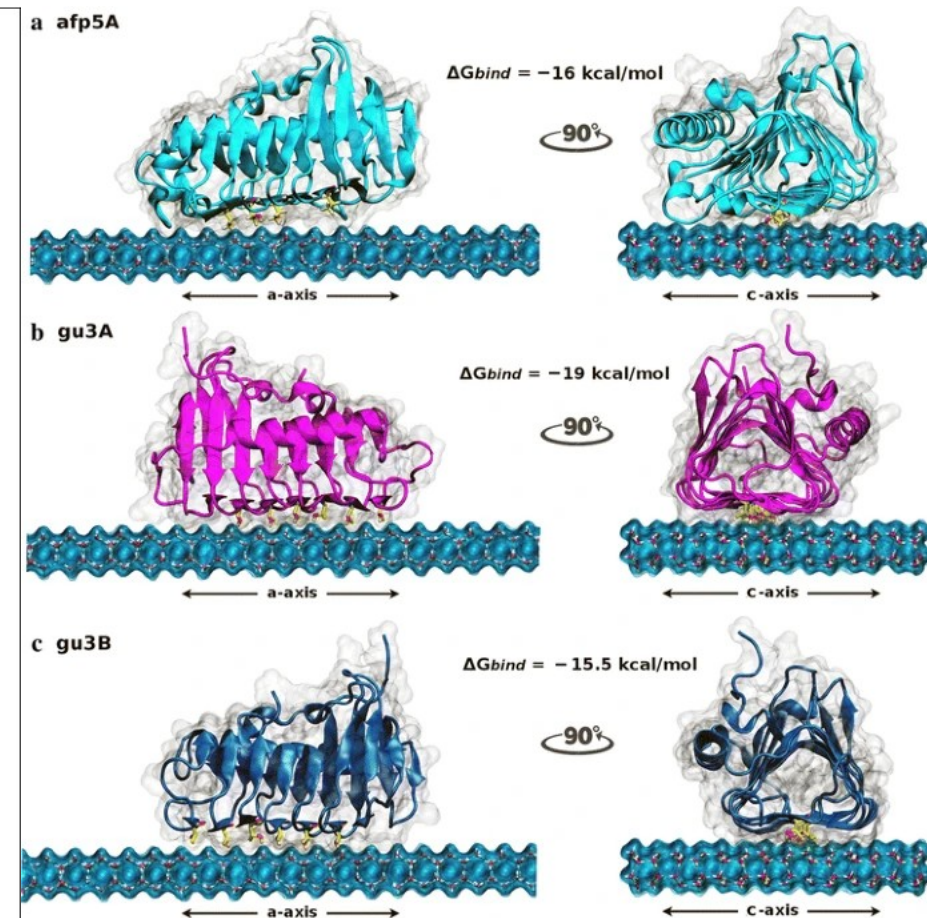
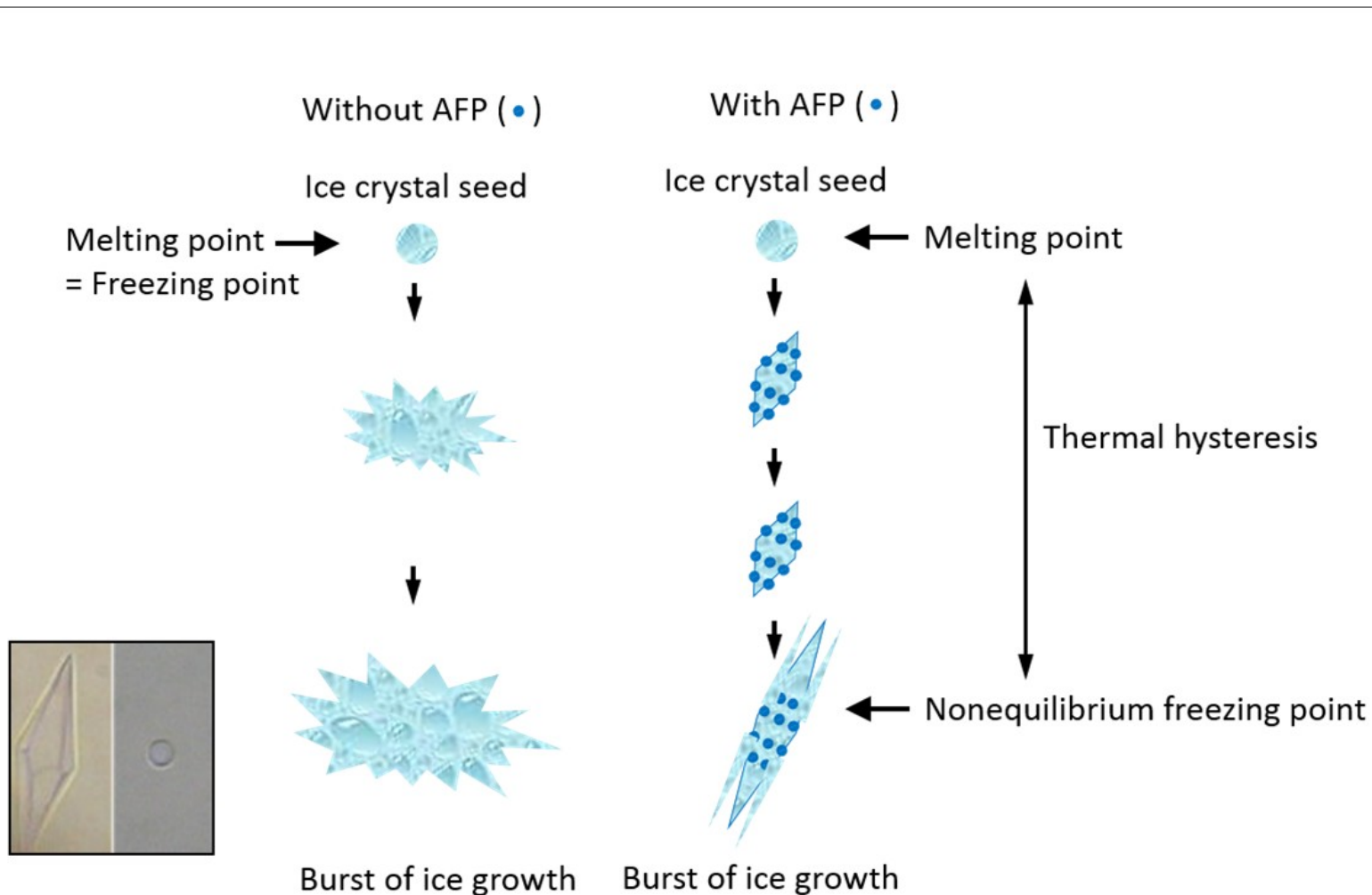
structurally characterized AFPs



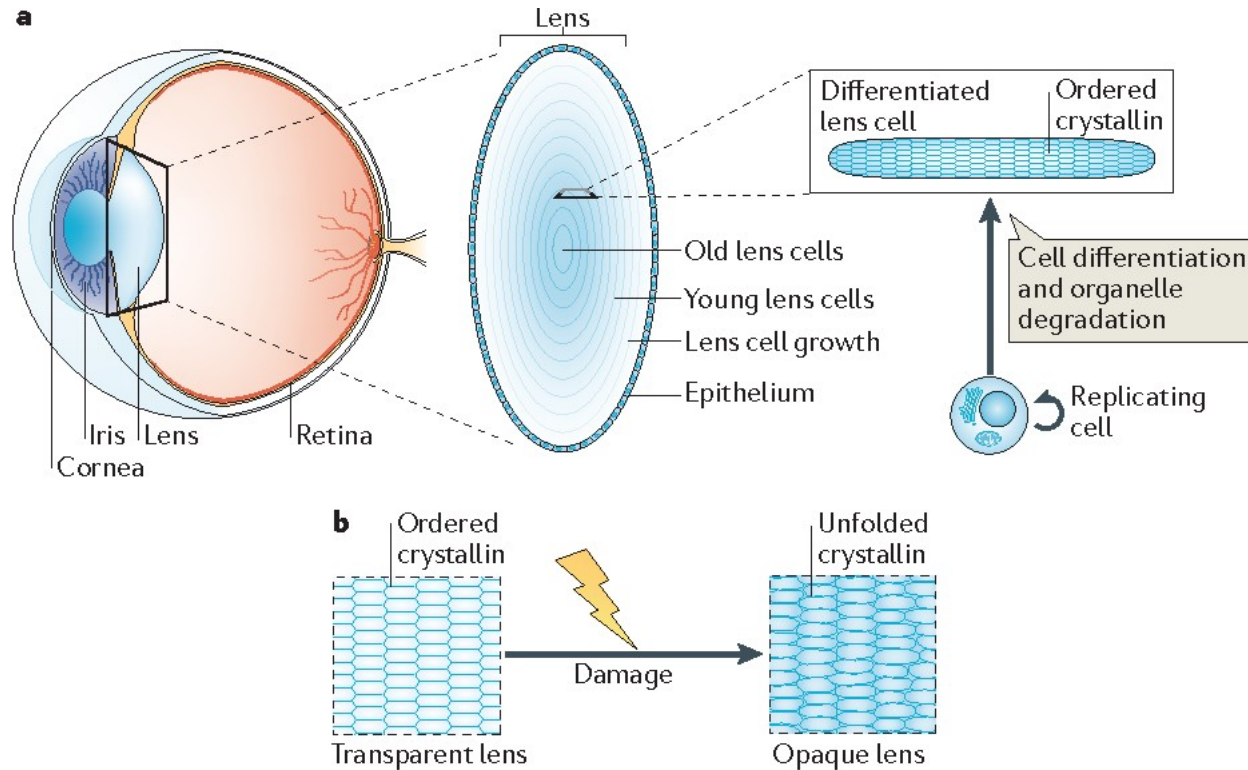
	Fish					Insect	Bacterium	Plant	
	Type I AFP			Type II AFP	Type III AFP	AFGP	DcAFP	MpAFP	LpAFP
Structure element	α -helix, Alanine rich	α -helix, Alanine rich	α -helix, Threonine-(Alanine rich)	Globular; S-S bonds	Globular; β -sandwich	AAT-repeat; Disaccharide	β -solenoid; S-S bonds	β -solenoid	β -solenoid
Representative structure									
Binding plane									
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

Η προστατευτική λειτουργία των AFPs επωφελείται από τις ιδιότητές τους, οι οποίες περιλαμβάνουν την συγγένεια με το επίπεδο του πάγου, τη θερμική υστέρηση, την αναστολή της ανακρυστάλλωσης του πάγου και την παροδική σύνδεση ενός οργανισμού με τον πάγο.

Effect



gene sharing



The lens proteins need to have three properties:

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

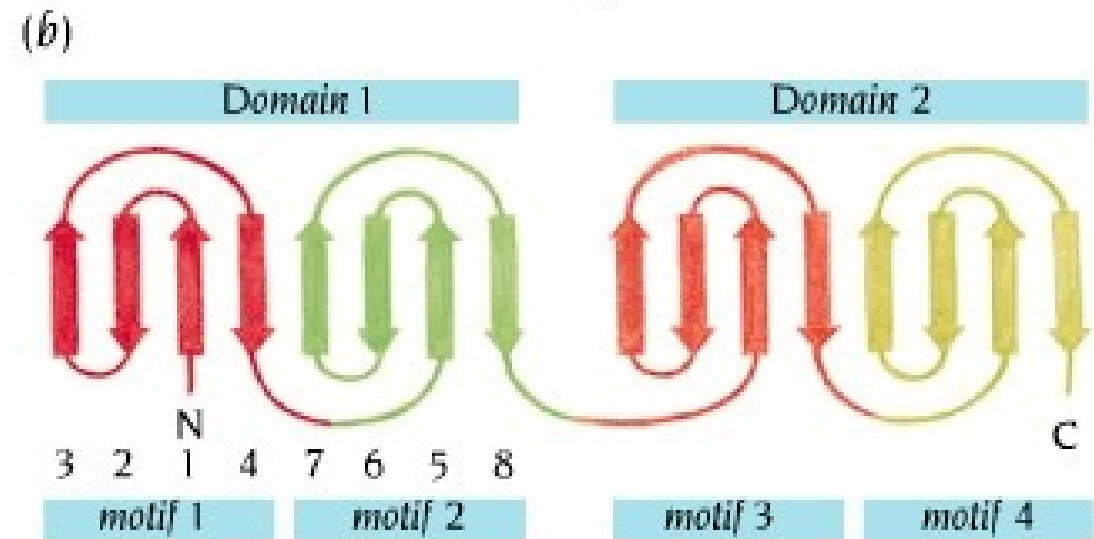
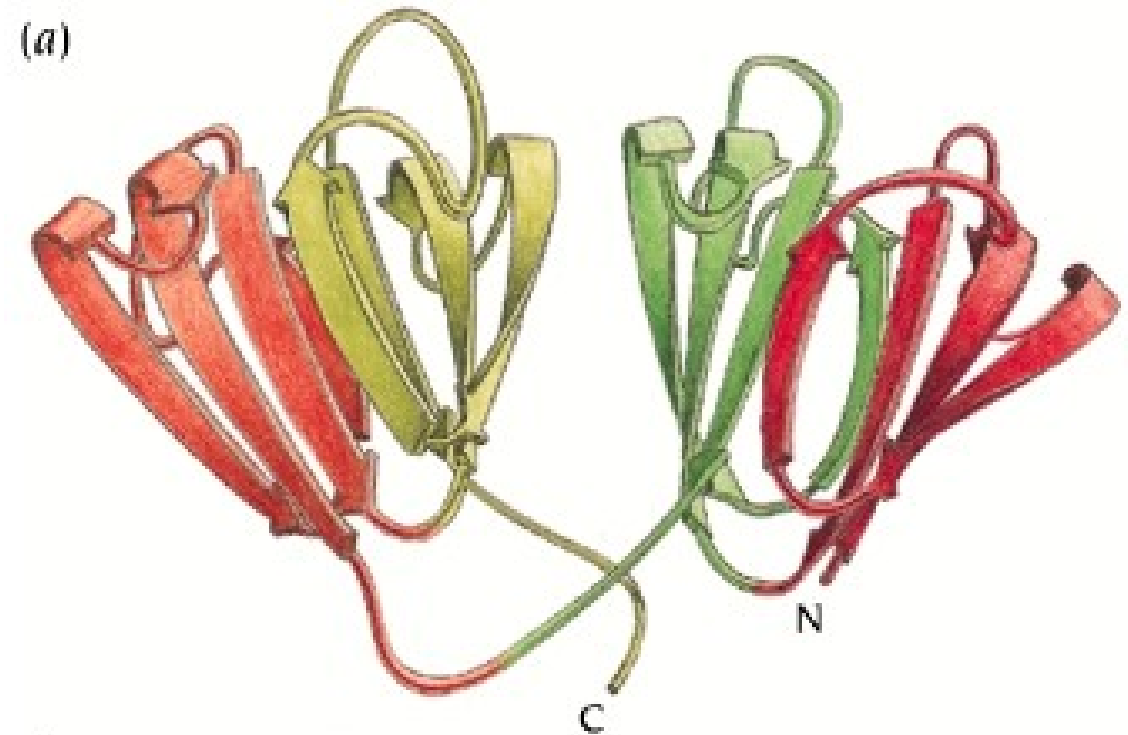
they should remain soluble and transparent throughout the life of the animal

they should be nontoxic in their new location and concentration.

γ crystallin

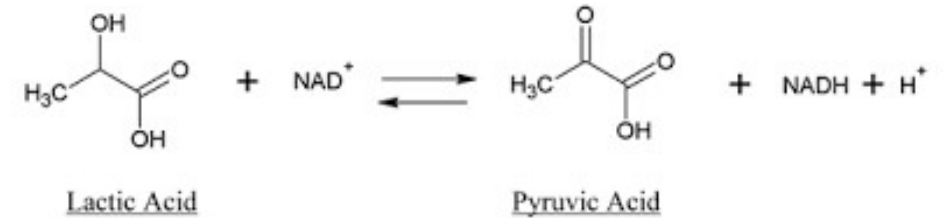


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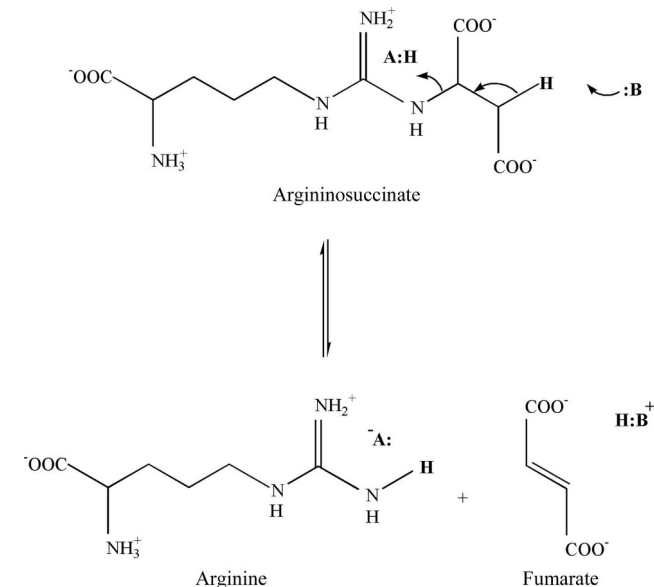
gene sharing



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

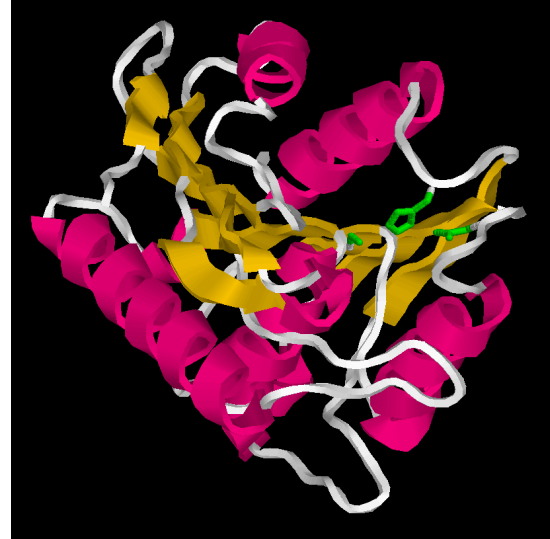
Convergent Evolution



Trypsin



Subtilisin

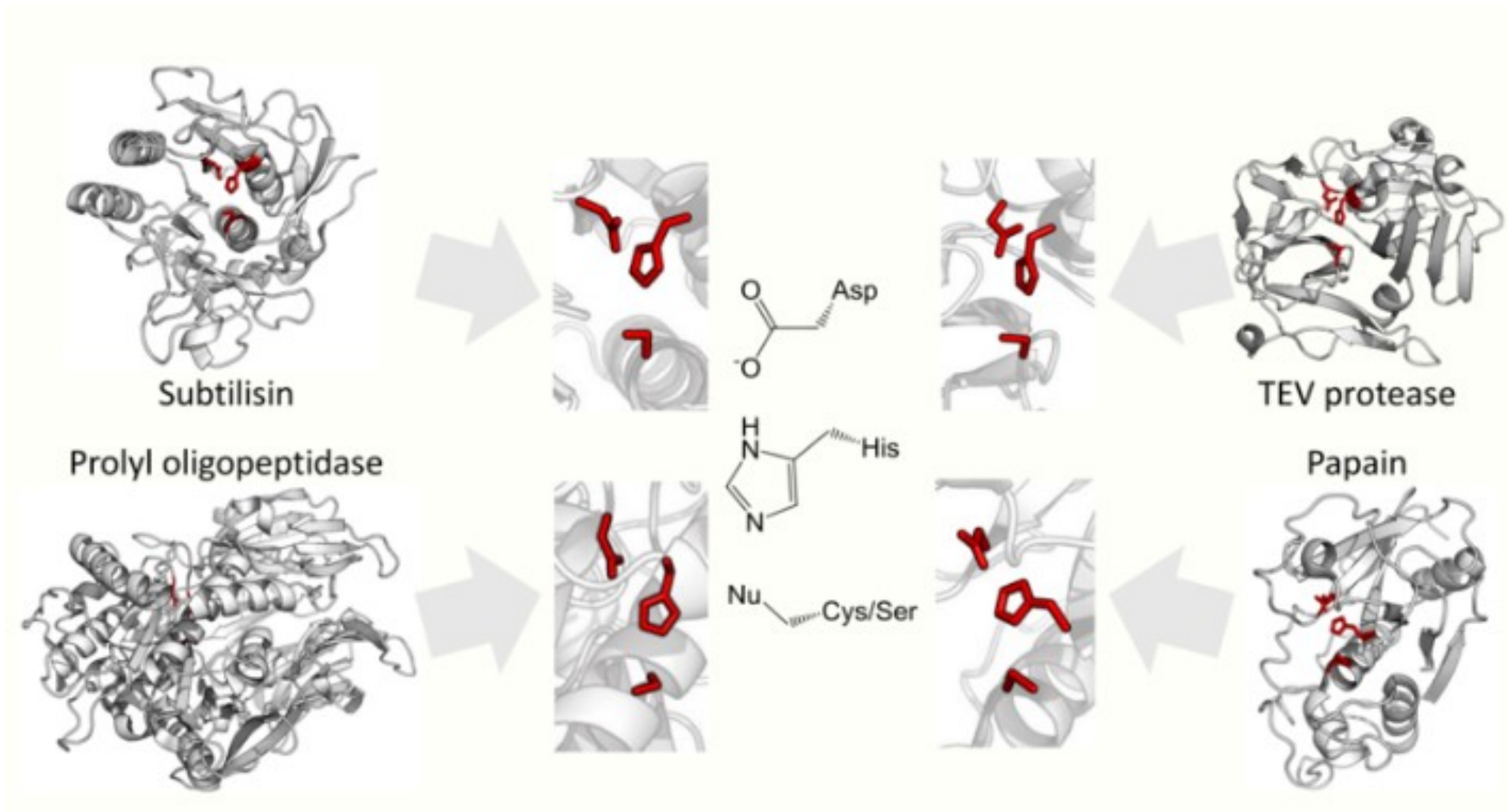


Alpha/beta hydrolase

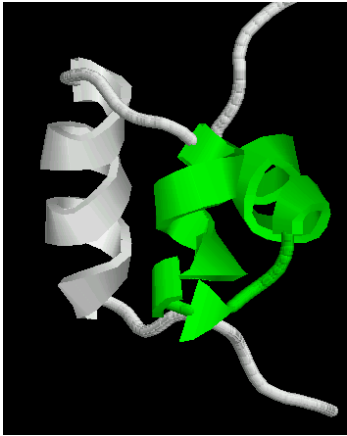


CheB methylesterase

Convergent Evolution



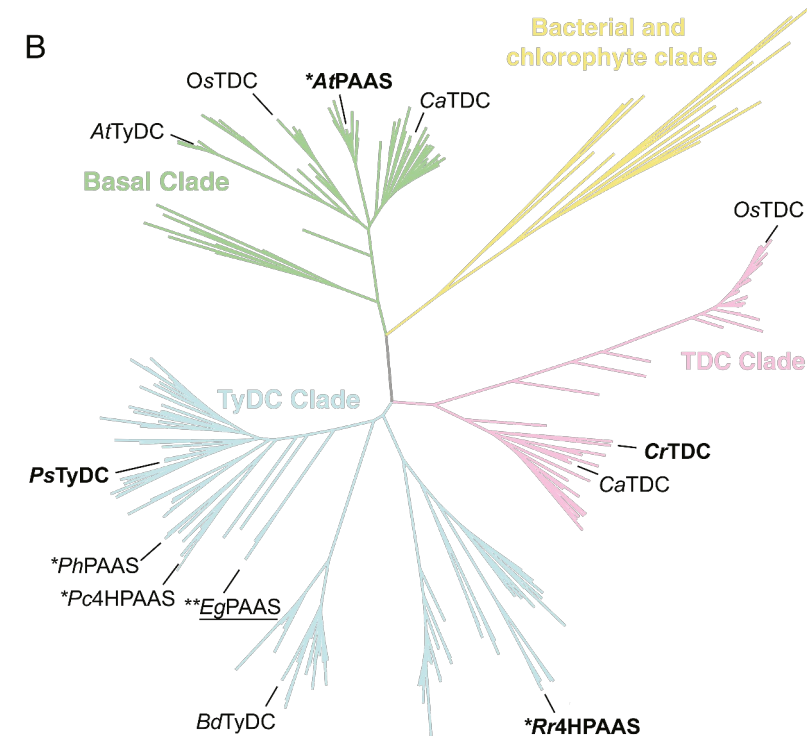
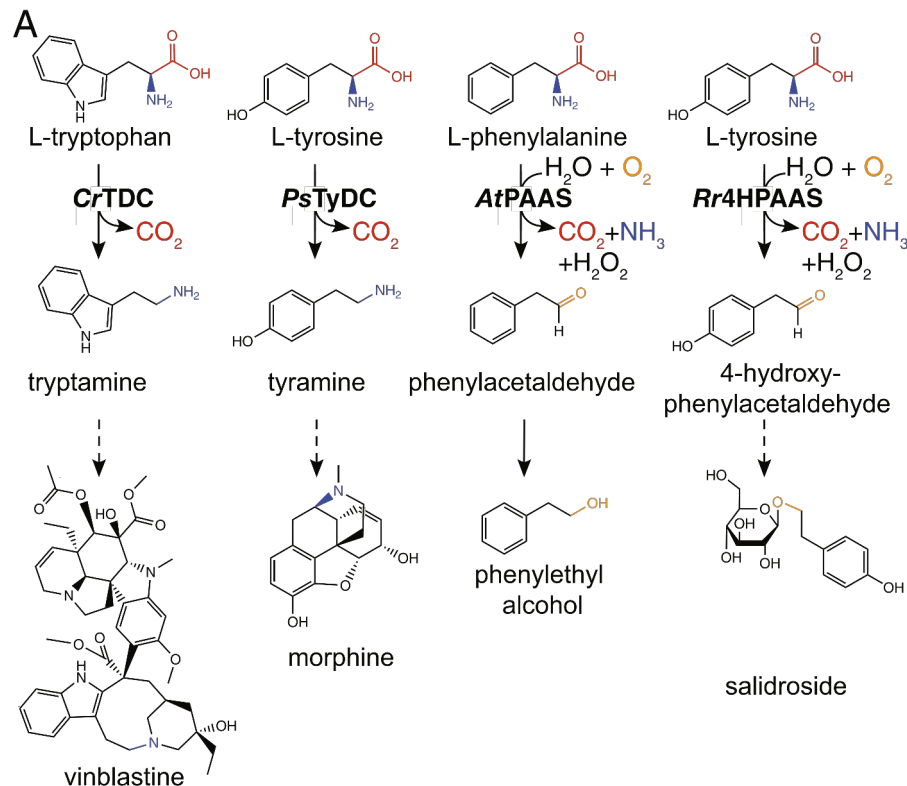
Convergent Evolution

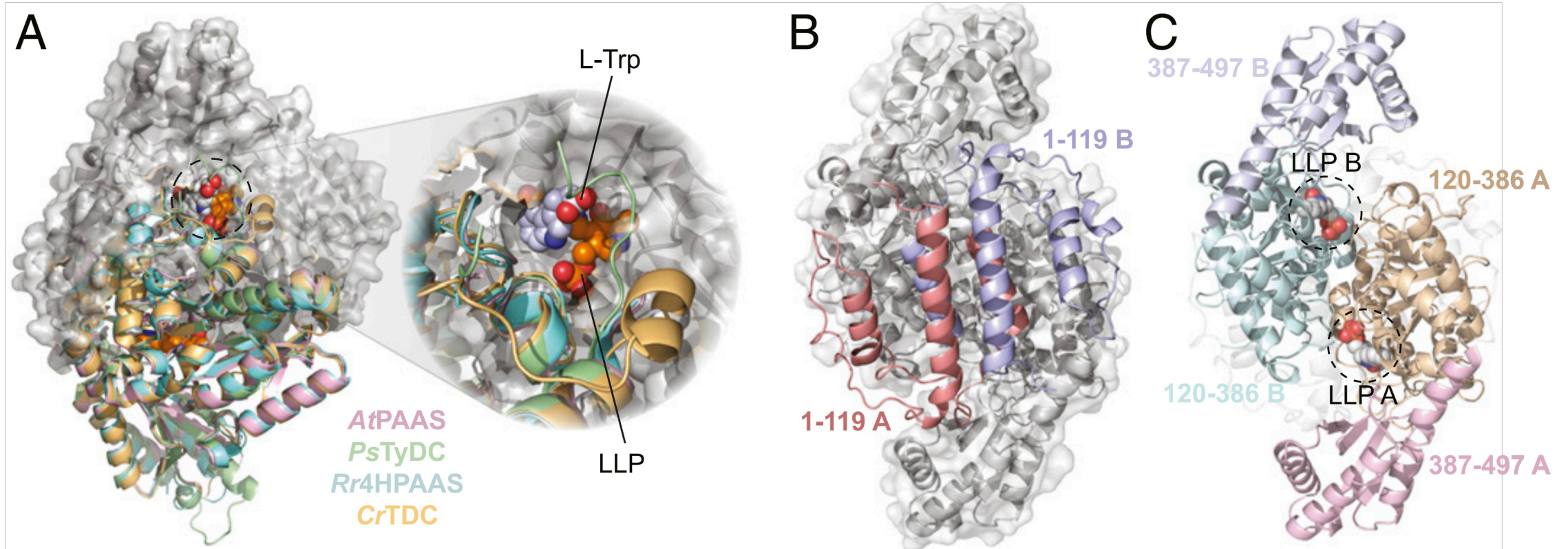


Divergent Evolution

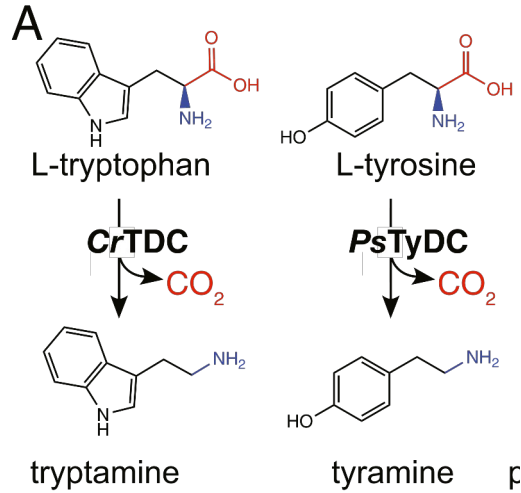
Related proteins can perform different functions – divergent evolution

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.

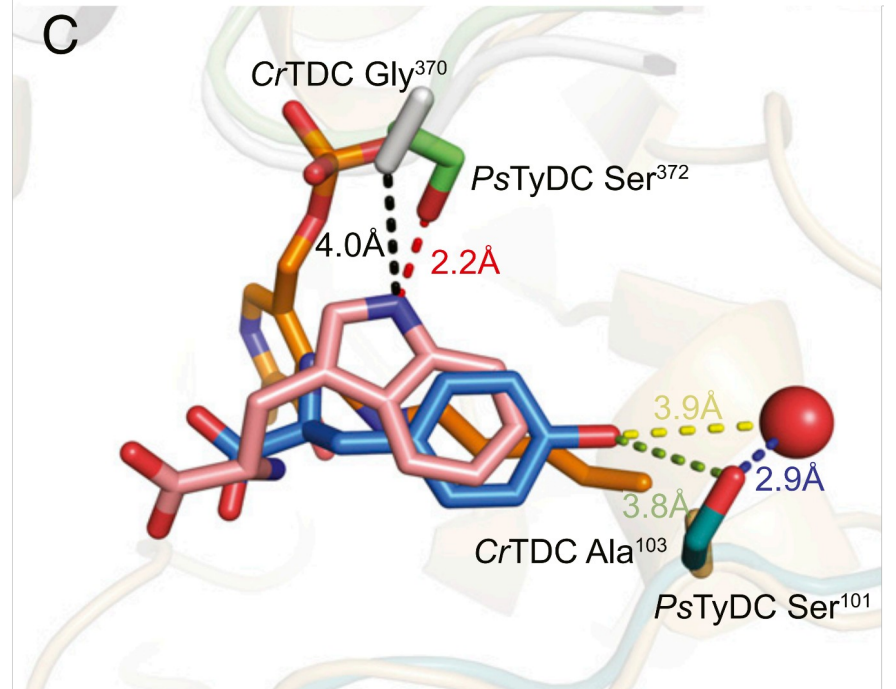
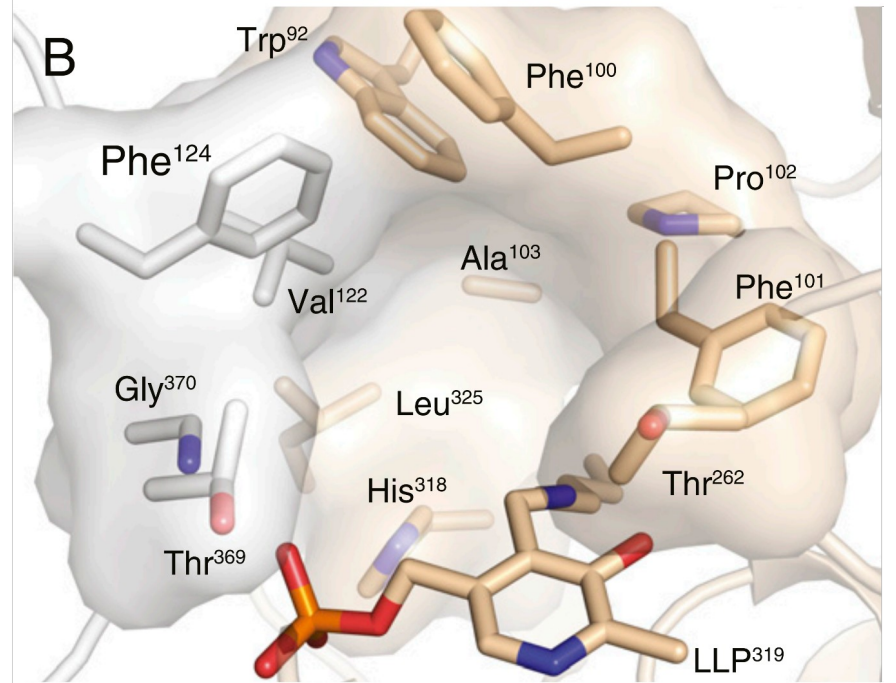




substrate selectivity



The CrTDC active-site pocket

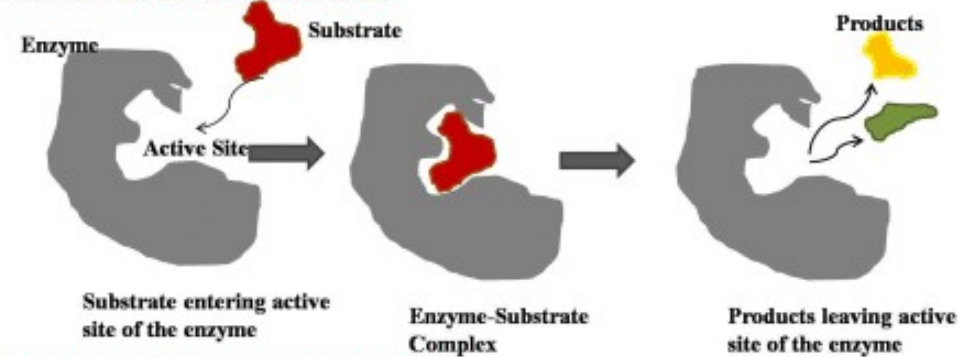


Promiscuous enzymes

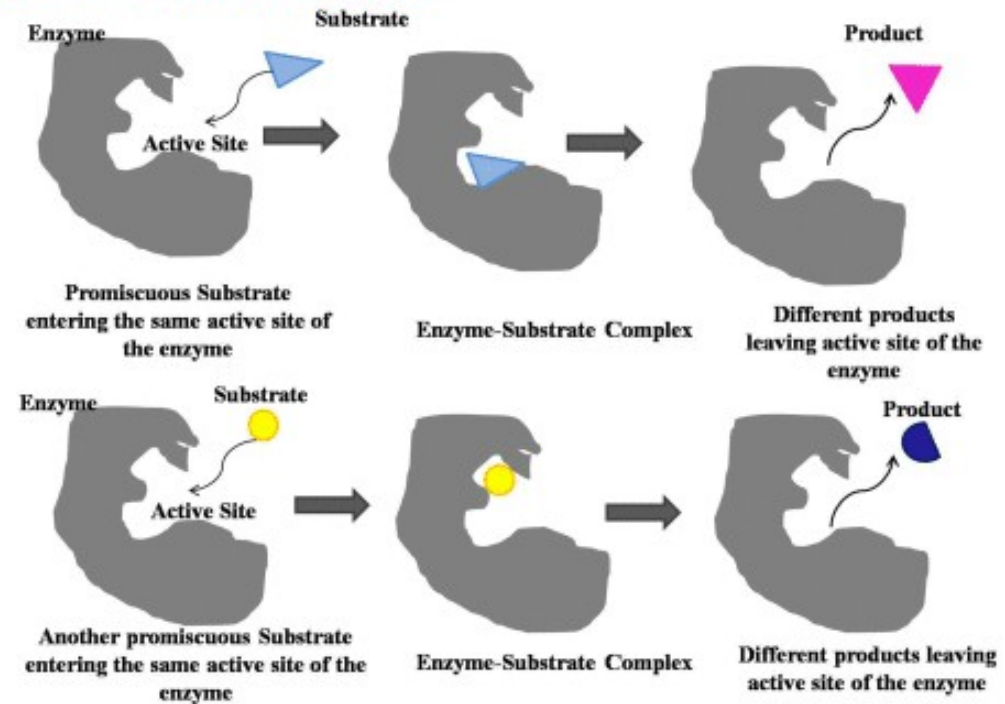
Promiscuous enzymes that catalyze two different reactions

They 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.

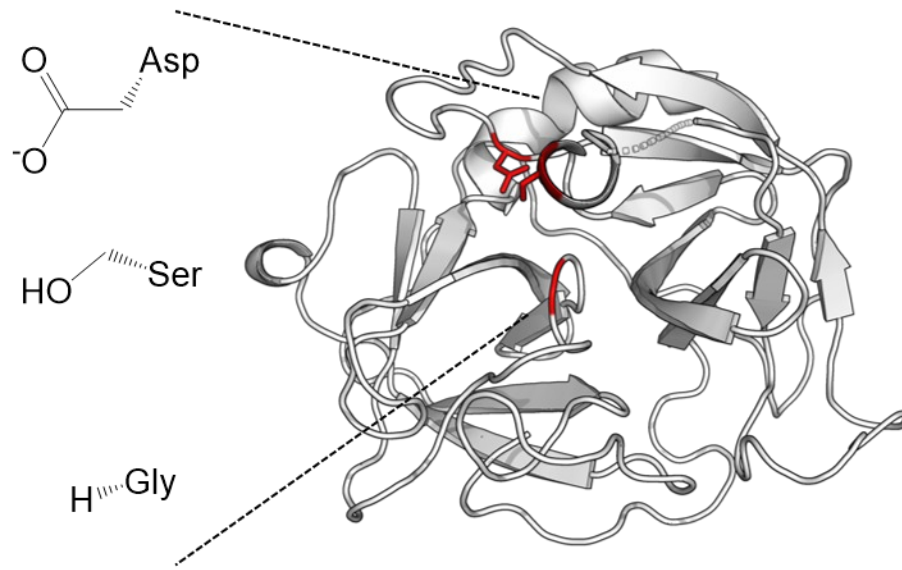
Promiscuous enzymes

TABLE 1.4 Promiscuous enzymes

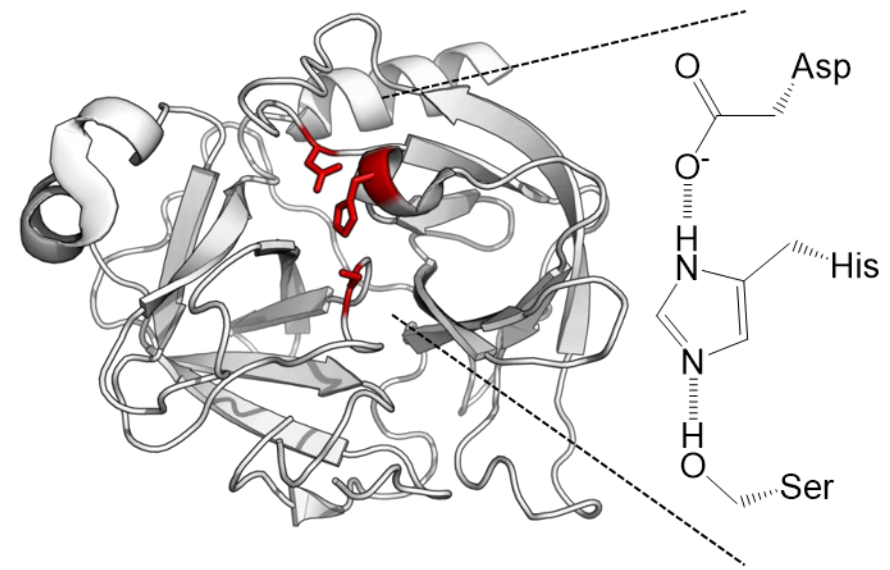
Enzyme	Normal reaction	Promiscuous reaction
α -Chymotrypsin	Peptide hydrolysis	Hydrolysis of esters and phosphate triesters
Alkaline phosphatase	Phosphate monoester hydrolysis	Hydrolysis of phosphate diesters, phosphonate monoesters, and sulfate esters; phosphate oxidation
Arylsulfatase A	Sulfate ester 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

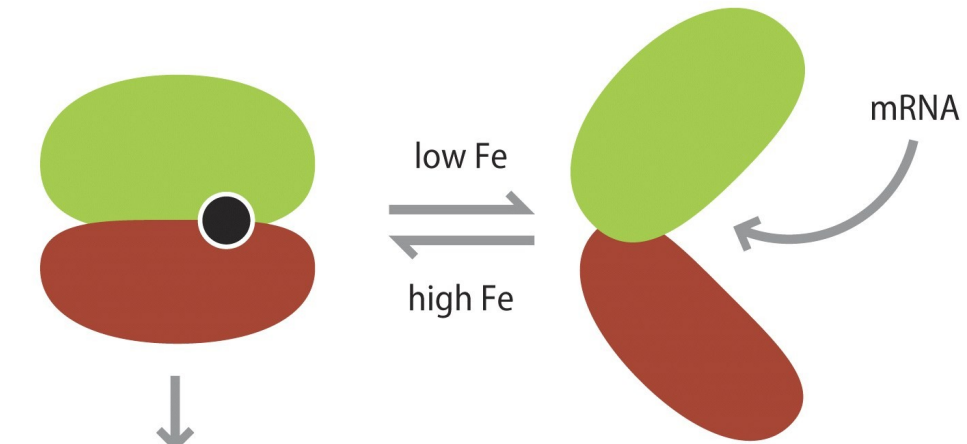
Moonlighting proteins that have two or more quite different functions:

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)

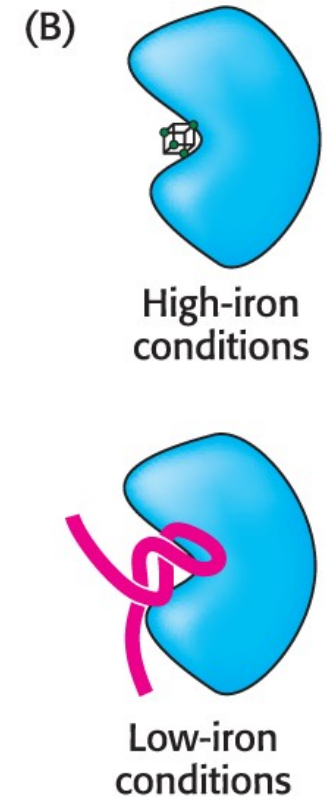
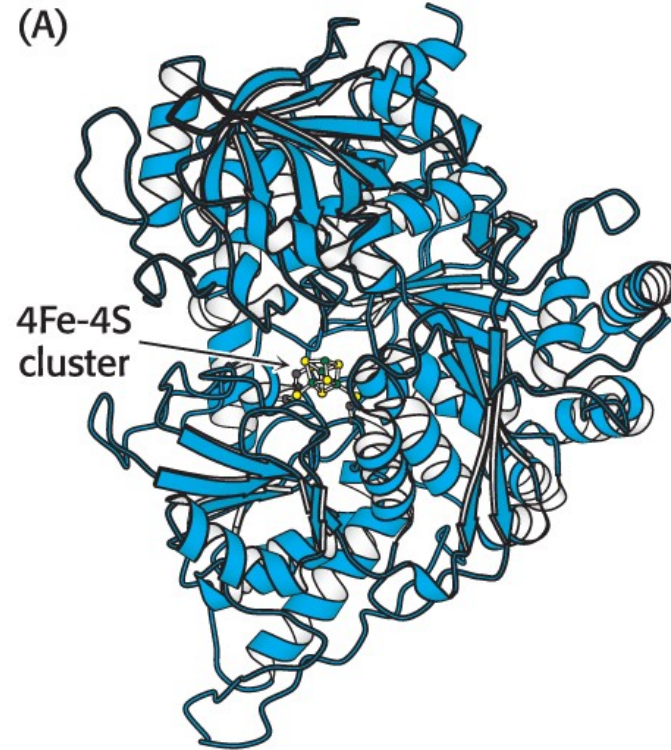
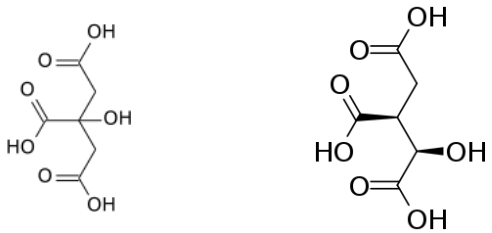
aconitase



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

Ο σίδηρος είναι βασικό συστατικό πολλών σημαντικών πρωτεϊνών, όπως η αιμοσφαιρίνη και τα κυτοχρώματα.

Ωστόσο, ο σίδηρος είναι επίσης ικανός να παράγει καταστροφικά δραστικά είδη οξυγόνου, επομένως η μεταφορά και η αποθήκευση του σιδήρου πρέπει να ρυθμίζονται προσεκτικά.

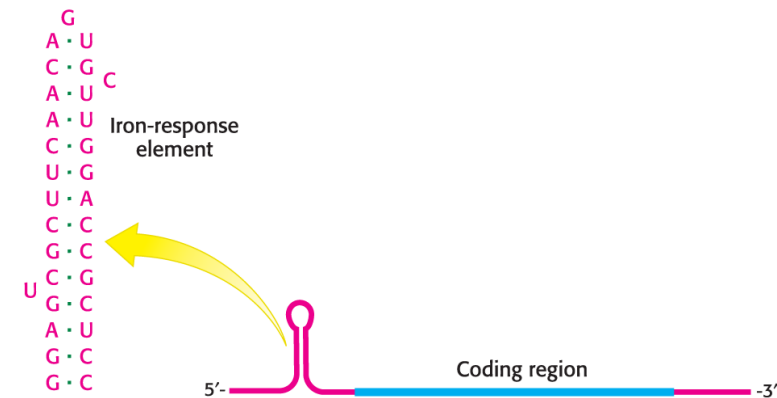
Σημαντικές πρωτεΐνες στο μεταβολισμό του σιδήρου είναι η τρανσφερίνη, μια πρωτεΐνη του αίματος που μεταφέρει σίδηρο, ο υποδοχέας τρανσφερίνης, μια μεμβρανική πρωτεΐνη που συνδέεται με την πλούσια σε σίδηρο τρανσφερίνη και διευκολύνει την είσοδό της στο κύτταρο, και η φερριτίνη, μια πρωτεΐνη αποθήκευσης σιδήρου στο κύτταρο

Το mRNA της φερριτίνης περιέχει μια δομή στελέχους-βρόχου στην 5' μη μεταφρασμένη περιοχή του, που ονομάζεται στοιχείο απόκρισης στο σίδηρο (IRE).

Σε περίπτωση απουσίας σιδήρου, η πρωτεΐνη IRE-binding protein (IRP) συνδέεται με το IRE και εμποδίζει τη μετάφραση.

Όταν υπάρχει σίδηρος, συνδέεται με την IRP, προκαλώντας τη διάσπασή της από το IRE και επιτρέποντας έτσι τη μετάφραση.

Ferritin mRNA



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Genes Associated with Iron Metabolism Are Translationally Regulated in Animals

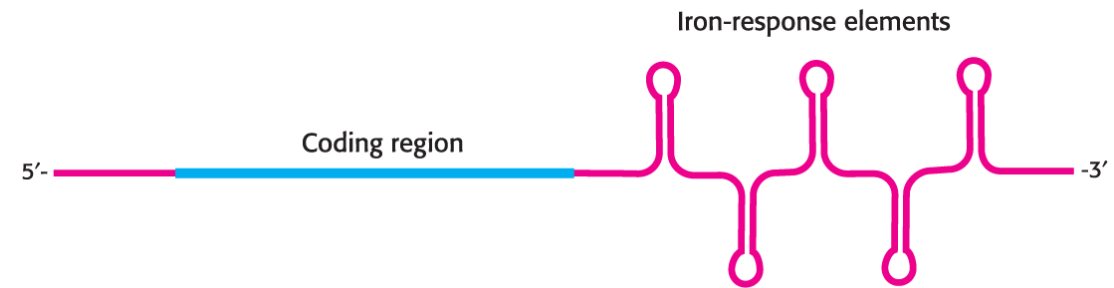
Το mRNA του υποδοχέα τρανσφερίνης έχει επίσης αρκετές IRE, που βρίσκονται στην 3' μη μεταφρασμένη περιοχή.

Όταν υπάρχει λίγος σίδηρος, το IRP συνδέεται με το IRE, επιτρέποντας τη μετάφραση του mRNA.

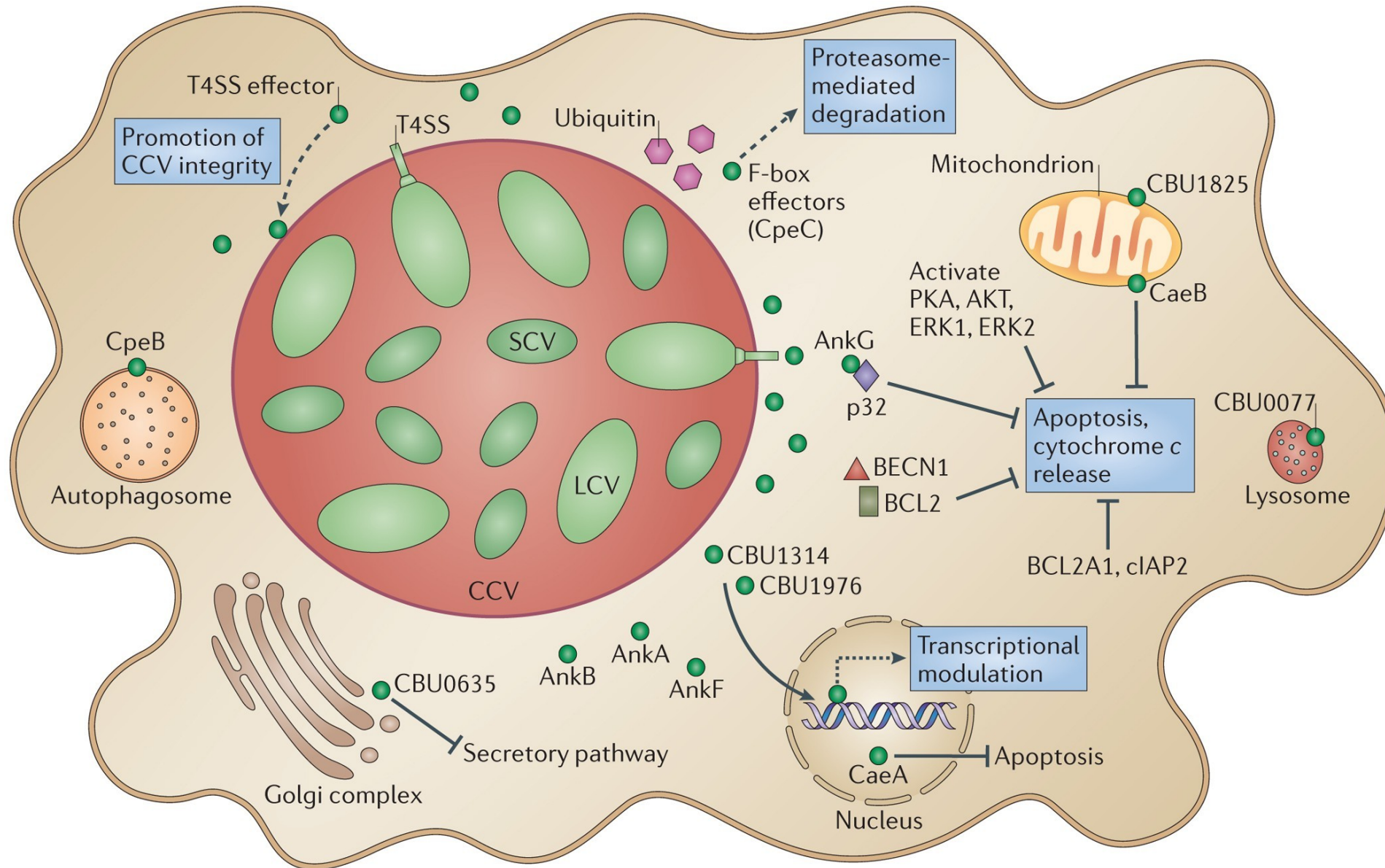
Όταν υπάρχει σίδηρος, αυτός συνδέεται με το IRP, προκαλώντας τη διάσπασή του από το mRNA του υποδοχέα τρανσφερίνης. Χωρίς το IRP, το mRNA του υποδοχέα αποικοδομείται.

Το IRP είναι μια ενεργή ακονιτάση που απαιτεί σίδηρο και υφίσταται διαμορφωτική αλλαγή όταν δεν συνδέεται με σίδηρο. Επομένως, μπορεί να λειτουργήσει ως αισθητήρας σιδήρου.

Transferrin-receptor mRNA



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Proteins began in an RNA world

