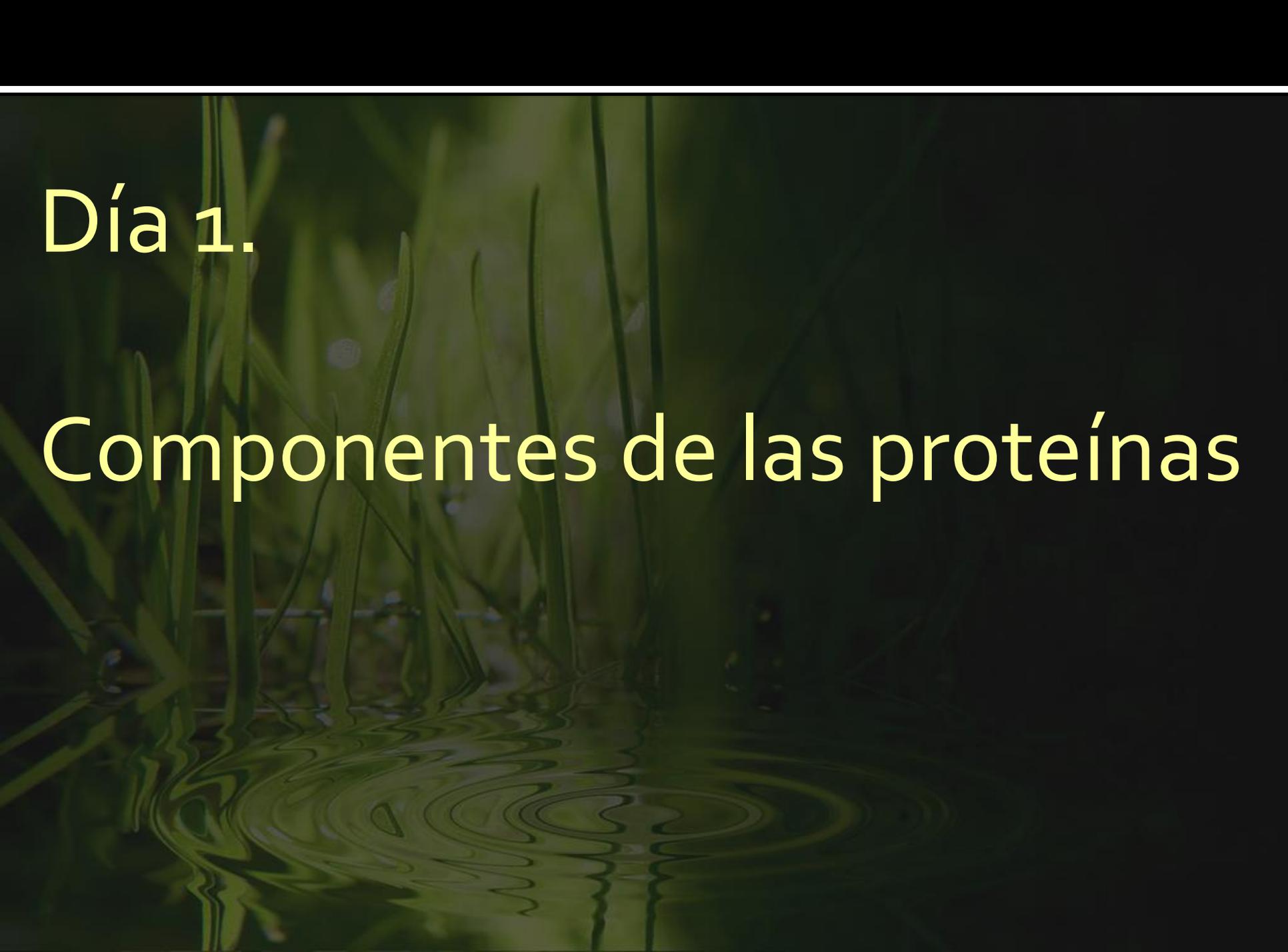


La Semana de la Ciencia en Chiapas 2012

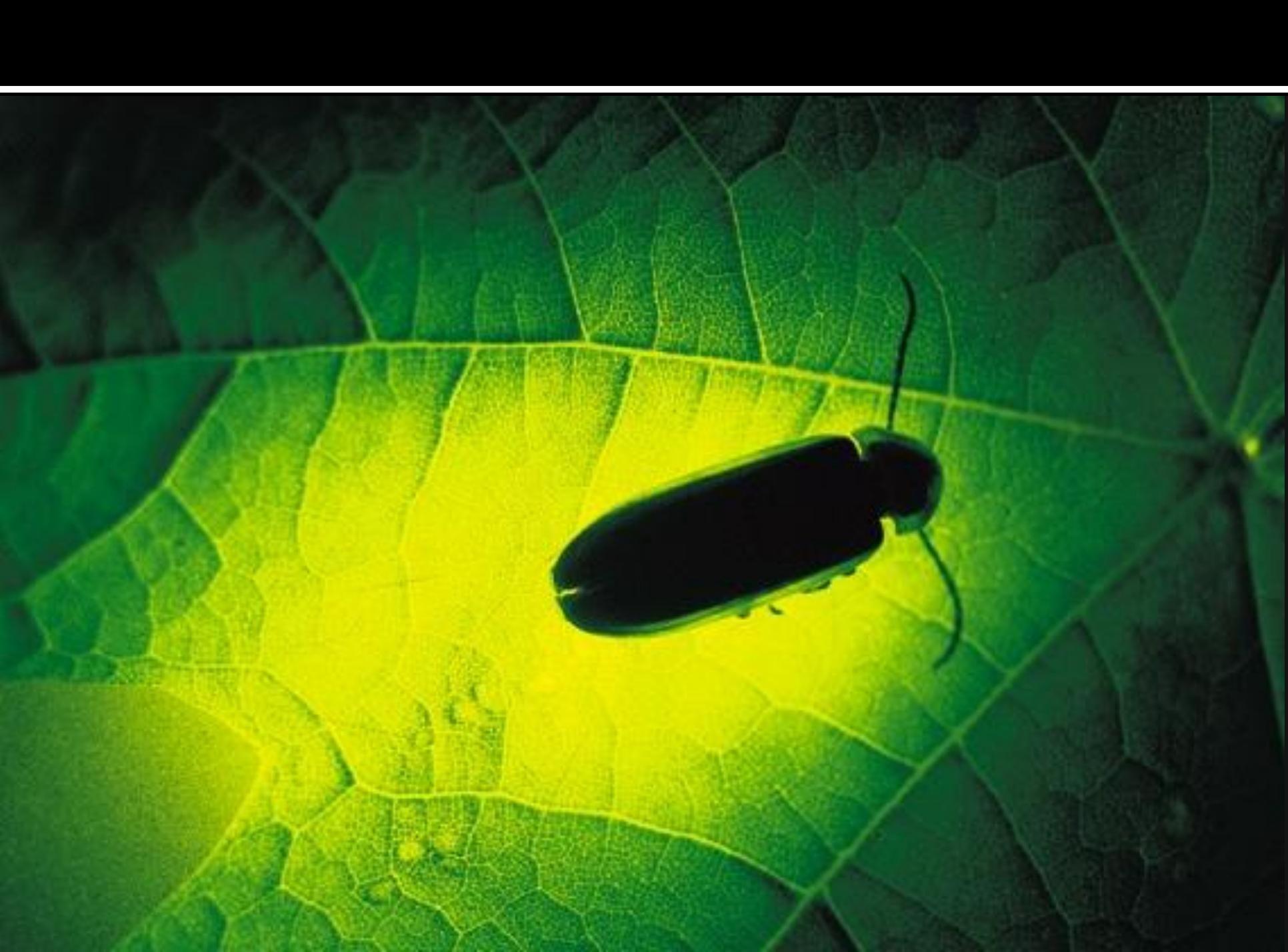
Curso de Biología Proteómica

Yuri Peña

The background of the slide features a close-up photograph of green grass blades. The grass is reflected in a body of water, creating a symmetrical, rippling effect. The overall color palette is dominated by various shades of green, from light lime to dark forest green, set against a dark, almost black background.

Día 1.

Componentes de las proteínas

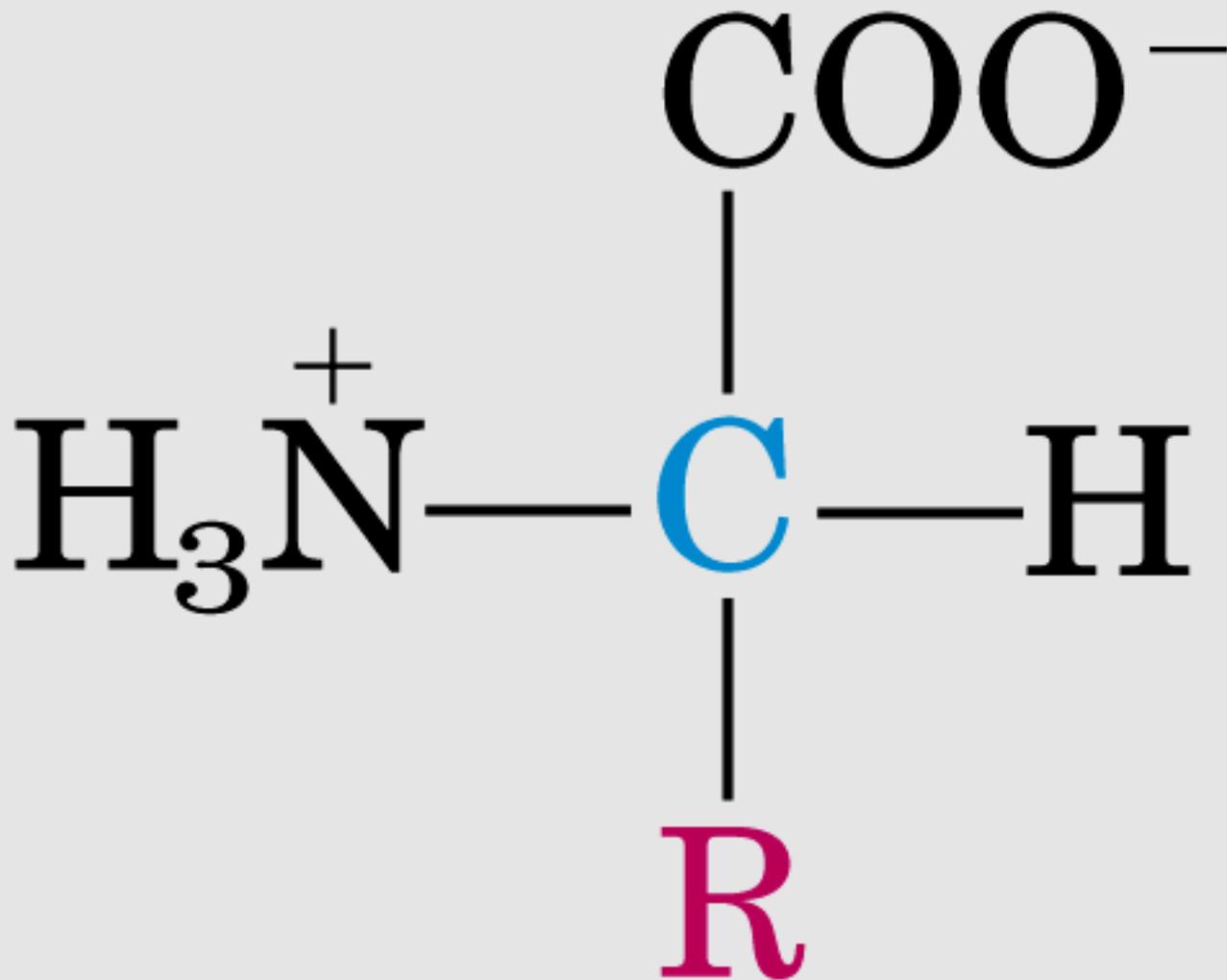


proteína.

(Del fr. *protéine*, y este del gr. πρωτεῖος, preeminente, de primera calidad, e *-ine*, *-ina*).

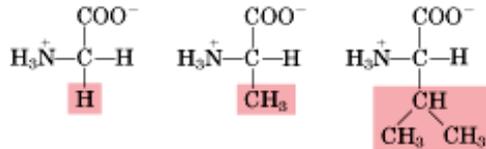
1. f. Sustancia constitutiva de la materia viva, formada por una o varias cadenas de aminoácidos

Aminoácidos



La caja bioquímica de herramientas

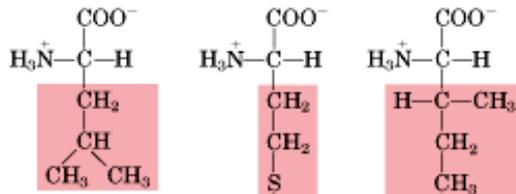
Nonpolar, aliphatic R groups



Glycine

Alanine

Valine

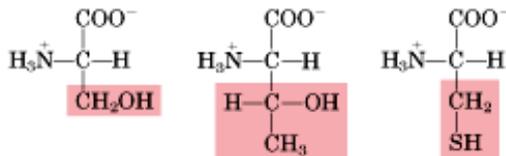


Leucine

Methionine

Isoleucine

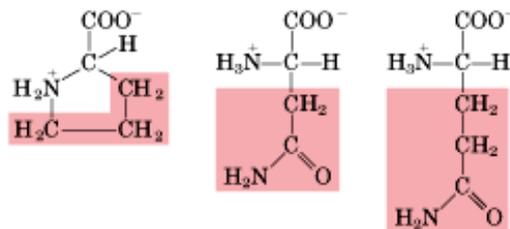
Polar, uncharged R groups



Serine

Threonine

Cysteine

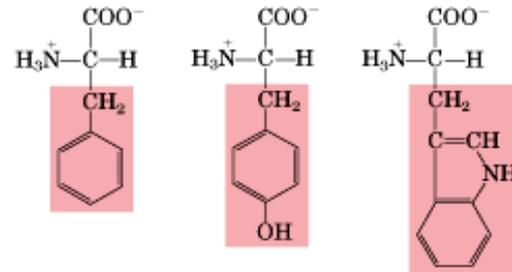


Proline

Asparagine

Glutamine

Aromatic R groups

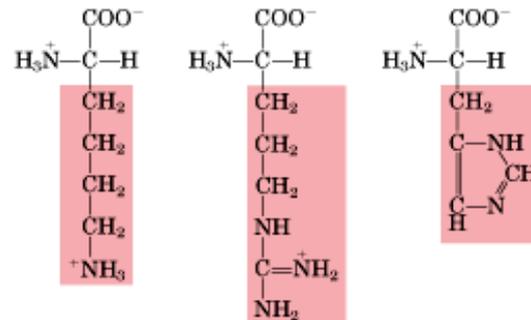


Phenylalanine

Tyrosine

Tryptophan

Positively charged R groups

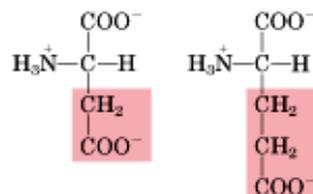


Lysine

Arginine

Histidine

Negatively charged R groups



Aspartate

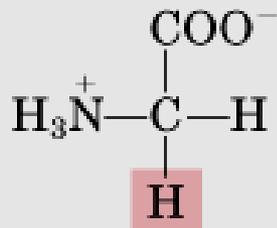
Glutamate

20 herramientas distintas

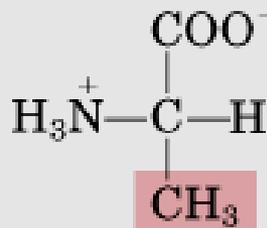


Aminoácidos alifáticos no polares

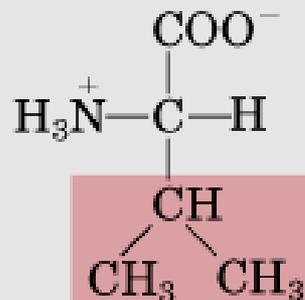
Nonpolar, aliphatic R groups



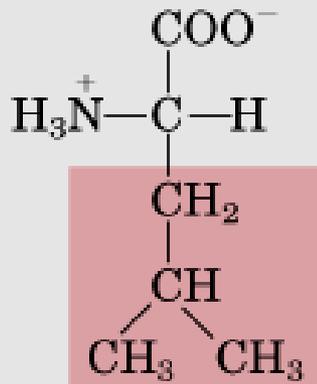
Glycine



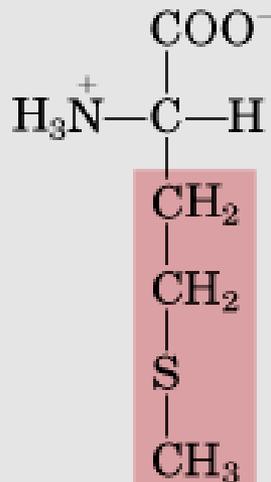
Alanine



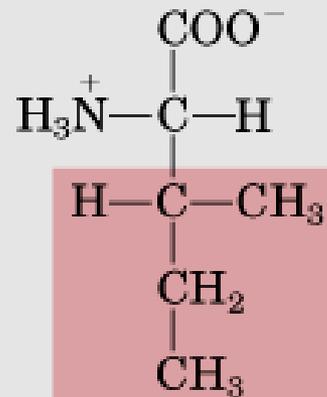
Valine



Leucine



Methionine



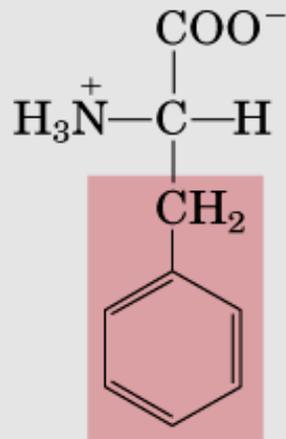
Isoleucine



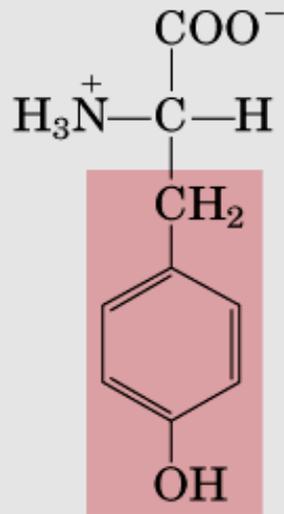
© School Division, Houghton Mifflin Company

Aminoácidos aromáticos

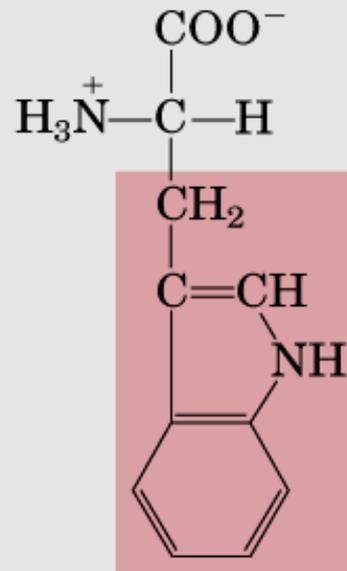
Aromatic R groups



Phenylalanine



Tyrosine

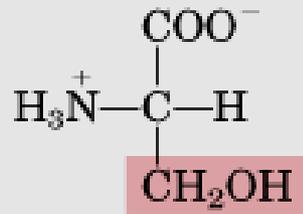


Tryptophan

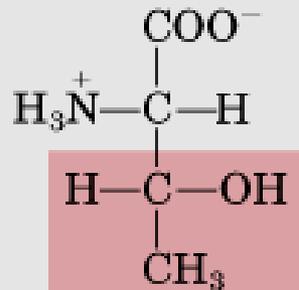


Aminoácidos polares sin carga

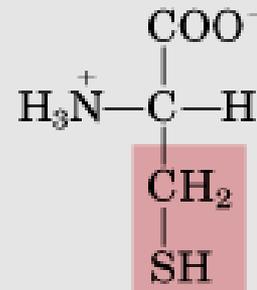
Polar, uncharged R groups



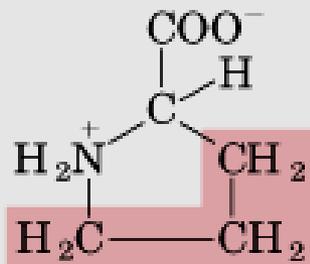
Serine



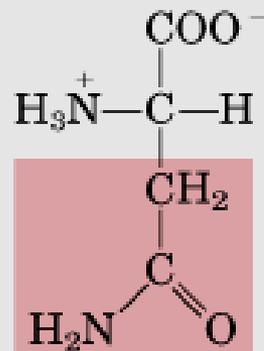
Threonine



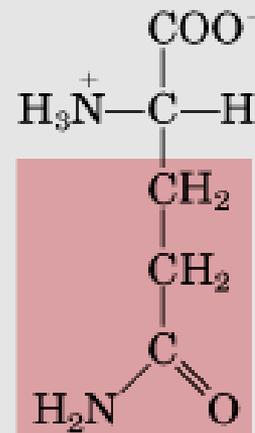
Cysteine



Proline



Asparagine

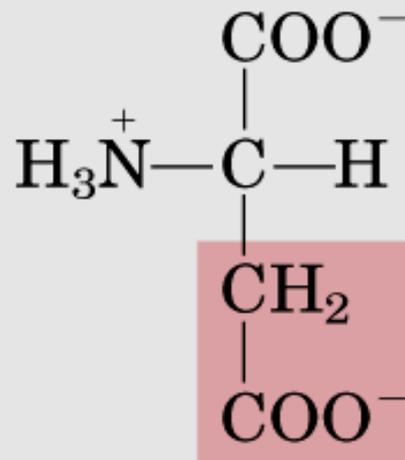


Glutamine

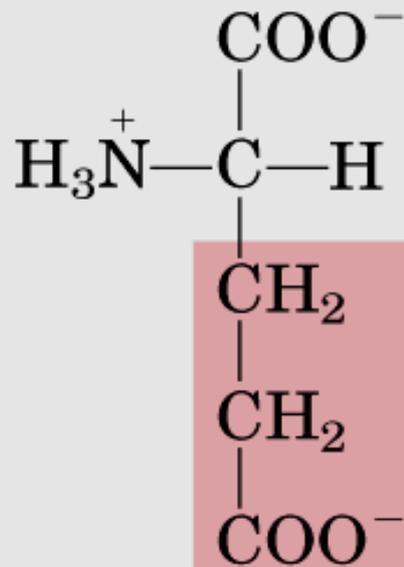


Aminoácidos con carga negativa

Negatively charged R groups



Aspartate



Glutamate



La estructura y las propiedades permiten la función:

1



2



3



4



5



() Apretar / aflojar tuercas

() Apretar / aflojar tornillos

() Perforar

() Recoger material

() Golpear, romper

La estructura y las propiedades permiten la función:

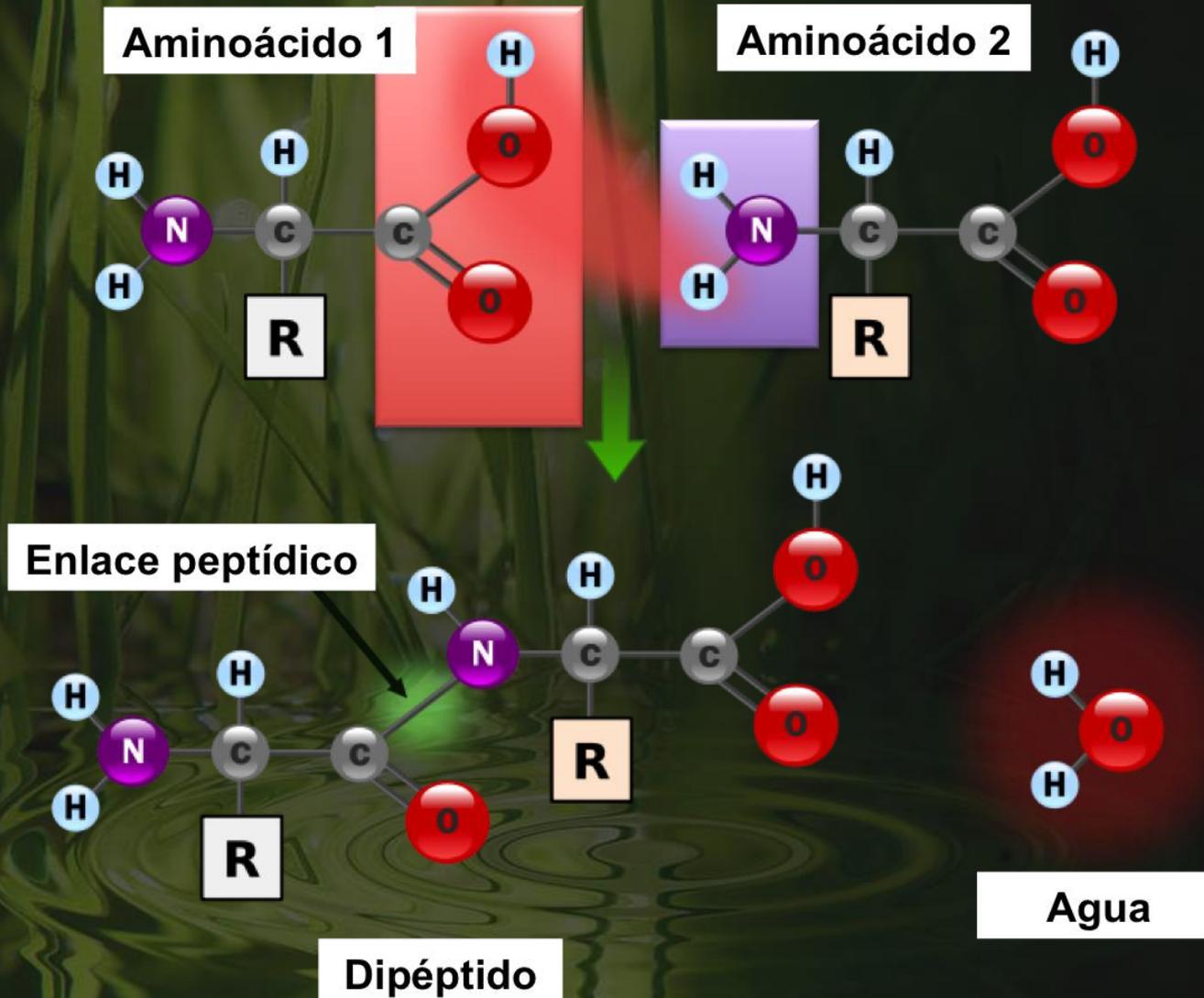
1. Aminoácidos no polares alifáticos Trabajan con moléculas negativas
2. Aminoácidos aromáticos Trabajan con moléculas que aceptan o ceden electrones
3. Aminoácidos polares no cargados Trabajan con moléculas positivas
4. Aminoácidos cargados positivamente Trabajan con moléculas hidrofóbicas
5. Aminoácidos cargados negativamente Trabajan con moléculas hidrofílicas

Un cinturón de herramientas:



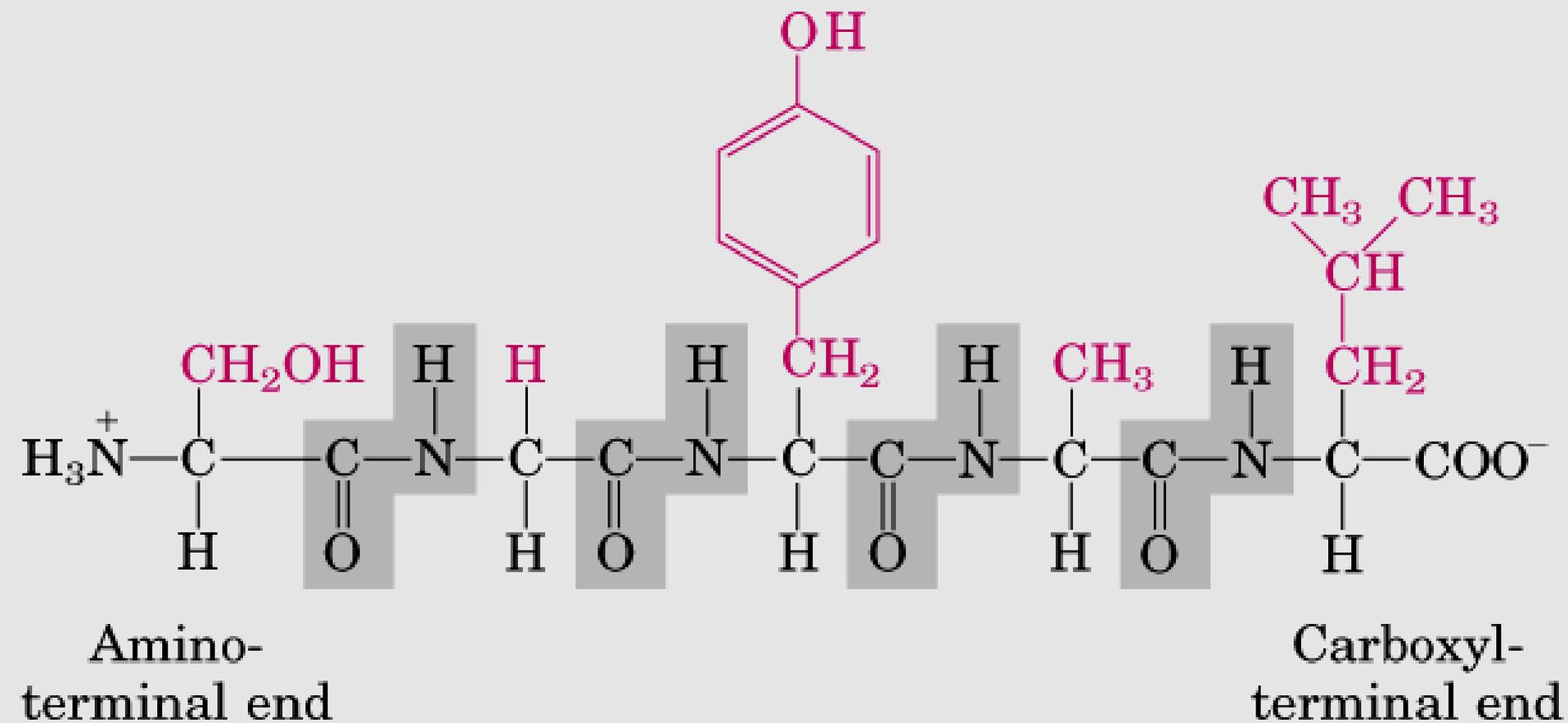
Un cinturón de herramientas bioquímicas

El enlace peptídico



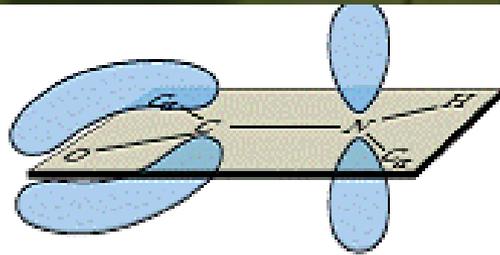
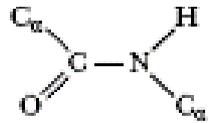
Un cinturón de herramientas bioquímicas

Las proteínas!!!



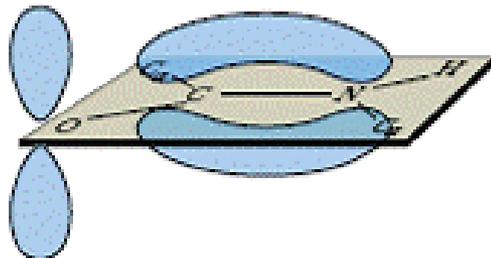
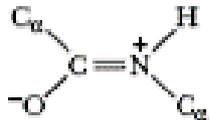
Naturaleza del enlace peptídico. Un enlace rígido.

(a)

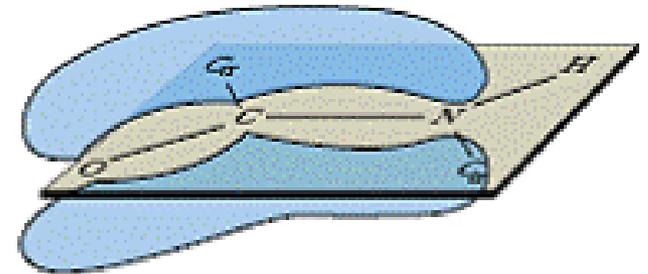


A pure double bond between C and O would permit free rotation around the C—N bond.

(b)

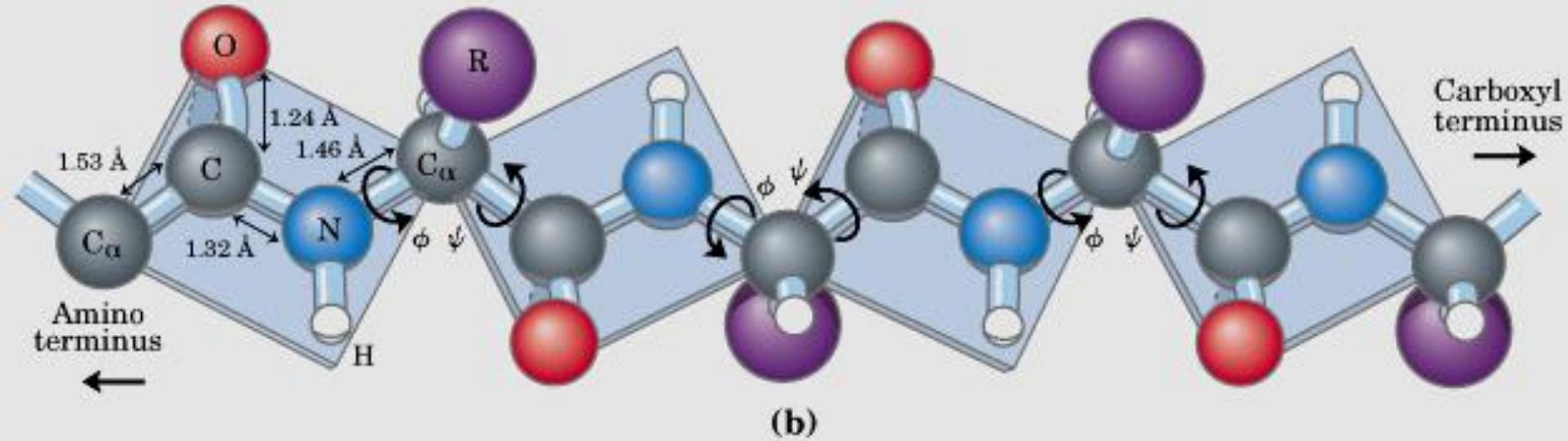


The other extreme would prohibit C—N bond rotation but would place too great a charge on O and N.



(c) The true electron density is intermediate. The barrier to C—N bond rotation of about 88 kJ/mol is enough to keep the amide group planar.

Naturaleza del enlace peptídico. Un enlace rígido.



Péptidos y proteínas

La representación de los péptidos y proteínas puede hacerse mediante la escritura del código de cada aminoácido de acuerdo a la secuencia de ellos en la cadena.

Ejemplo:

Un tripéptido de Glicina: GGG

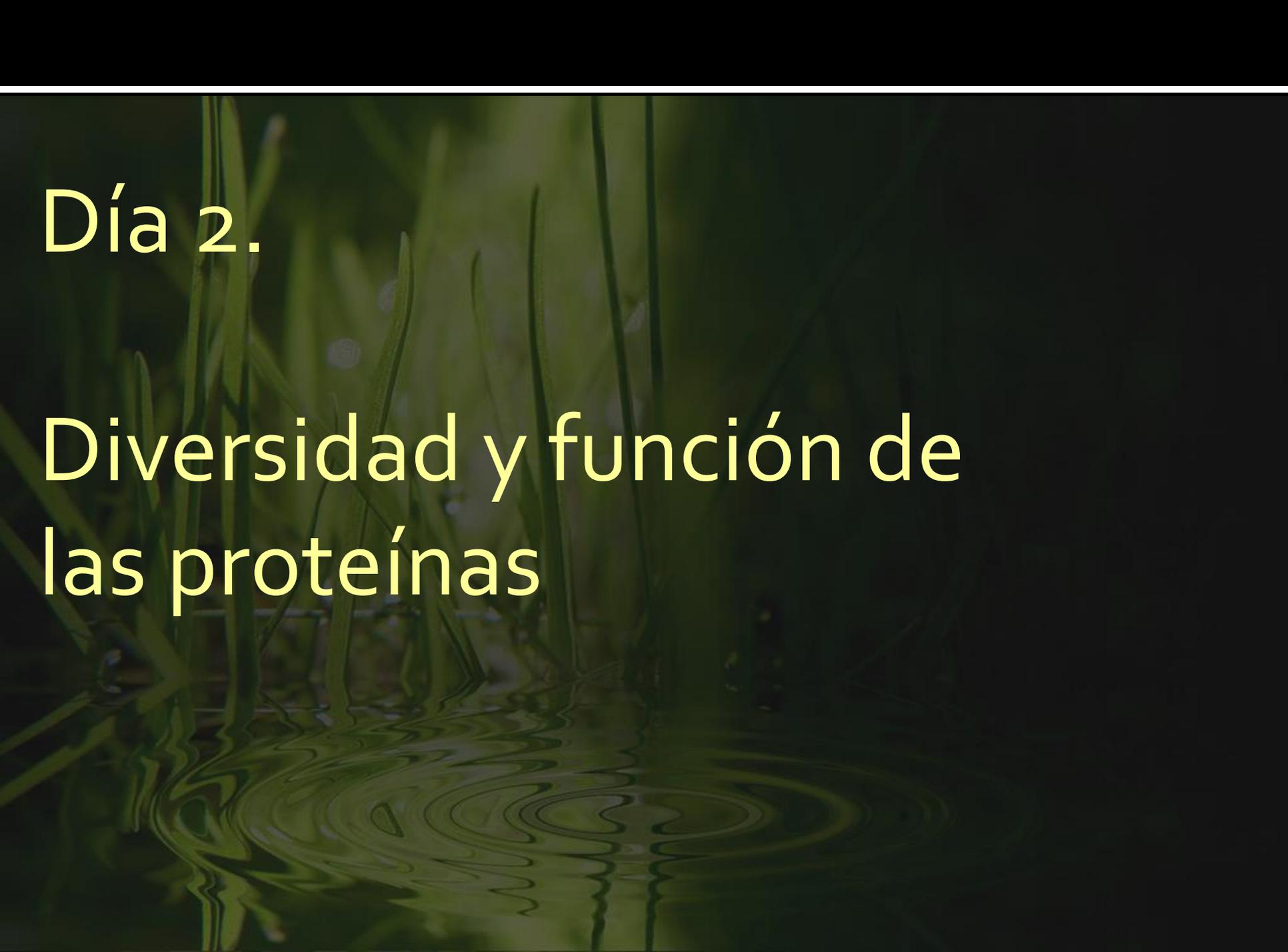
Un decapeptido de Alanina y Prolina: APAPAPAPAP

Números astronómicos!

El universo conocido se estima que tiene 10^{80} núcleos de protones ó 10^{80} Daltones



Si multiplicamos la masa de una proteína promedio de 100 aminoácidos ($\approx 13,800$ Daltones) por las distintas probabilidades, obtenemos 1.75^{134} Daltones. Necesitaríamos 10^{54} universos para tener la materia necesaria para construir cada combinación única.

The background of the slide features a close-up photograph of green grass blades. The lower portion of the image is dominated by a series of concentric, wavy ripples in a dark green liquid, likely water, which creates a textured, shimmering effect. The overall color palette is various shades of green, from light to dark, with a white horizontal line at the top edge.

Día 2.

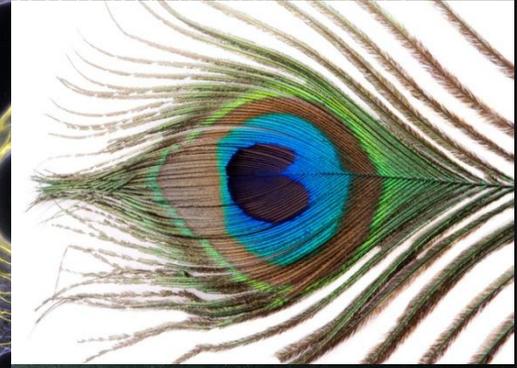
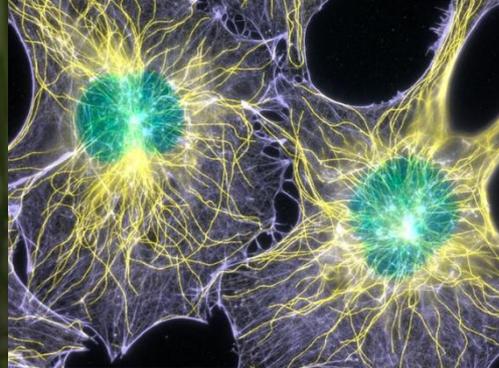
Diversidad y función de las proteínas

Diversidad en tamaño de las proteínas

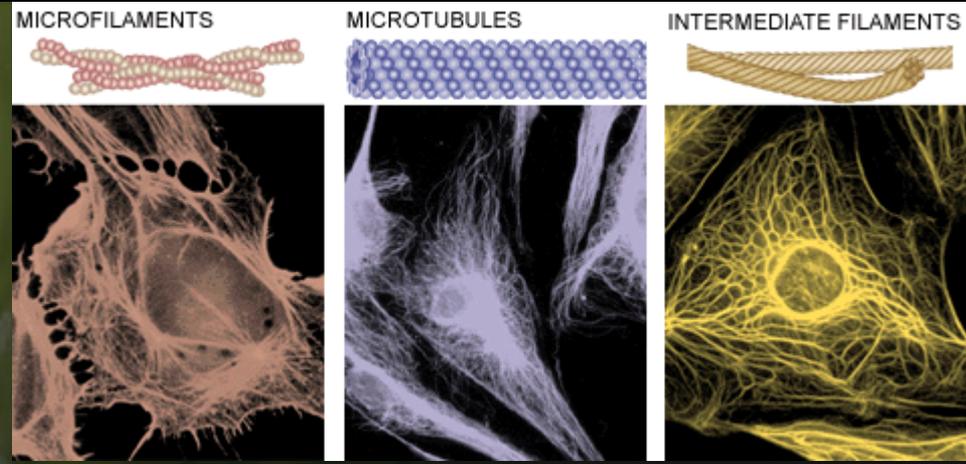
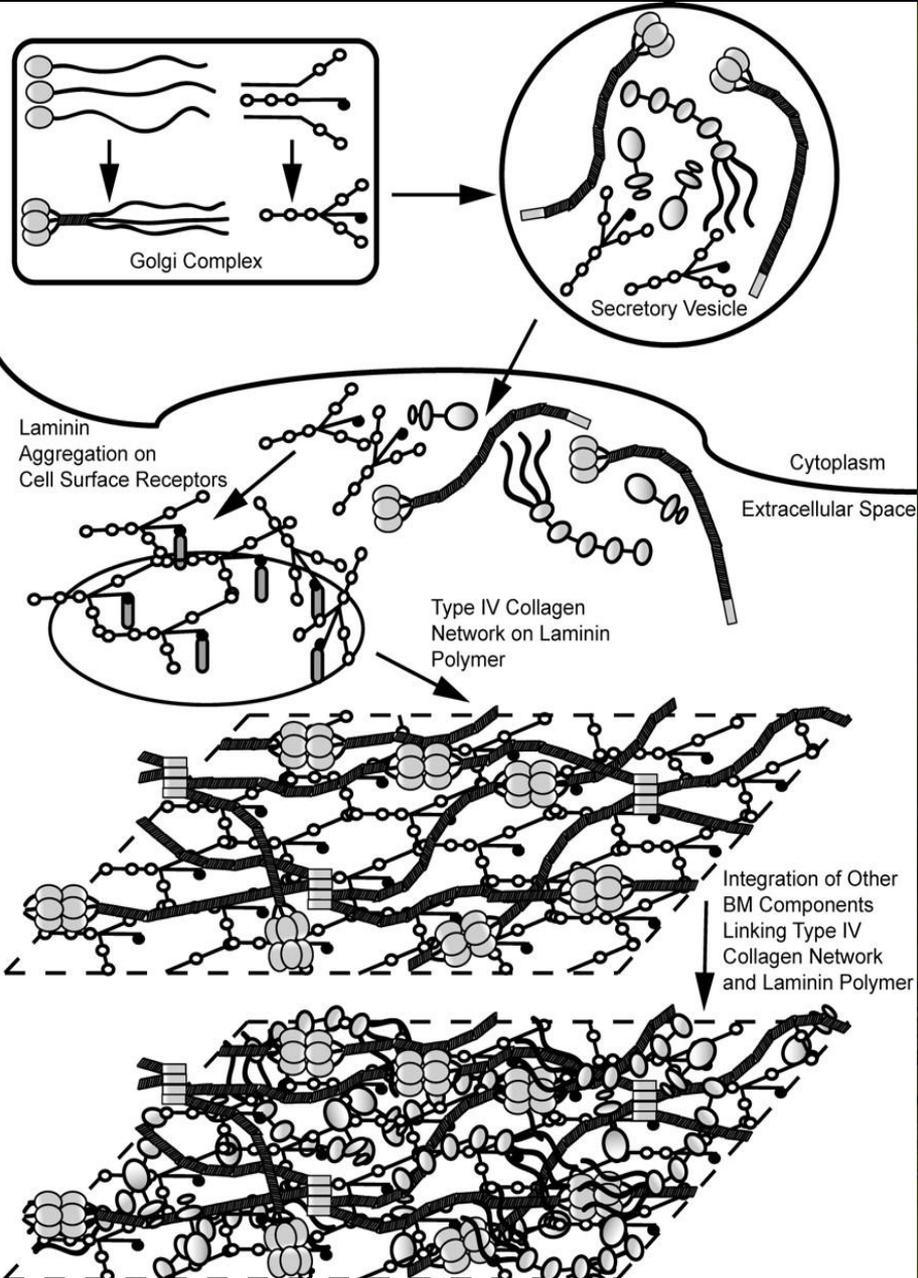
Proteína	Número de Aminoácidos	Peso Molecular (Da)
Insulina	47	5733
Citocromo	103	12500
Ribonucleasa A	104	12640
Lisosima	115	13930
Mioglobina	140	16980
Quimiotripsina	187	22600
Hemoglobina	533	64500
Albúmina sérica	566	68500
Hexocinasa	790	96000
Gamma globulina	1239	149900
Glutamato deshidrogenasa	2750	332694
Miosina	3884	470000
Ribulosa bifosfato carboxilasa	4628	560000
Glutamino sintetasa	4959	600000
Taitina	31539	3,816,188

Diversidad en función de las proteínas

1) Proteínas de estructura



1) Proteínas de estructura



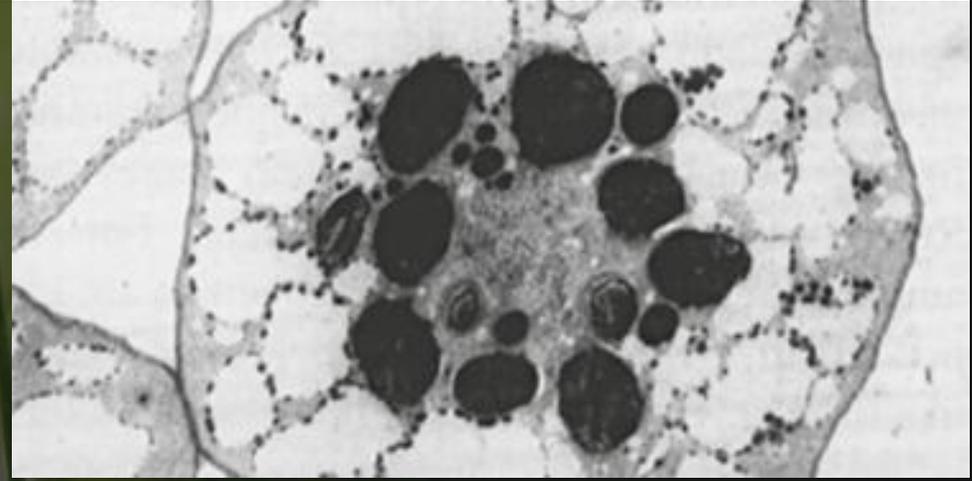
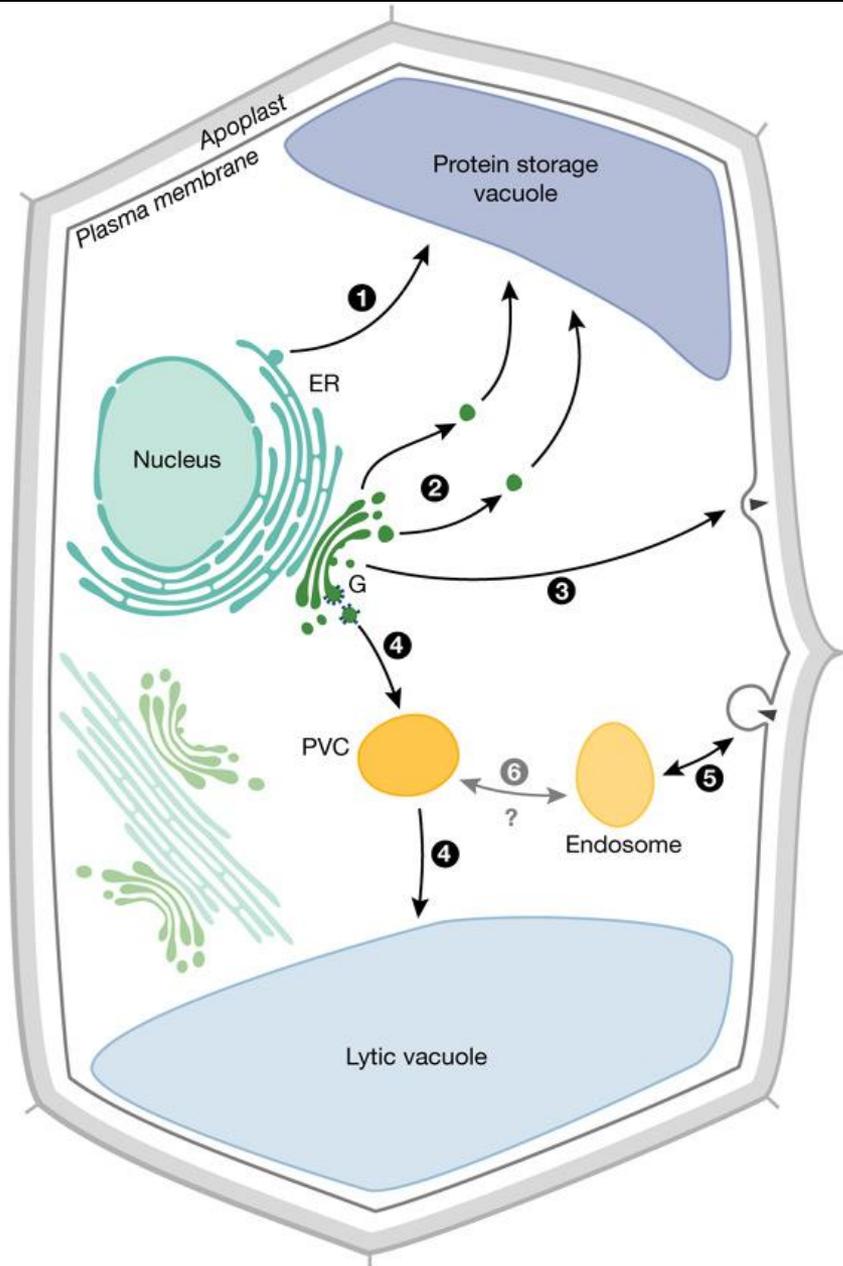
Colágeno
Elastina
Dentina
Queratina
Fibroina

Diversidad en función de las proteínas

2) Proteínas de almacén



2) Proteínas de almacén



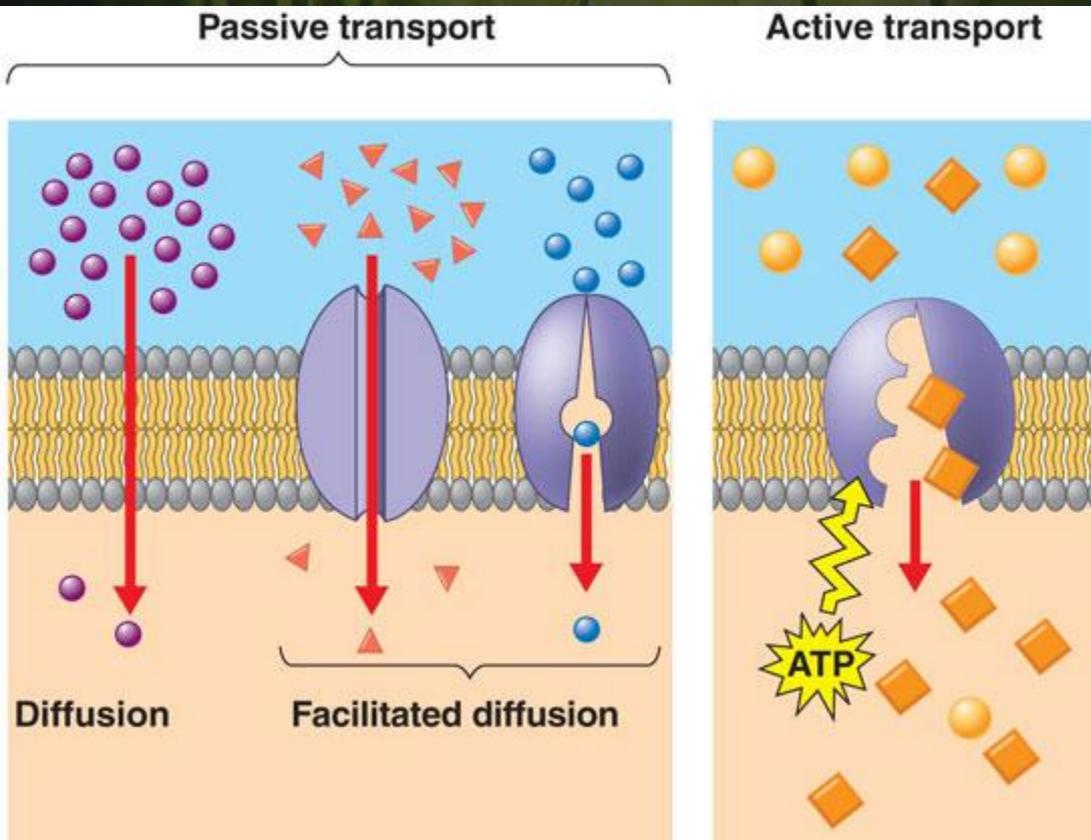
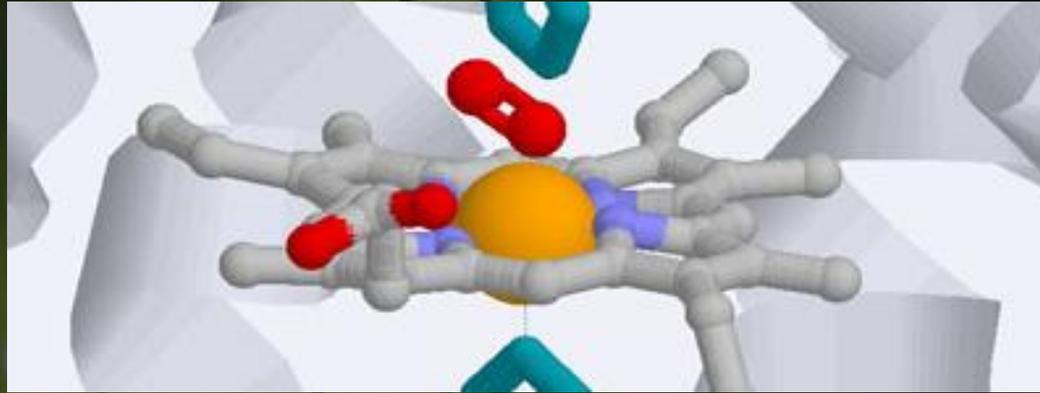
Albúmina
Gluteina
Miosina
Ferritina
Caseina

Diversidad en función de las proteínas

3) Proteínas de transporte



2) Proteínas de transporte



Hemoglobina
Canales
iónicos
Porinas
Ferritina

Diversidad en función de las proteínas

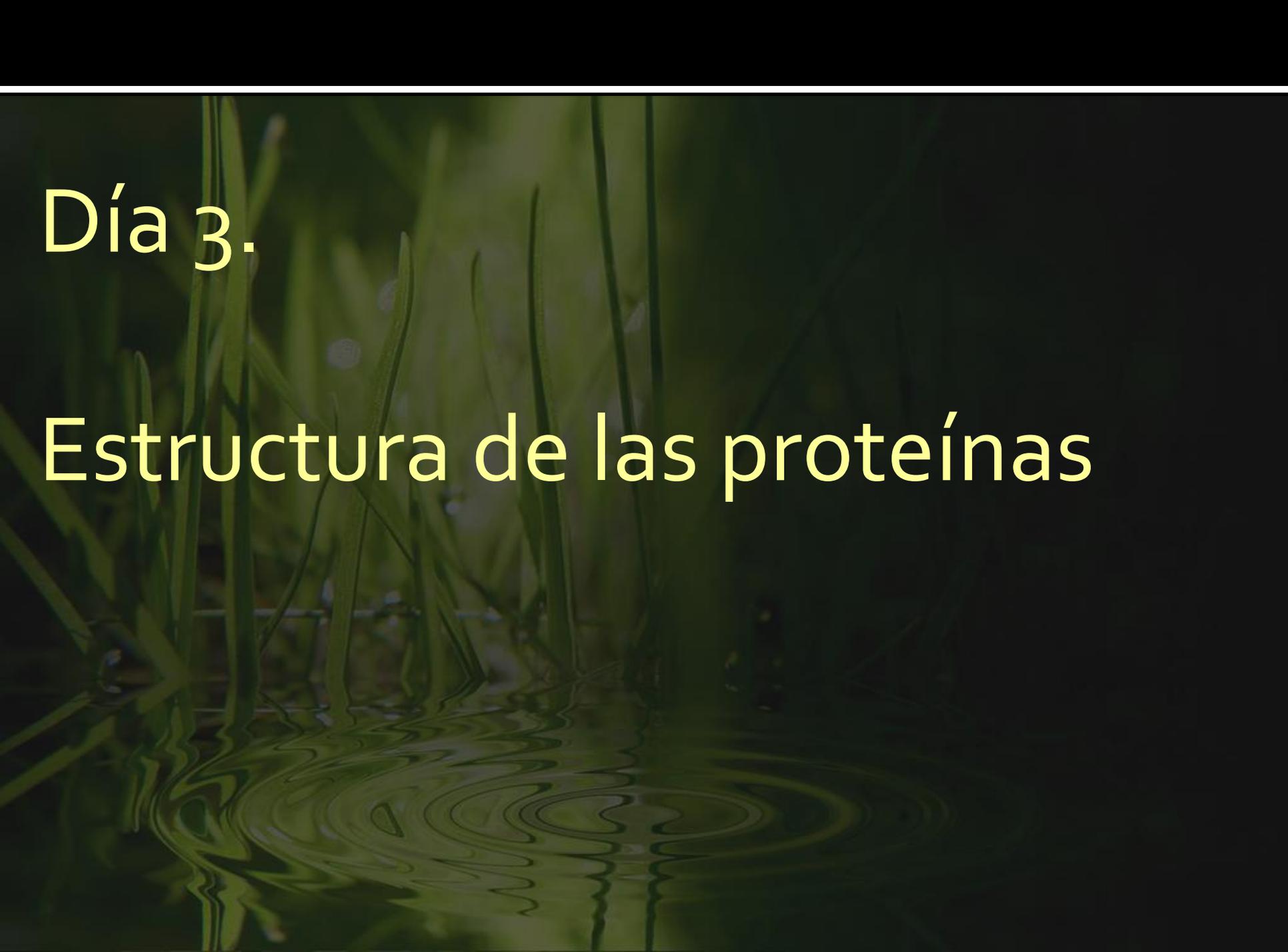
4) Proteínas de defensa



2) Proteínas de defensa

Cn3D

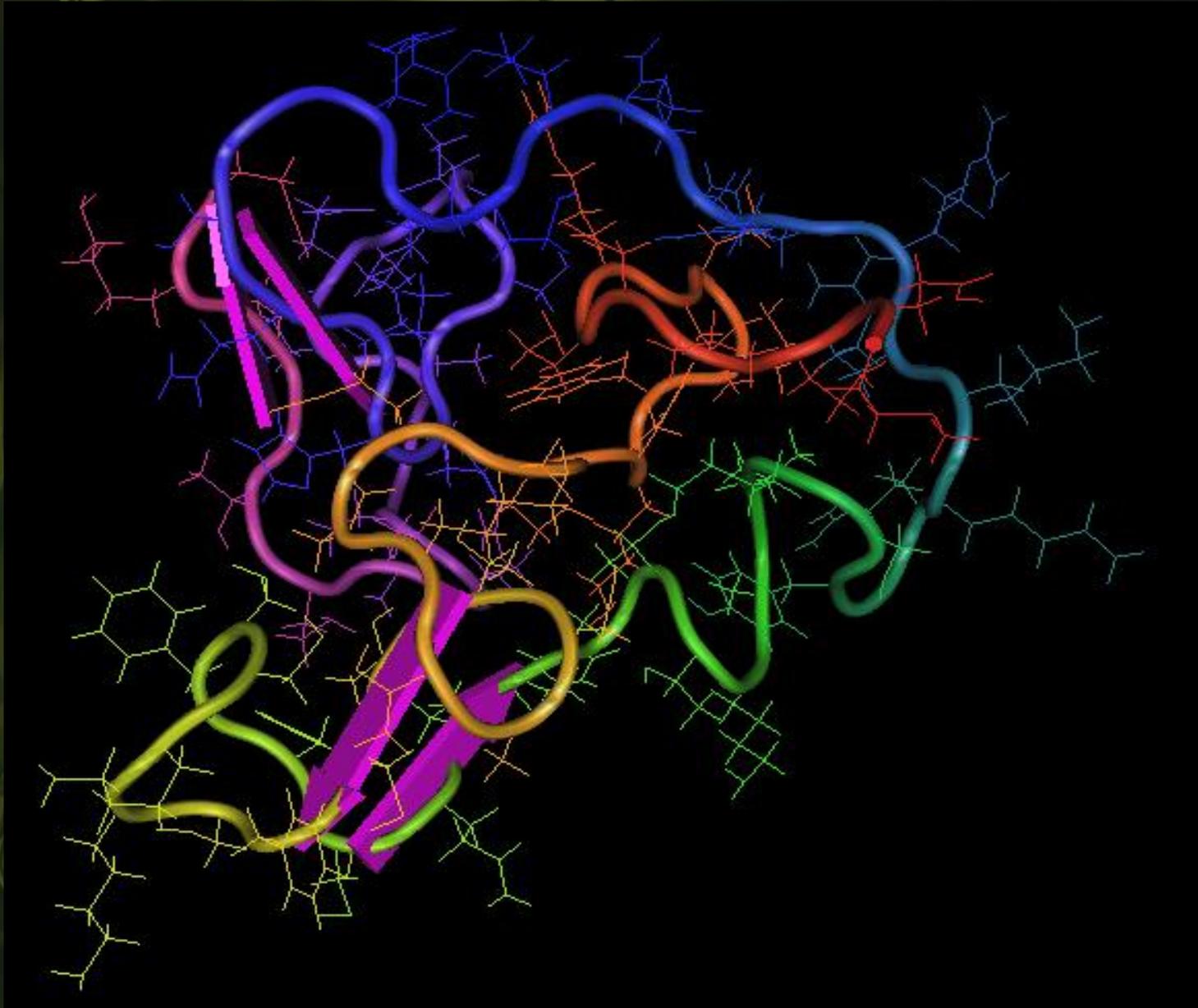
Muscina
Inmuno-
globulinas
Defensinas

The background of the slide features a close-up photograph of green grass blades. The lower portion of the image is dominated by a series of concentric, wavy ripples in a body of water, which reflect the green color of the grass above. The overall lighting is soft and natural, creating a serene and organic atmosphere.

Día 3.

Estructura de las proteínas

Estructura tridimensional de las proteínas



Estructura tridimensional de las proteínas

La estructura tridimensional de las proteínas se estudia por complejidad.

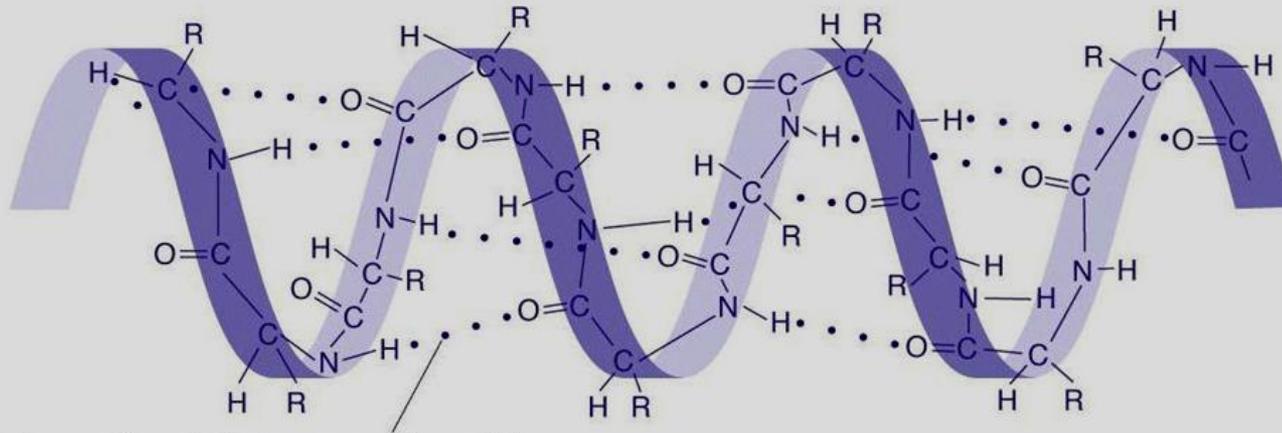
Estructura
Primaria
Secundaria
Terciaria
Cuaternaria

Descriptor
Secuencia de AAs
Plegamientos locales, Dominios
Estructura péptidos completos
Estructura polipéptidos

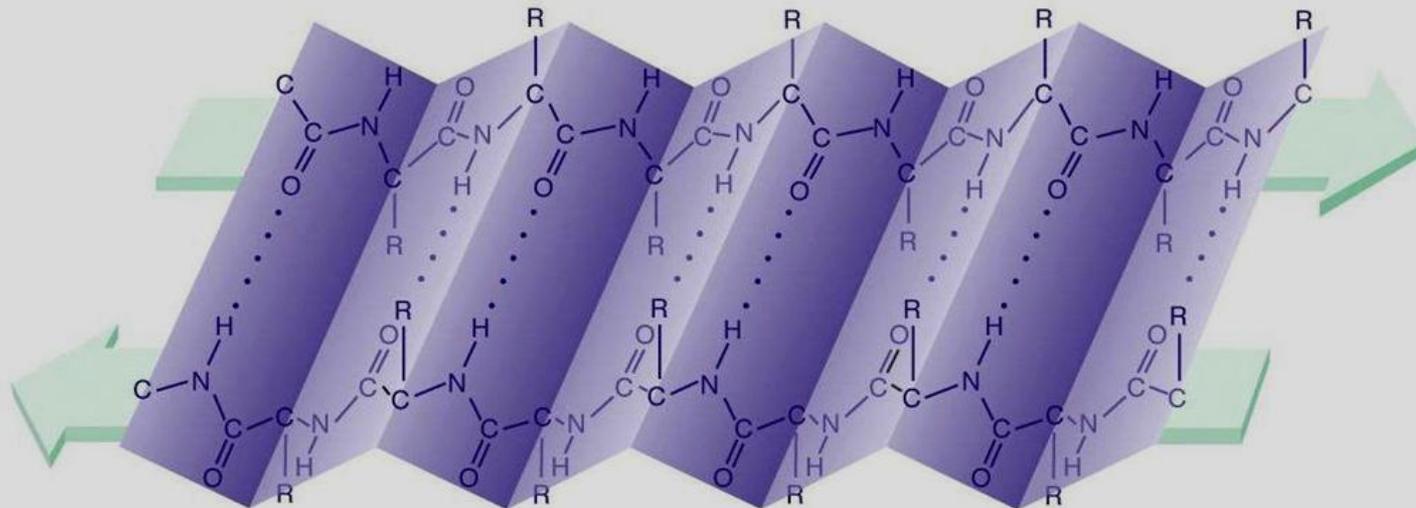
Plegamiento

¿La SECUENCIA DE LOS AMINOÁCIDOS en una proteína es determinante en su estructura tridimensional?

Estructura secundaria: Hélices α y placas β

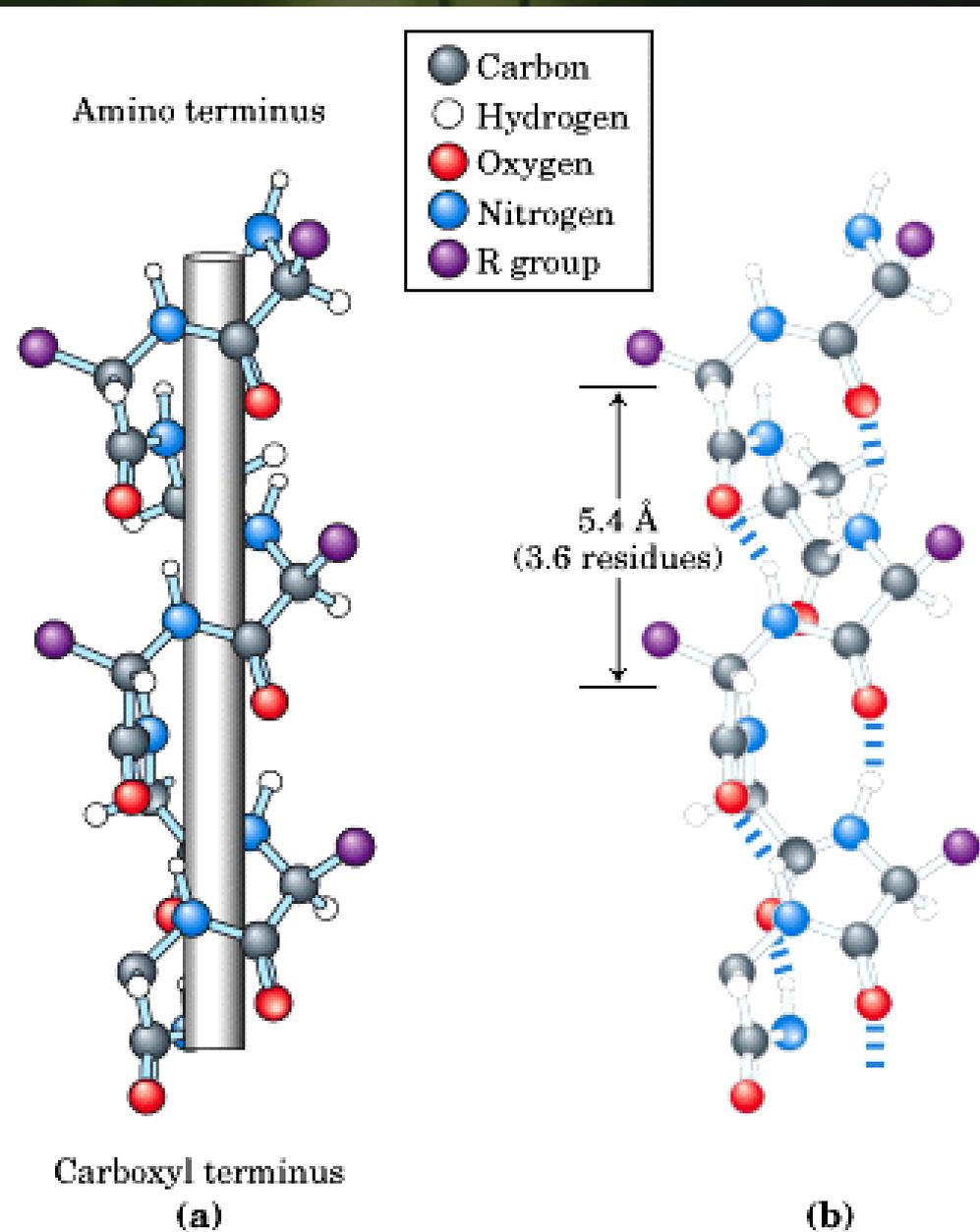


Hydrogen bonds between amino acids at different locations in polypeptide chain α helix

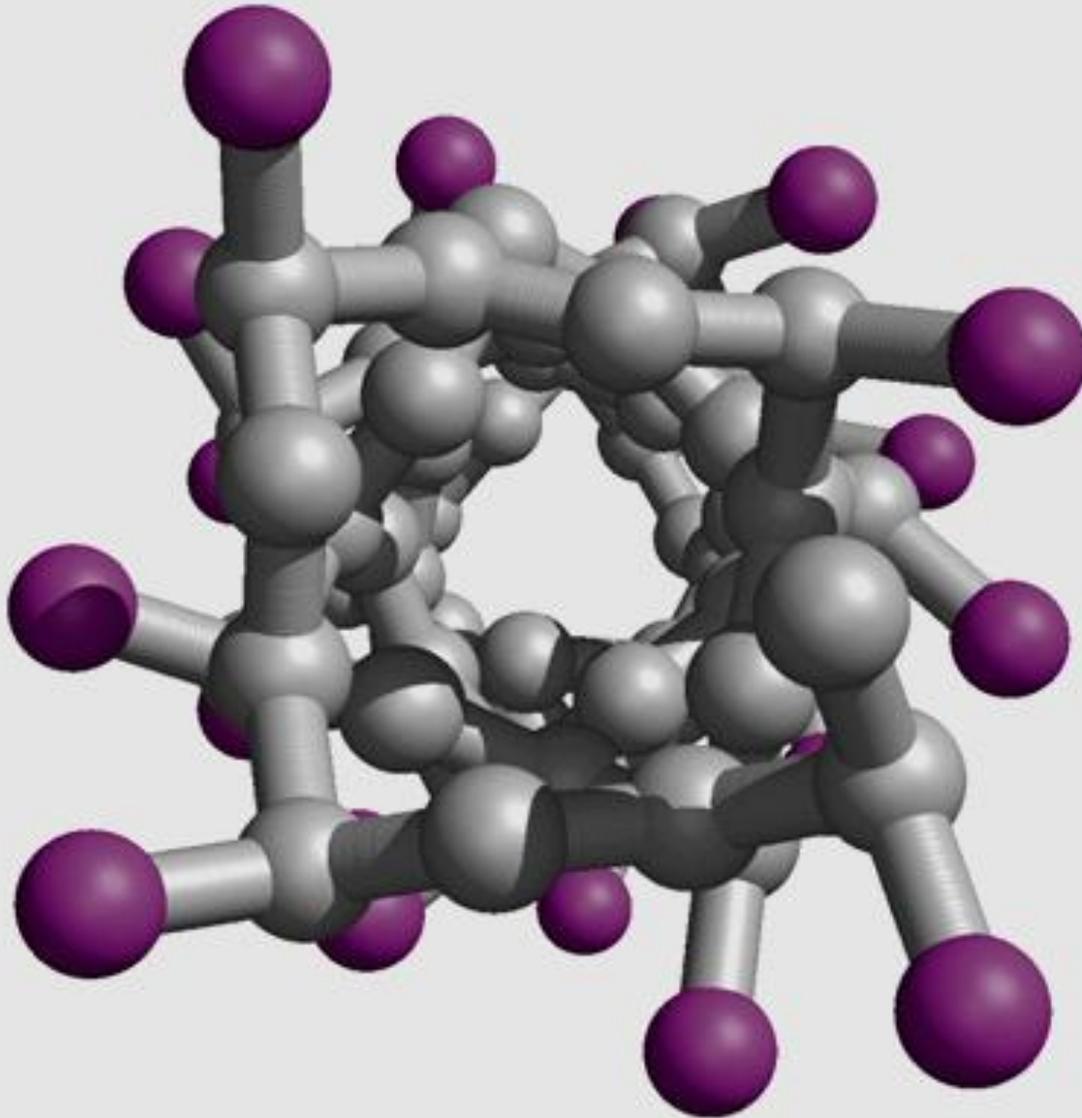


Pleated sheet

Estructura secundaria: Hélices α



Estructura secundaria: Hélices α

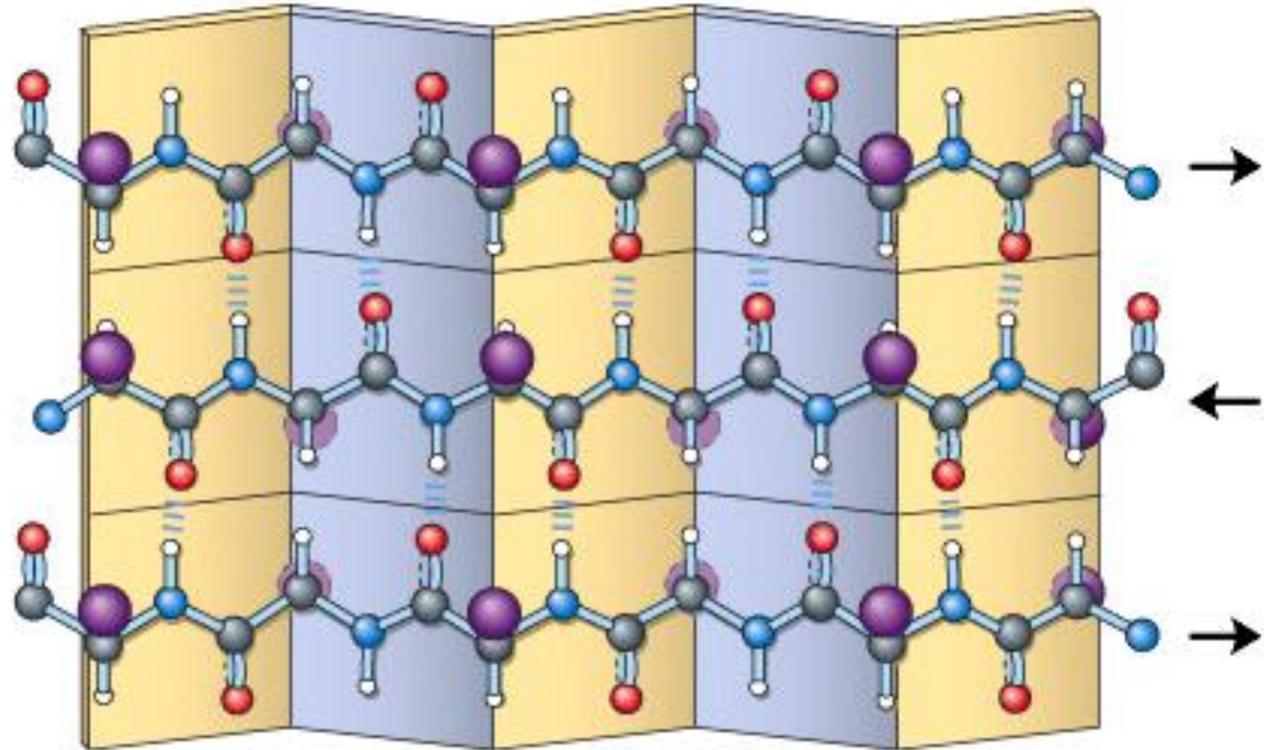


(c)

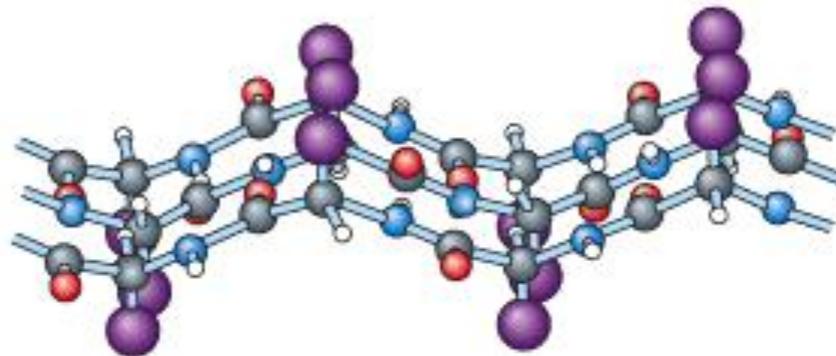
Estructura secundaria: placas β

(a) Antiparalel

Top view

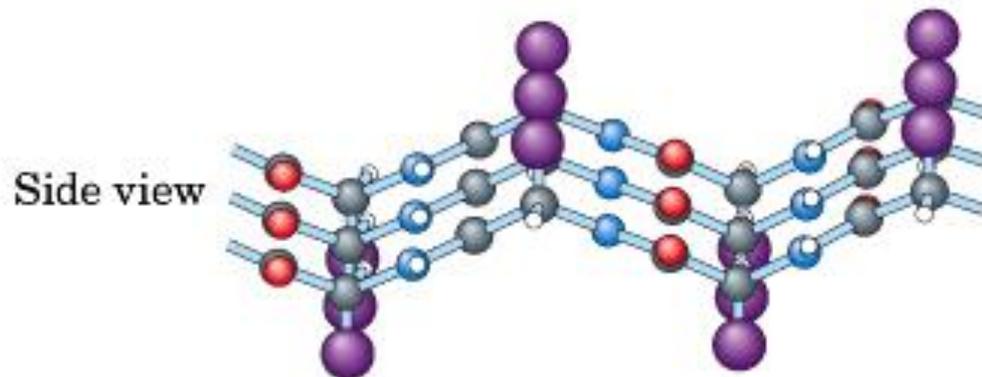
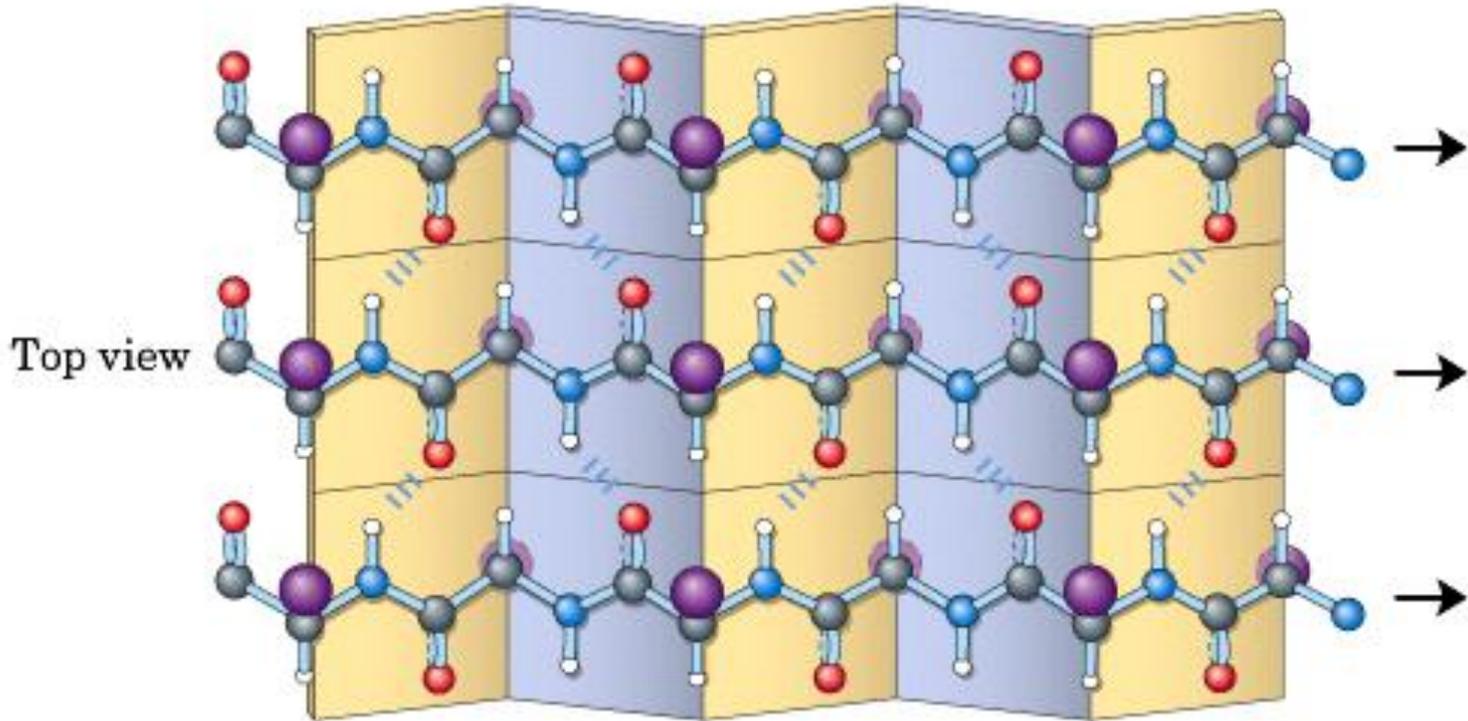


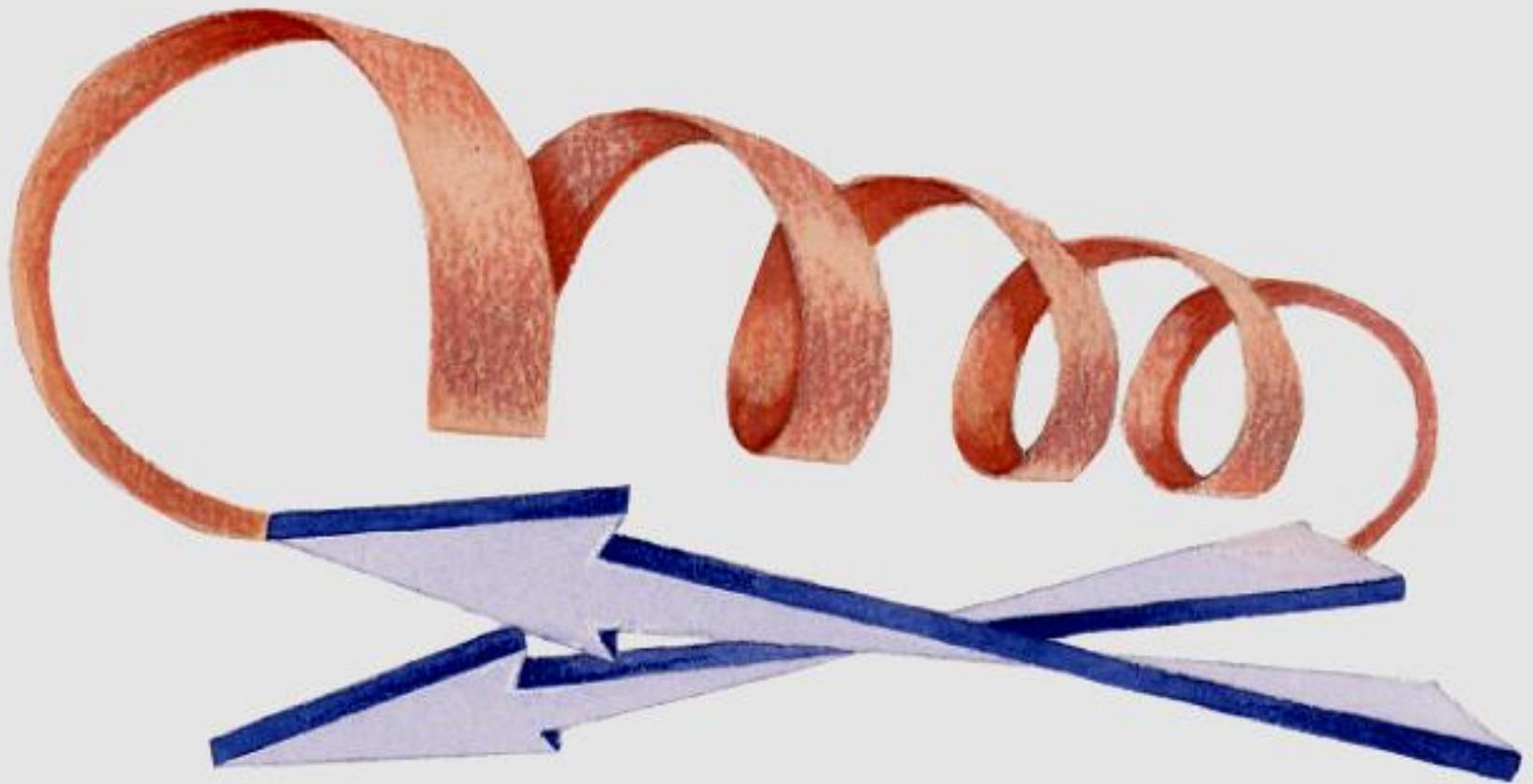
Side view



Estructura secundaria: placas β

(b) Parallel



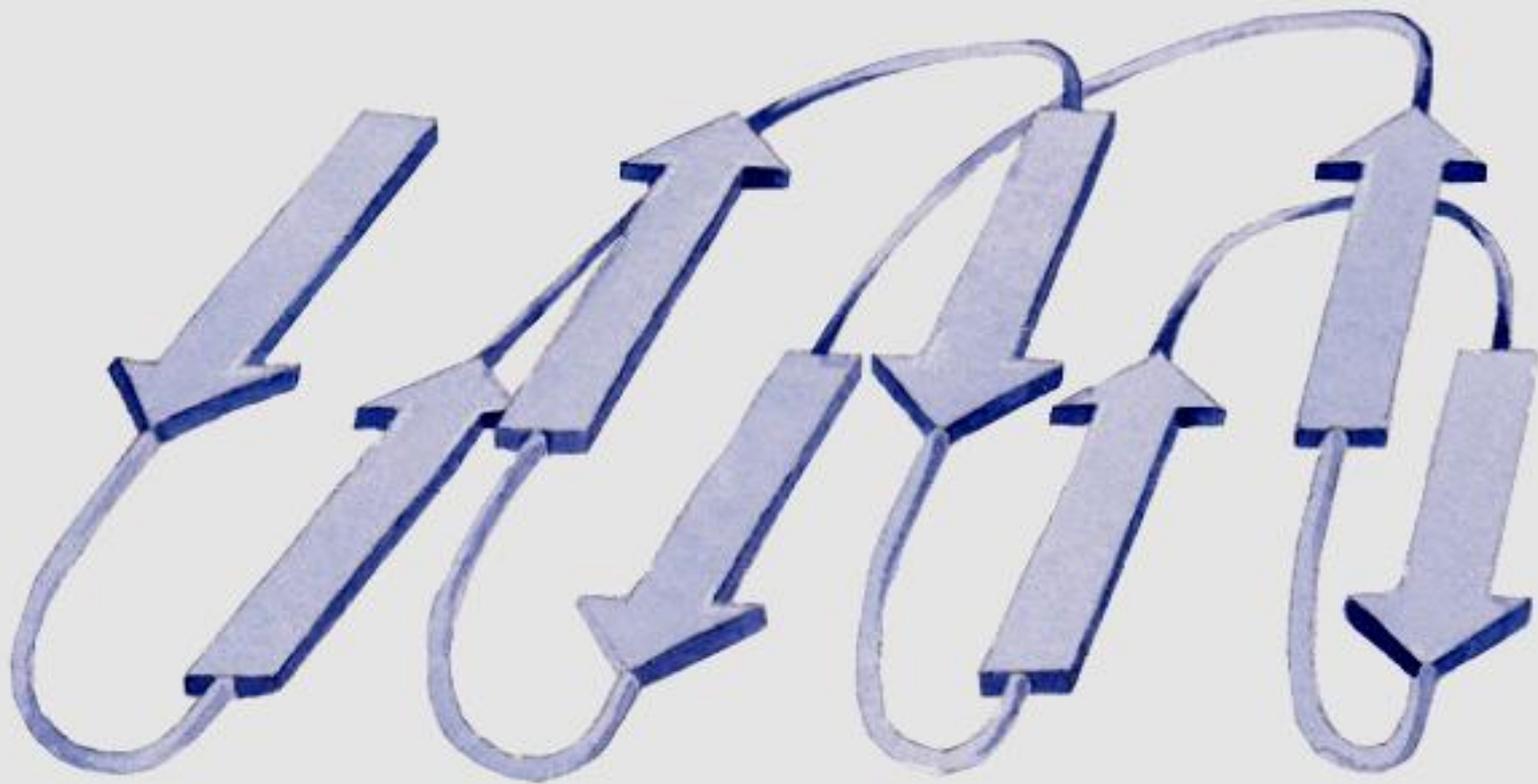


(a)

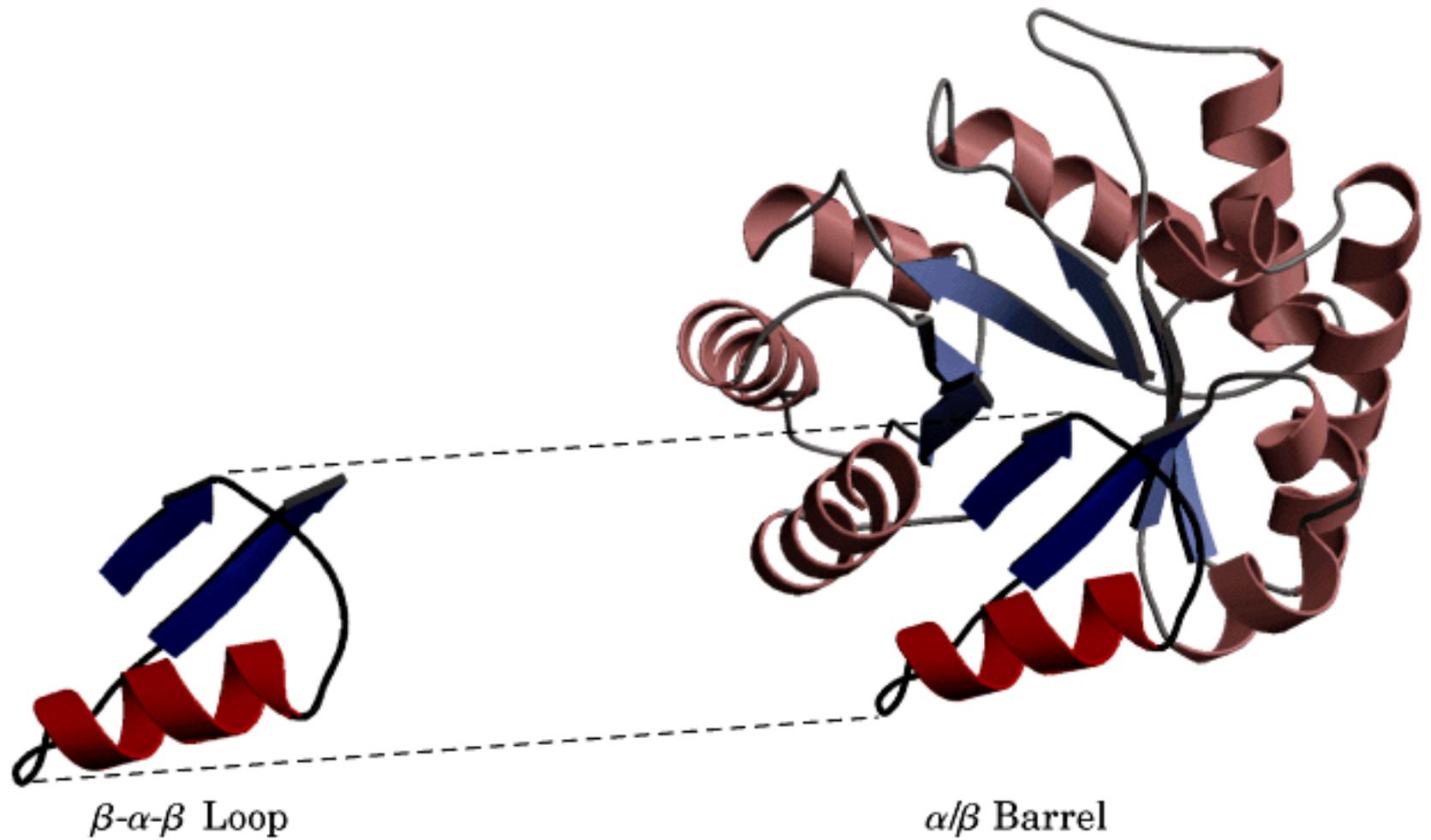
β - α - β Loop



α - α Corner



(b) Typical connections
in an all- β motif

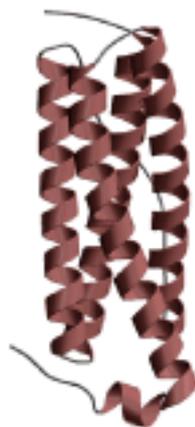




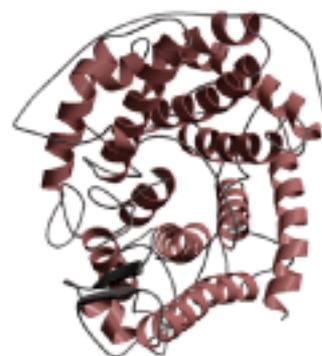
All α



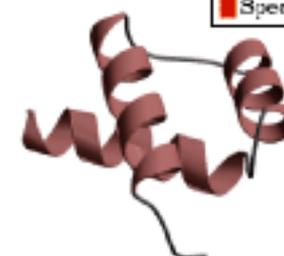
1a06
 Serum albumin
 Serum albumin
 Serum albumin
 Serum albumin
 Human (*Homo sapiens*)



1bef
 Ferritin-like
 Ferritin-like
 Ferritin
 Bacterioferritin (cytochrome b_1)
Escherichia coli



1gai
 α/α toroid
 Glycosyltransferases of the
 superhelical fold
 Glucoamylase
 Glucoamylase
Aspergillus awamori, variant x100



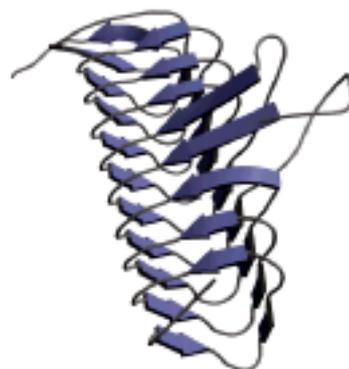
1enh
 DNA-binding 3-helical bundle
 Homeodomain-like
 Homeodomain
 engrailed Homeodomain
Drosophila melanogaster

Key	
■	PDB Identifier
■	Fold
■	Superfamily
■	Family
■	Protein
■	Species

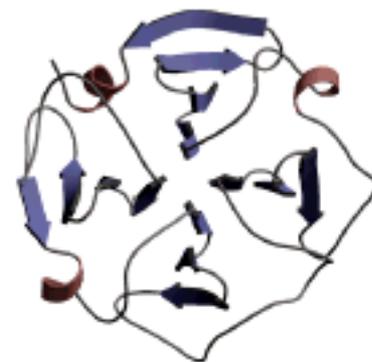
All β



1hoe
 α -Amylase inhibitor
 α -Amylase inhibitor
 α -Amylase inhibitor
 HOE-467A
Streptomyces tendae 4158



1lxe
 Single-stranded left-handed β helix
 Trimeric LpxA-like enzymes
 UDP *N*-acetylglucosamine acyltransferase
 UDP *N*-acetylglucosamine acyltransferase
Escherichia coli



1pex
 Four-bladed β propeller
 Hemopexin-like domain
 Hemopexin-like domain
 Collagenase-3 (MMP-13),
 carboxyl-terminal domain
 Human (*Homo sapiens*)



1jpc
 β -Prism II
 α -D-Mannose-specific plant lectins
 α -D-Mannose-specific plant lectins
 Lectin (agglutinin)
 Snowdrop (*Galanthus nivalis*)



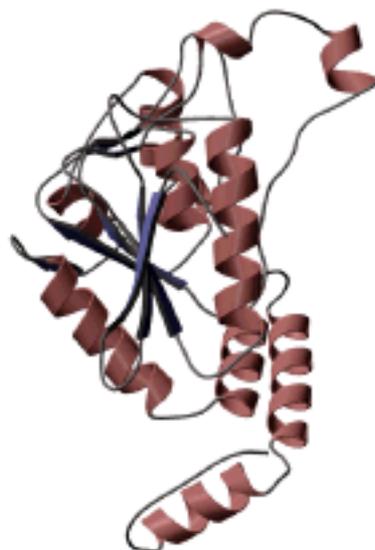
1cd8
 Immunoglobulin-like β sandwich
 Immunoglobulin
 Antibody variable domain-like
 CD8
 Human (*Homo sapiens*)

Key	
█	PDB Identifier
█	Fold
█	Superfamily
█	Family
█	Protein
█	Species

$\alpha\beta$

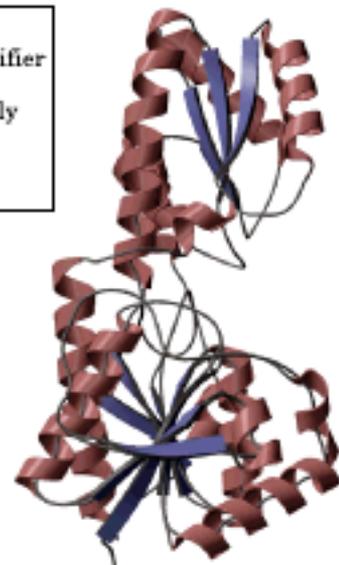


- 1deh
- NAD(P)-binding Rossmann-fold domains
- NAD(P)-binding Rossmann-fold domains
- Alcohol/glucose dehydrogenases, carboxyl-terminal domain
- Alcohol dehydrogenase
- Human (*Homo sapiens*)



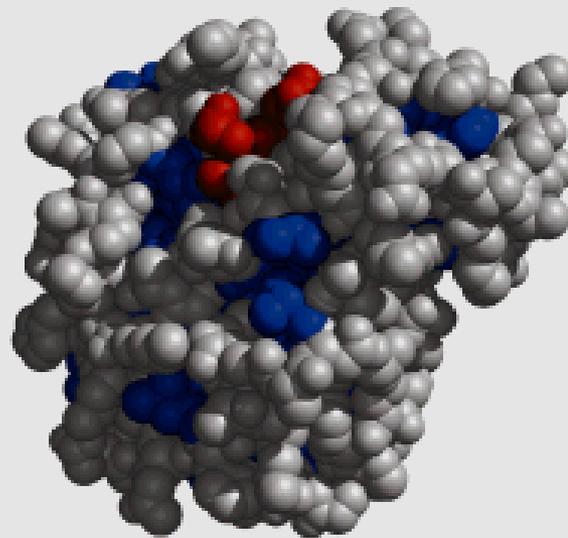
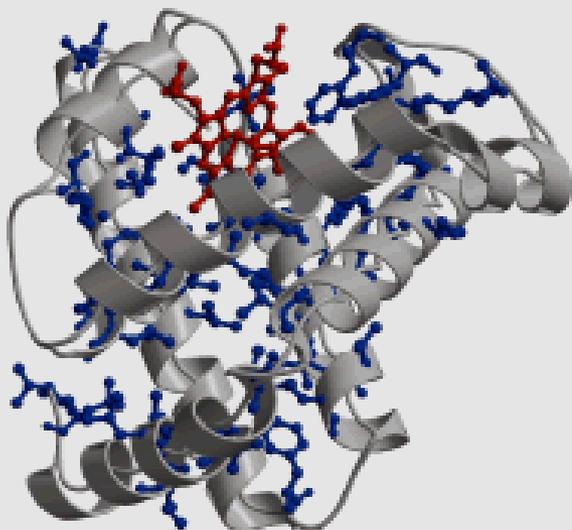
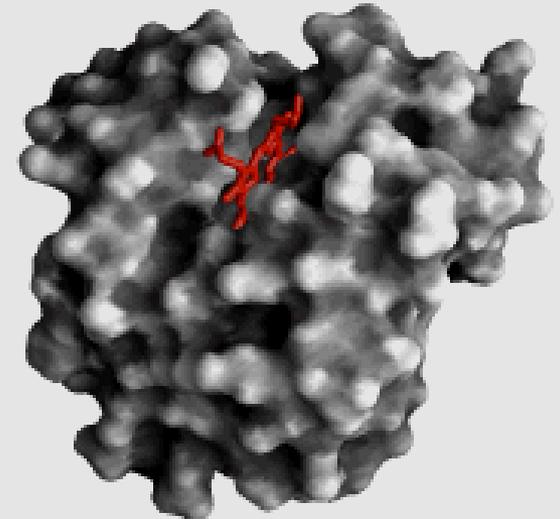
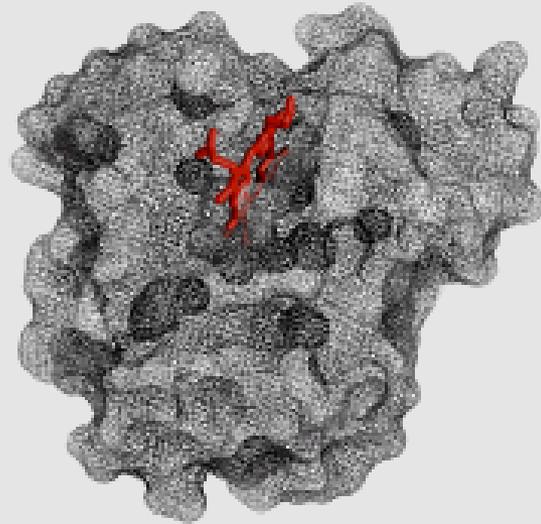
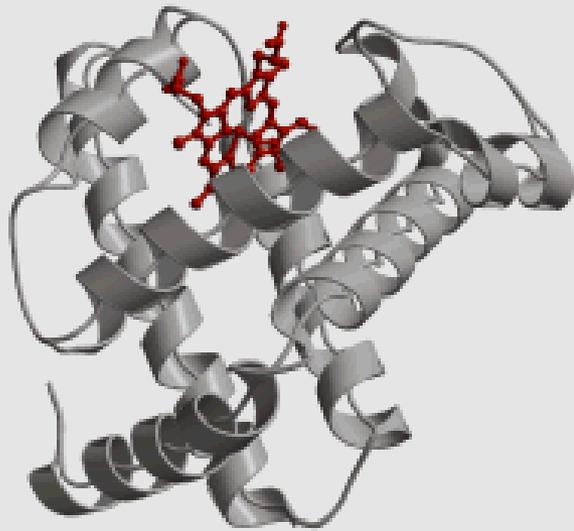
- 1dub
- Crotonase-like
- Crotonase-like
- Crotonase-like
- Enoyl-CoA hydratase
- Rat (*Rattus norvegicus*)

Key	
█	PDB Identifier
█	Fold
█	Superfamily
█	Family
█	Protein
█	Species



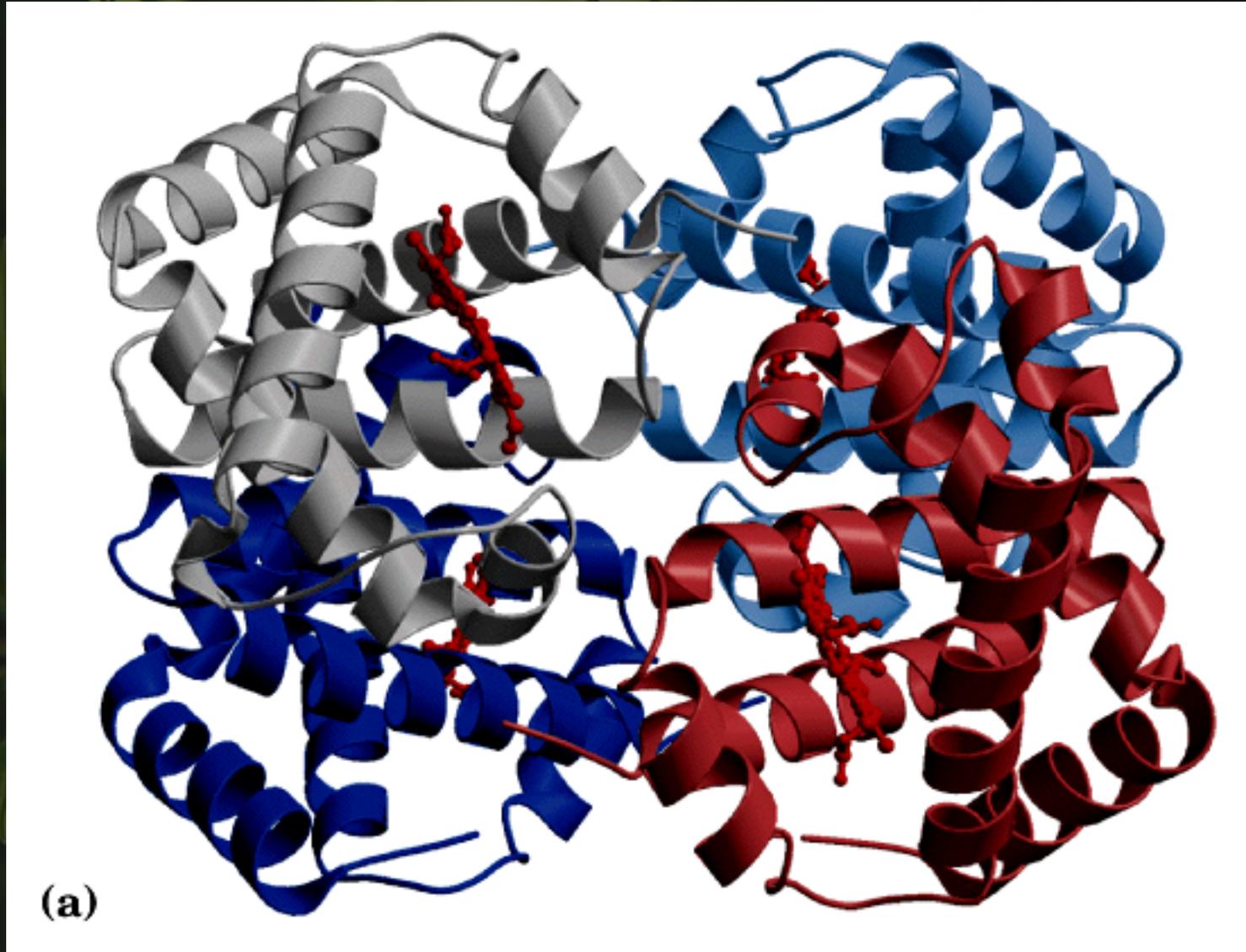
- 1pfk
- Phosphofructokinase
- Phosphofructokinase
- Phosphofructokinase
- Phosphofructokinase
- Phosphofructokinase
- Escherichia coli*

Estructura terciaria. Distintas representaciones

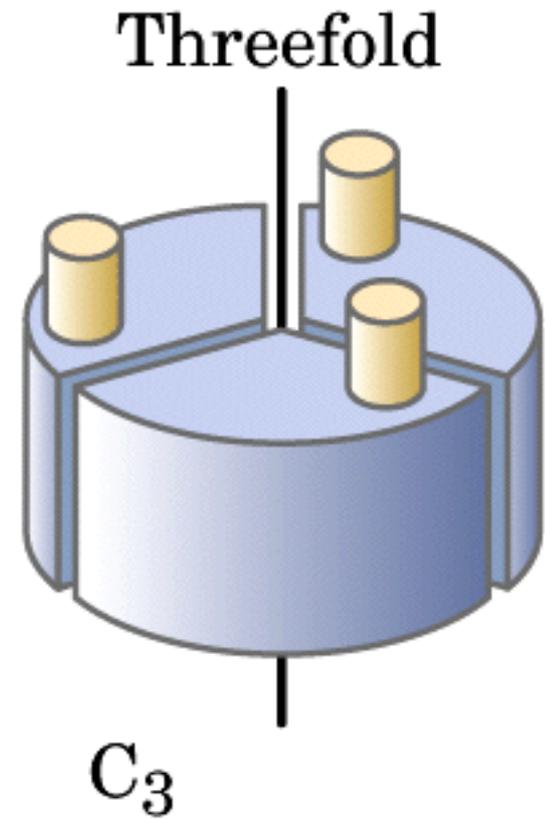
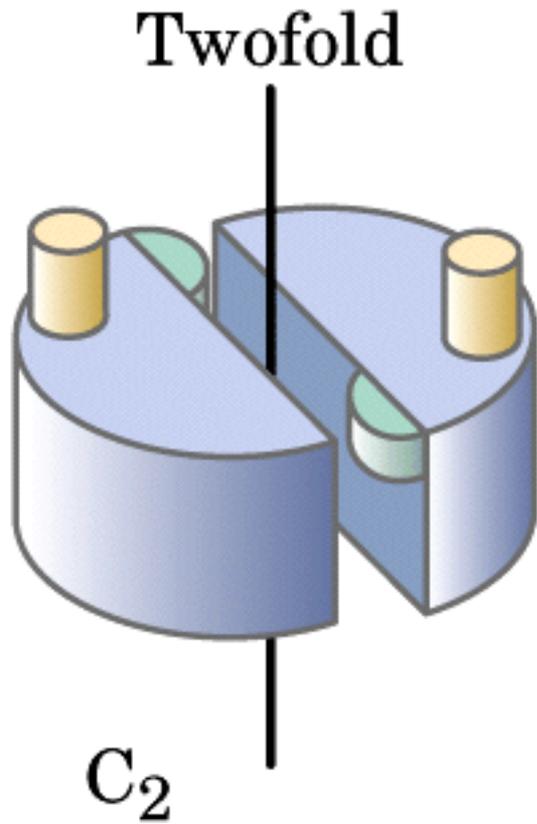


Cn3D

Estructura cuaternaria. Polipéptidos

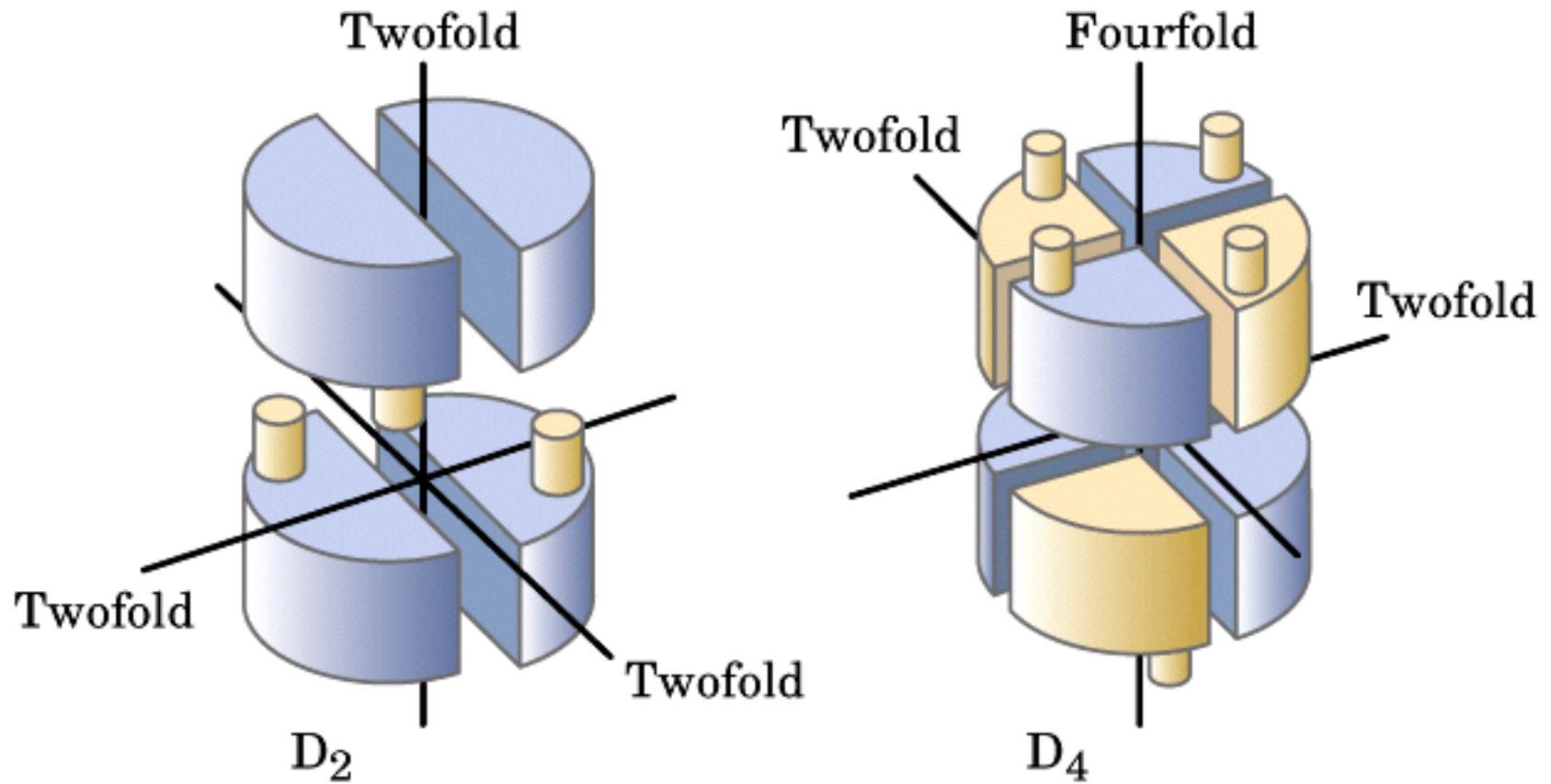


Estructura cuaternaria. Simetrías

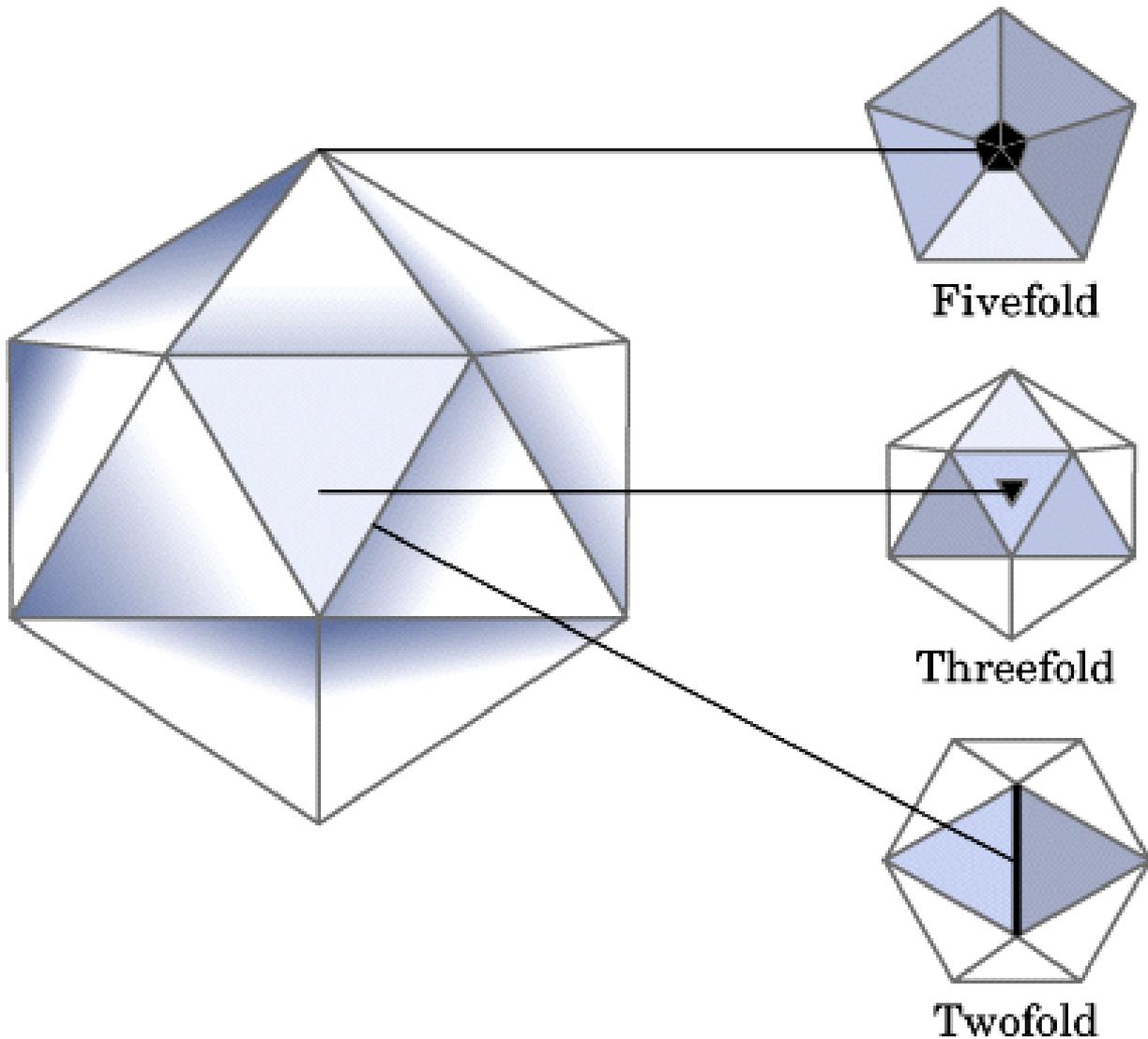


**Two types of cyclic symmetry
(a)**

Estructura cuaternaria. Simetrías

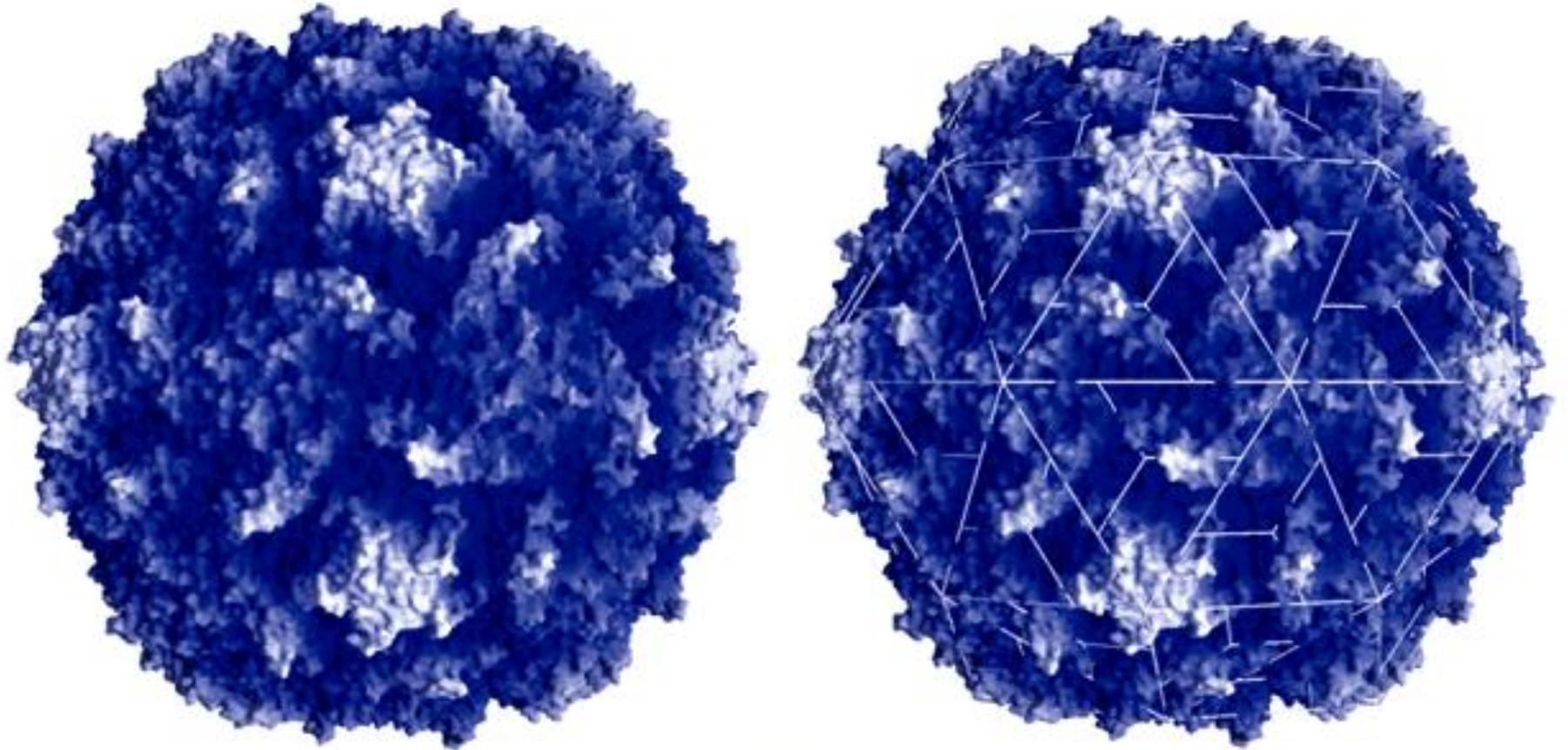


Two types of dihedral symmetry
(b)



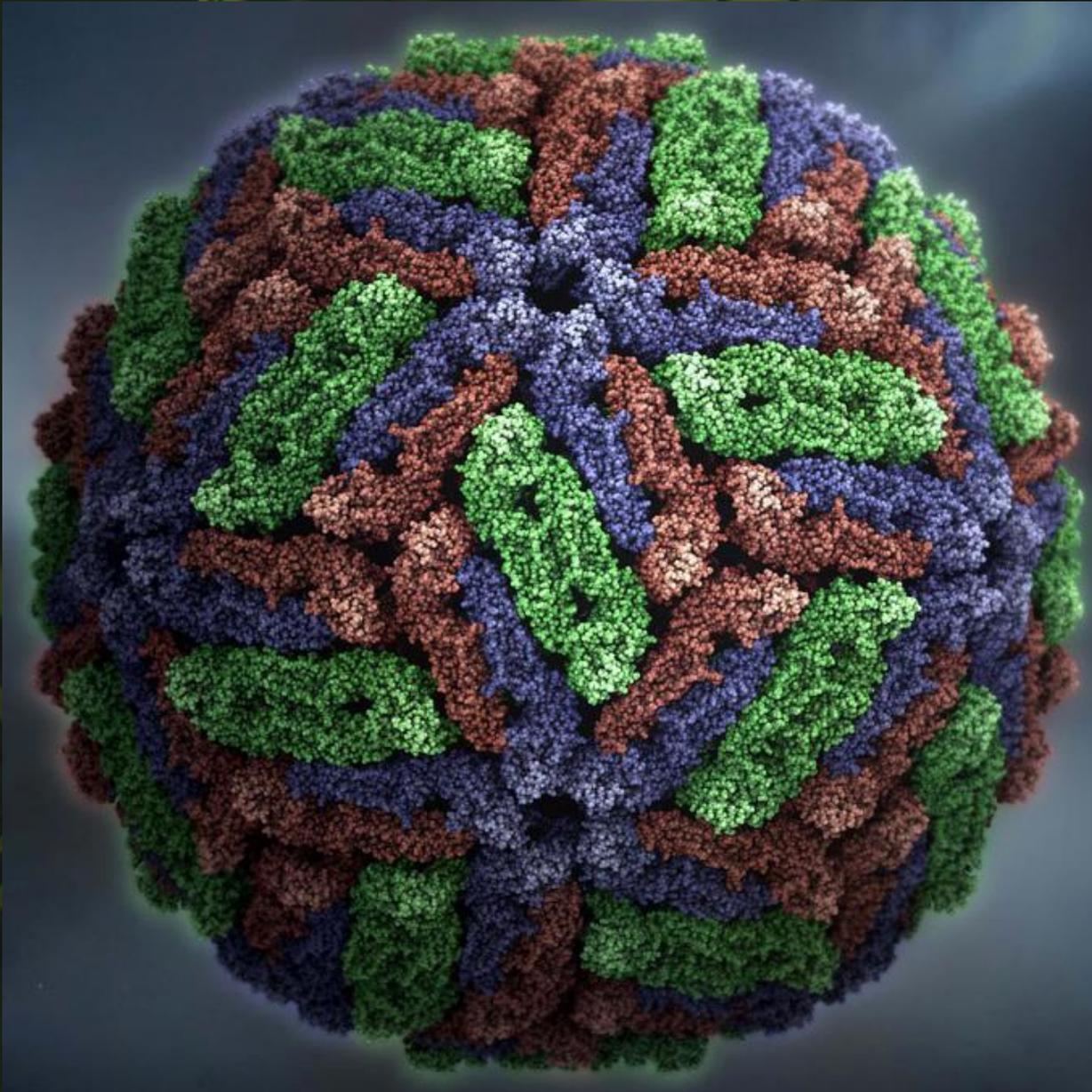
Icosahedral symmetry
(c)

Estructura cuaternaria. Simetrías macromoleculares



(a)

Estructura cuaternaria. Simetrías macromoleculares



Virus del dengue

Estructura de proteínas. Resumen.

Primary structure



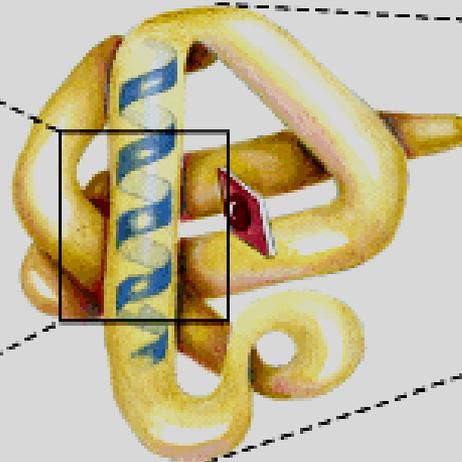
Amino acid residues

Secondary structure



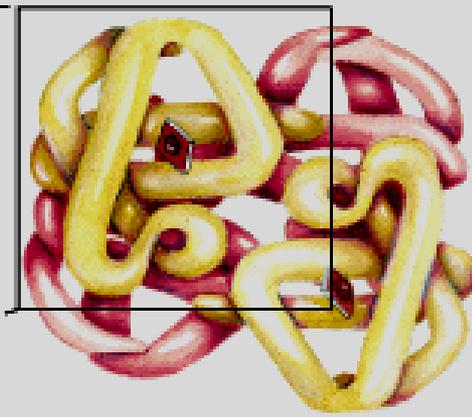
α Helix

Tertiary structure

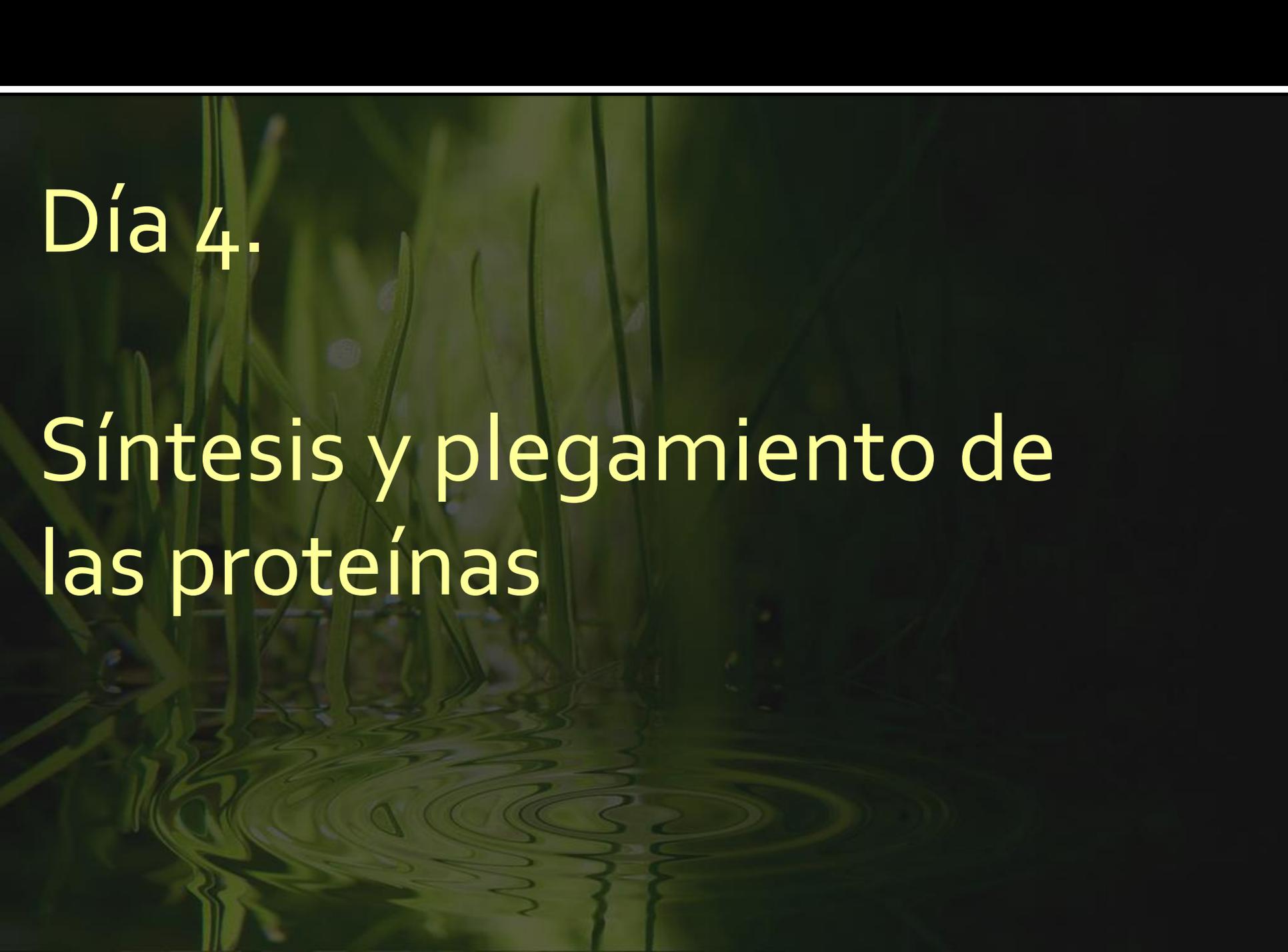


Polypeptide chain

Quaternary structure



Assembled subunits

The background of the slide features a dark green, slightly blurred image of tall grass. In the lower portion, there are concentric ripples on a dark surface, likely water, reflecting the green light. The overall color palette is monochromatic, ranging from deep black to vibrant green.

Día 4.

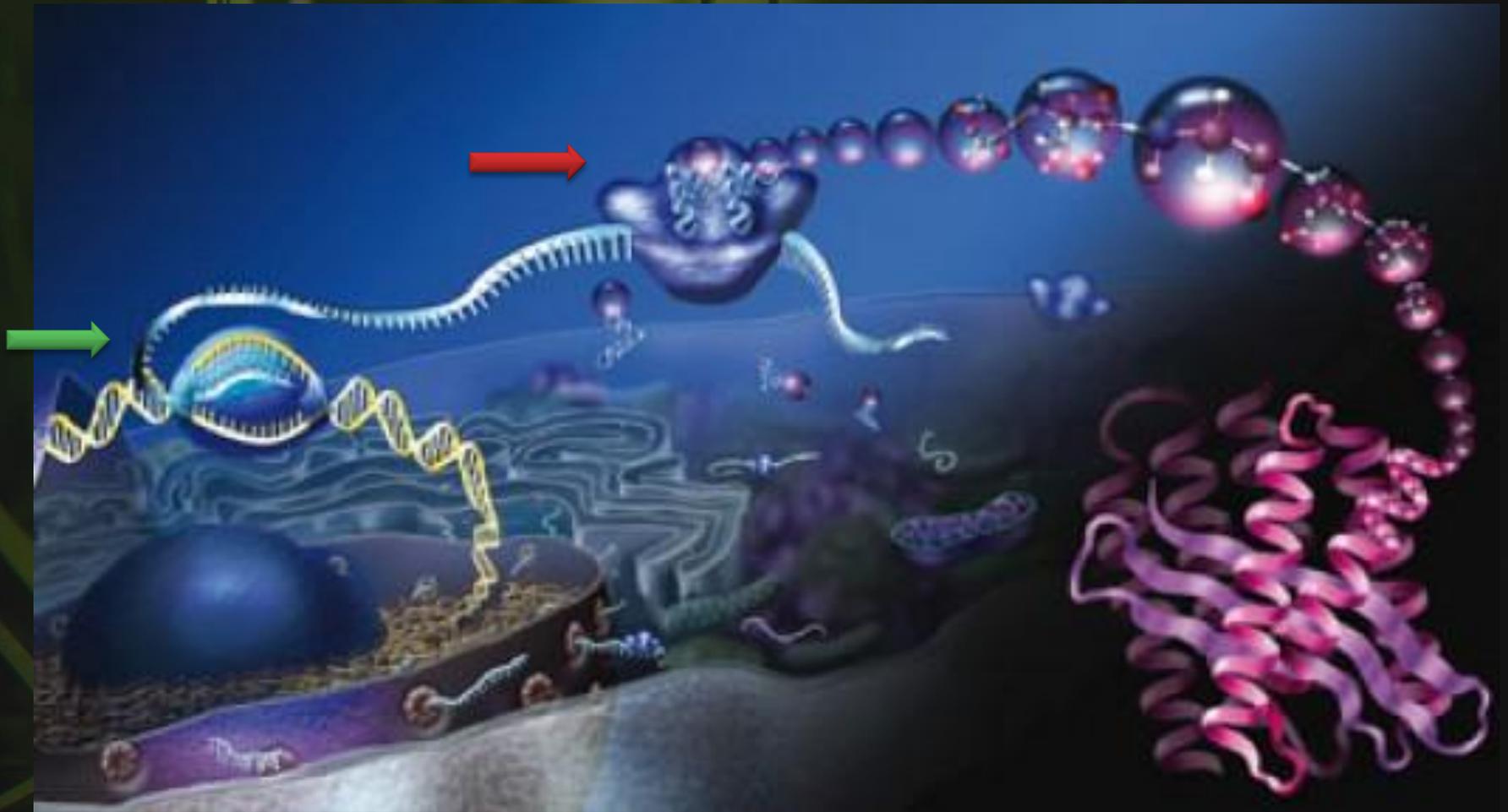
Síntesis y plegamiento de las proteínas

Plegamiento de proteínas

Cómo una proteína logra adquirir esas estructuras tan complejas?

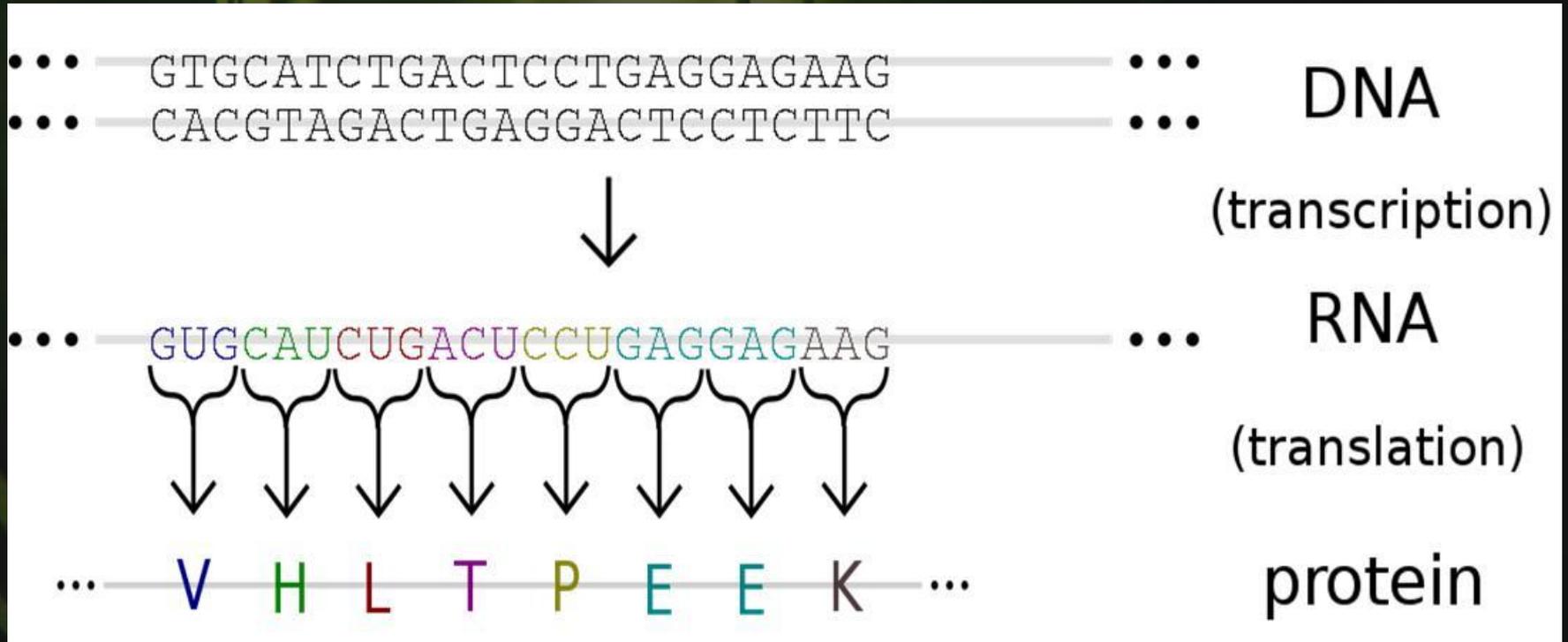
Veamos primero cómo se sintetizan.

Síntesis de proteínas. El dogma central.



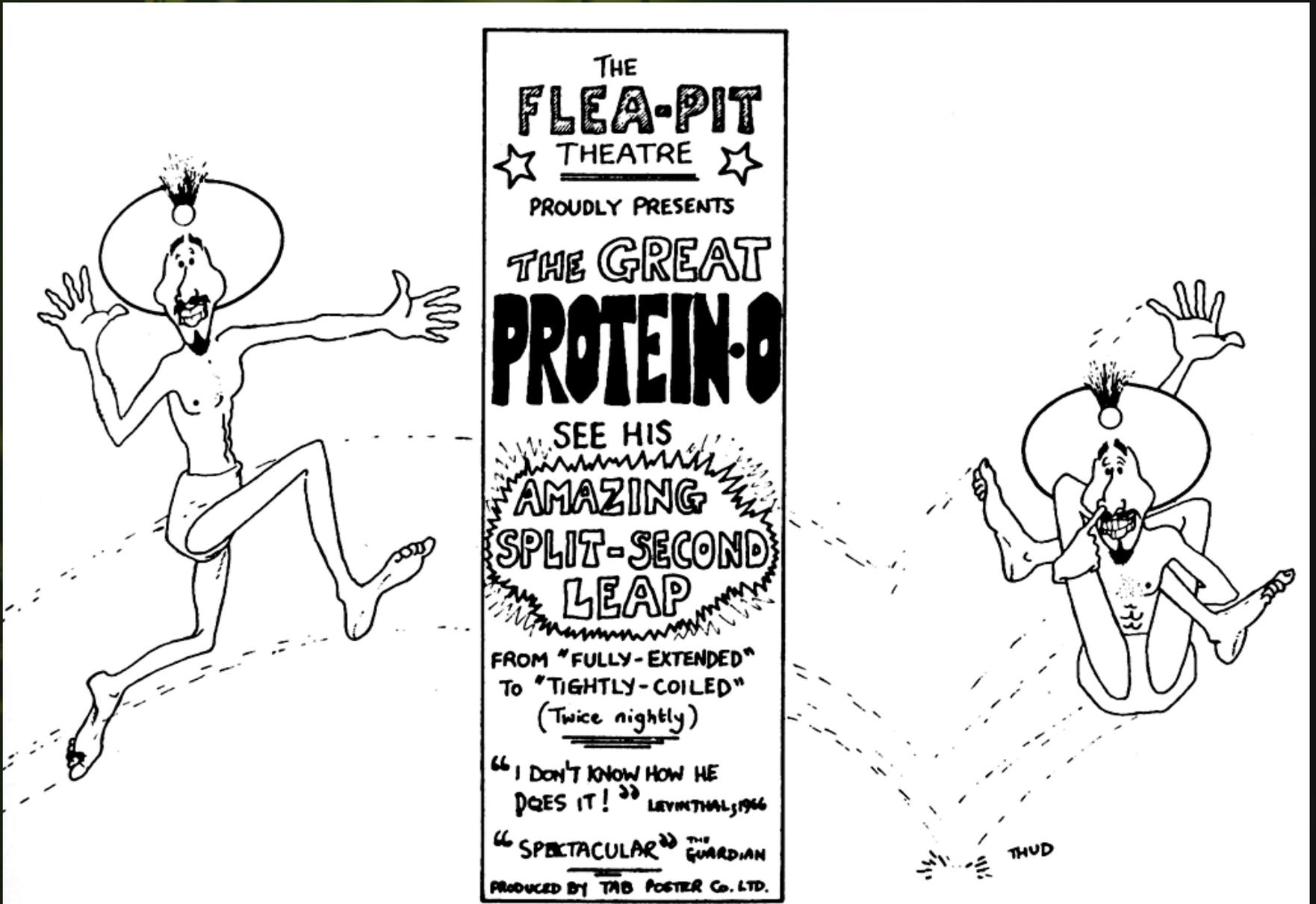
Un gen en el ADN es transcrito a ARN y éste es empleado como molde para ser traducido a una secuencia de aminoácidos

Actividad:



Escribe tu nombre en código genético. Cambia las B por V; las J por G; las Ñ por N; las O por Q; las U por V y las W, X y Z por N.

Plegamiento de proteínas



THE
FLEA-PIT
★ THEATRE ★
PROUDLY PRESENTS
THE GREAT
PROTEIN-O

SEE HIS
AMAZING
SPLIT-SECOND
LEAP

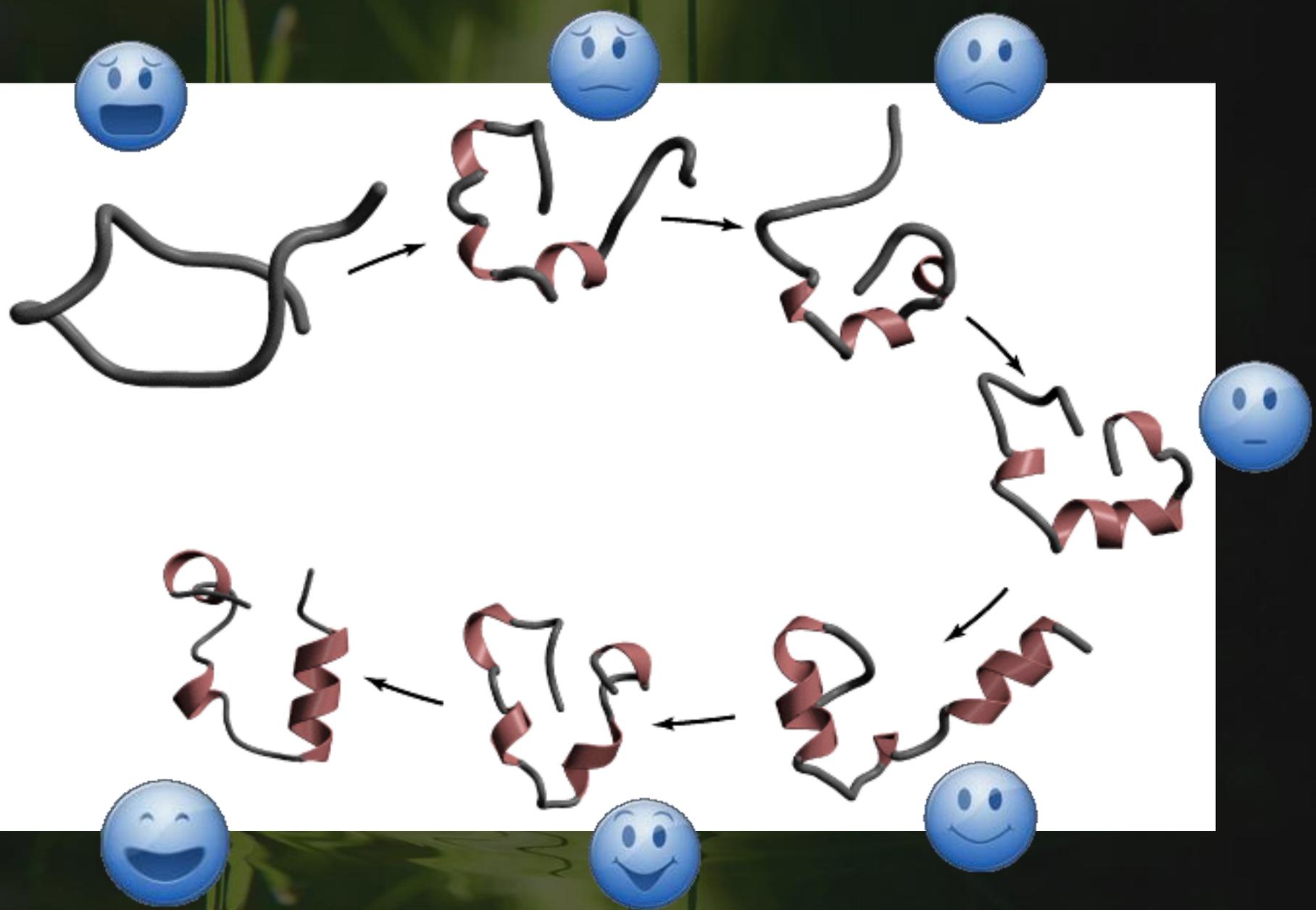
FROM "FULLY-EXTENDED"
TO "TIGHTLY-COILED"
(Twice nightly)

"I DON'T KNOW HOW HE
DOES IT!" LEVINTHAL, 1966

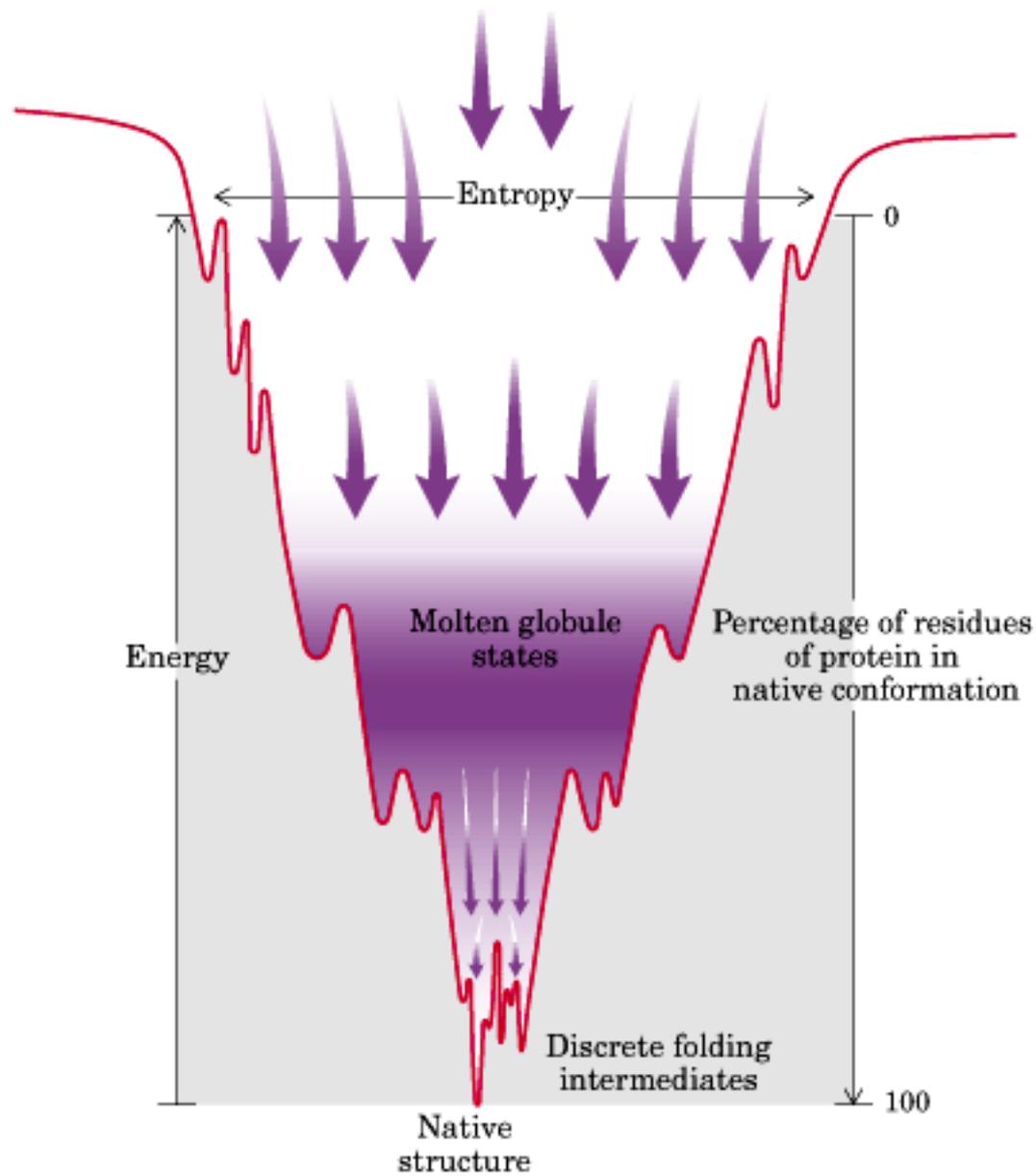
"SPECTACULAR" THE GUARDIAN

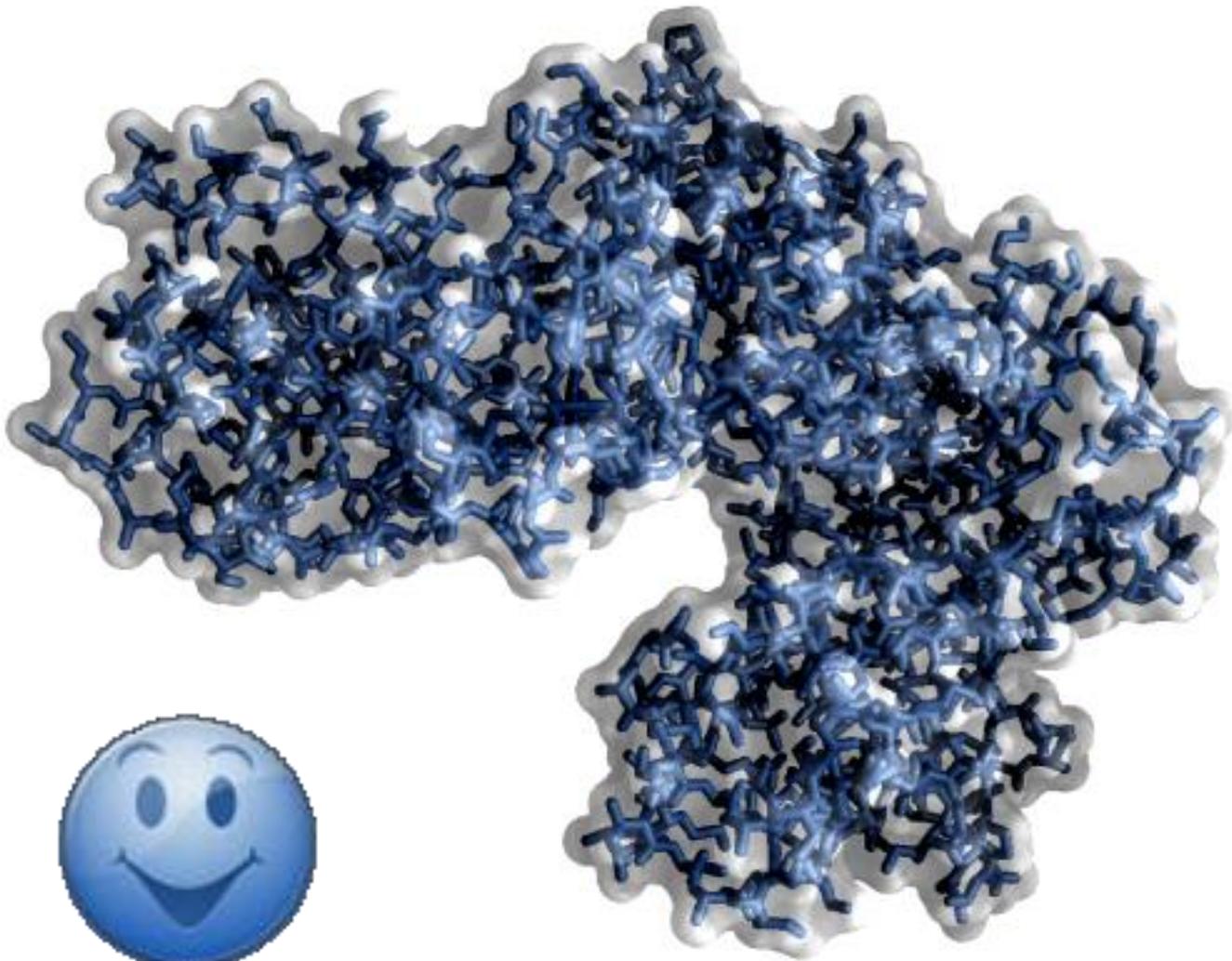
PRODUCED BY TAB POSTER CO. LTD.

THUD

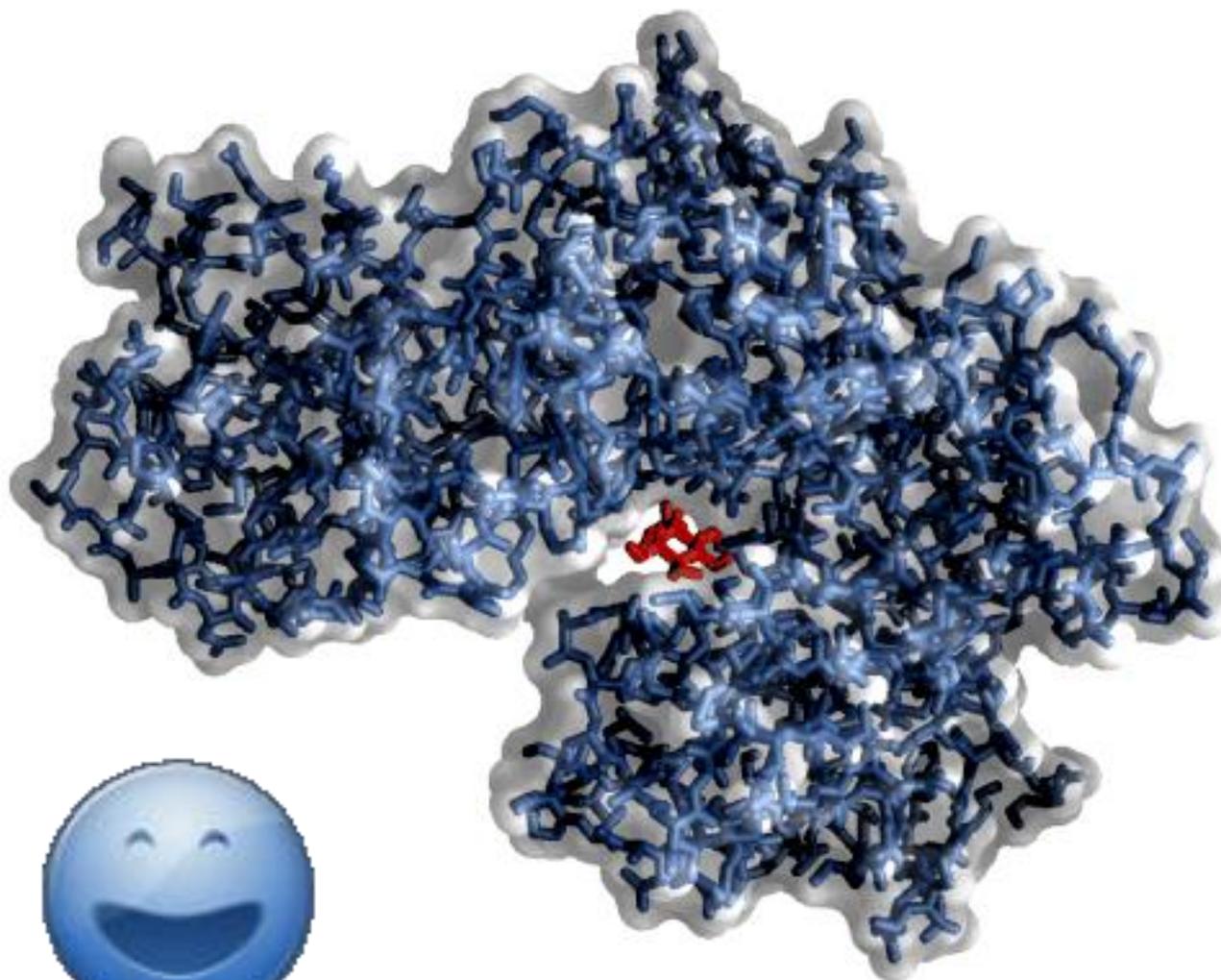


Beginning of helix formation and collapse





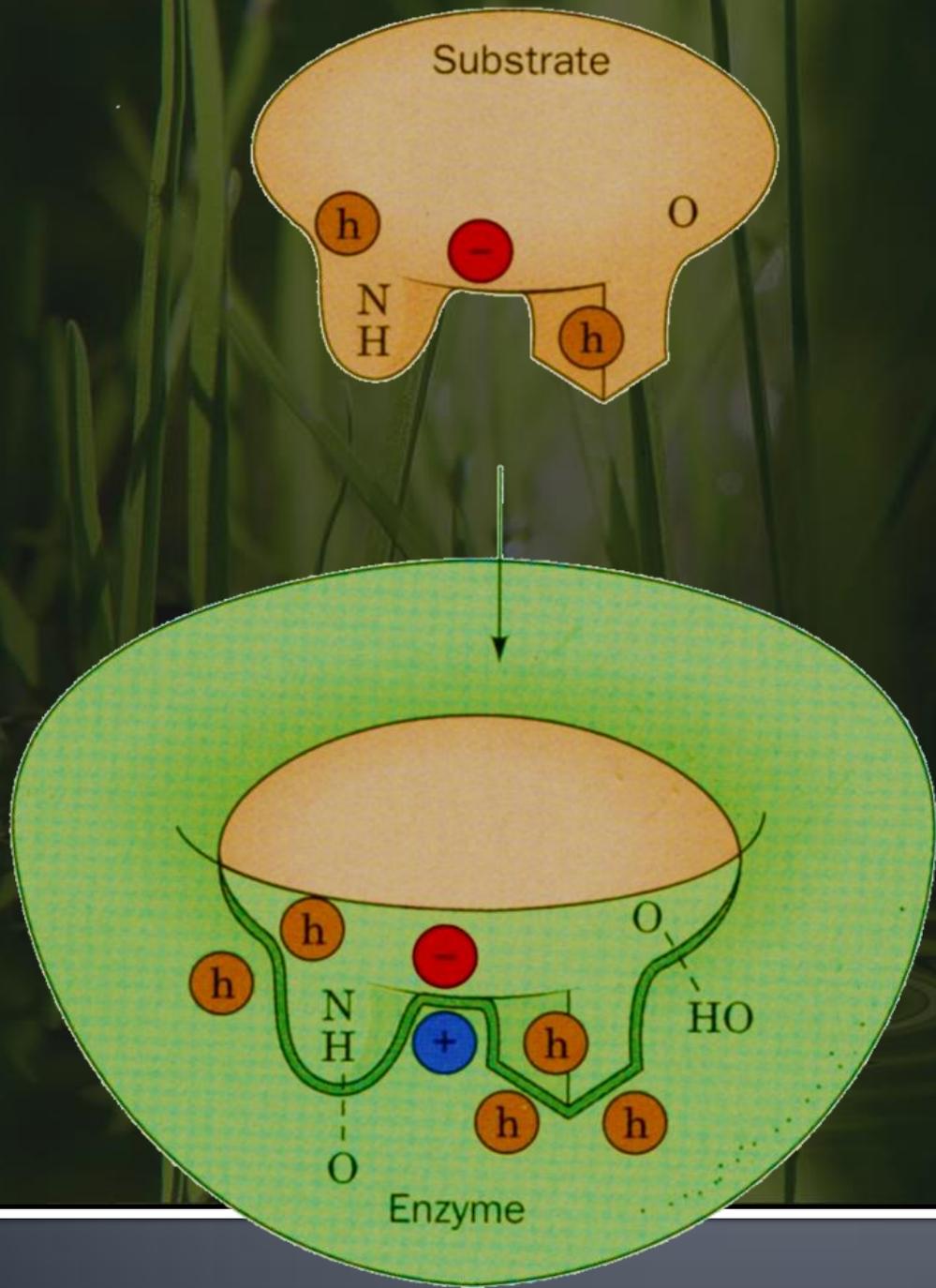
(a)



(b)

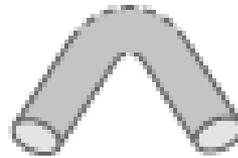


Enzimas



Reacción química

(a) No enzyme



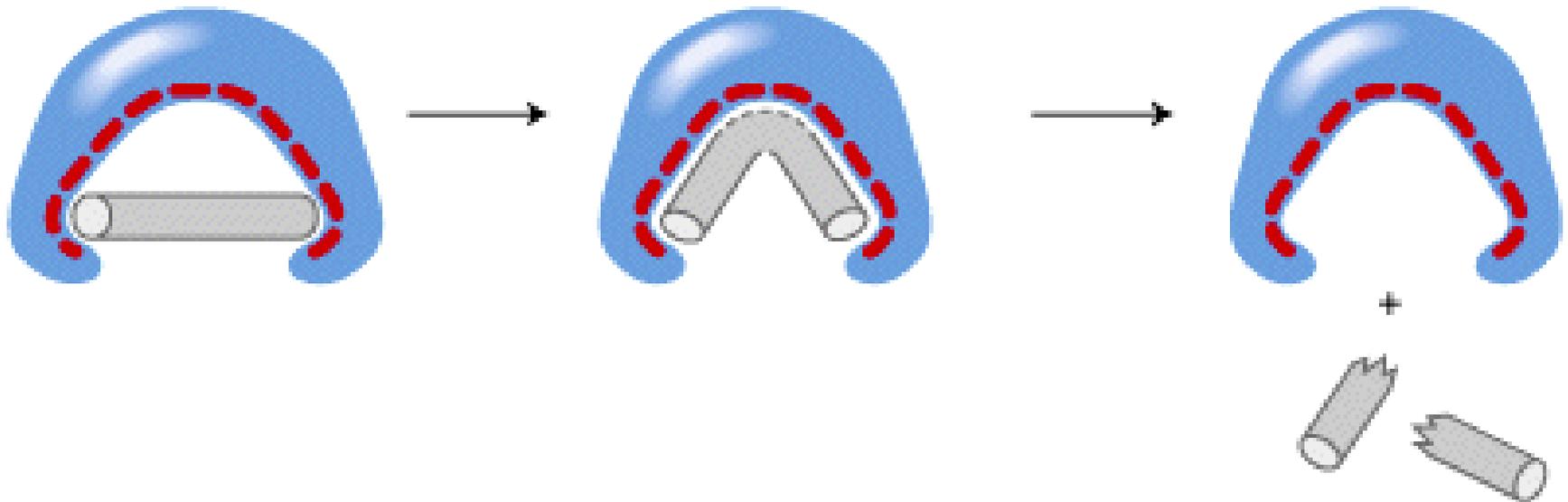
Substrate
(metal stick)

Transition state
(bent stick)

Products
(broken stick)

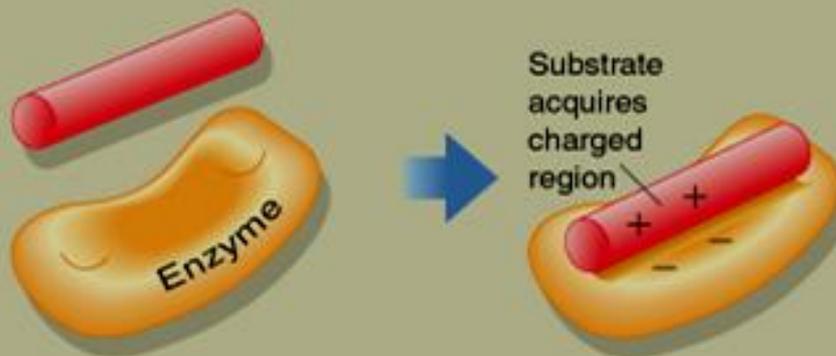
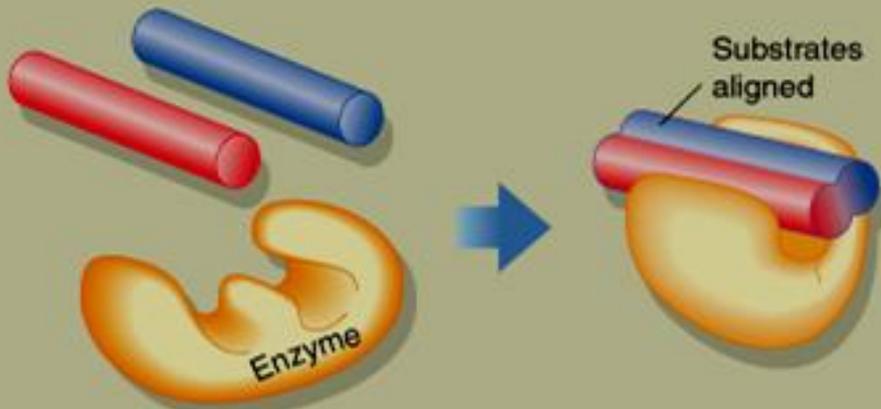
Reacción bioquímica (catalizada por una enzima)

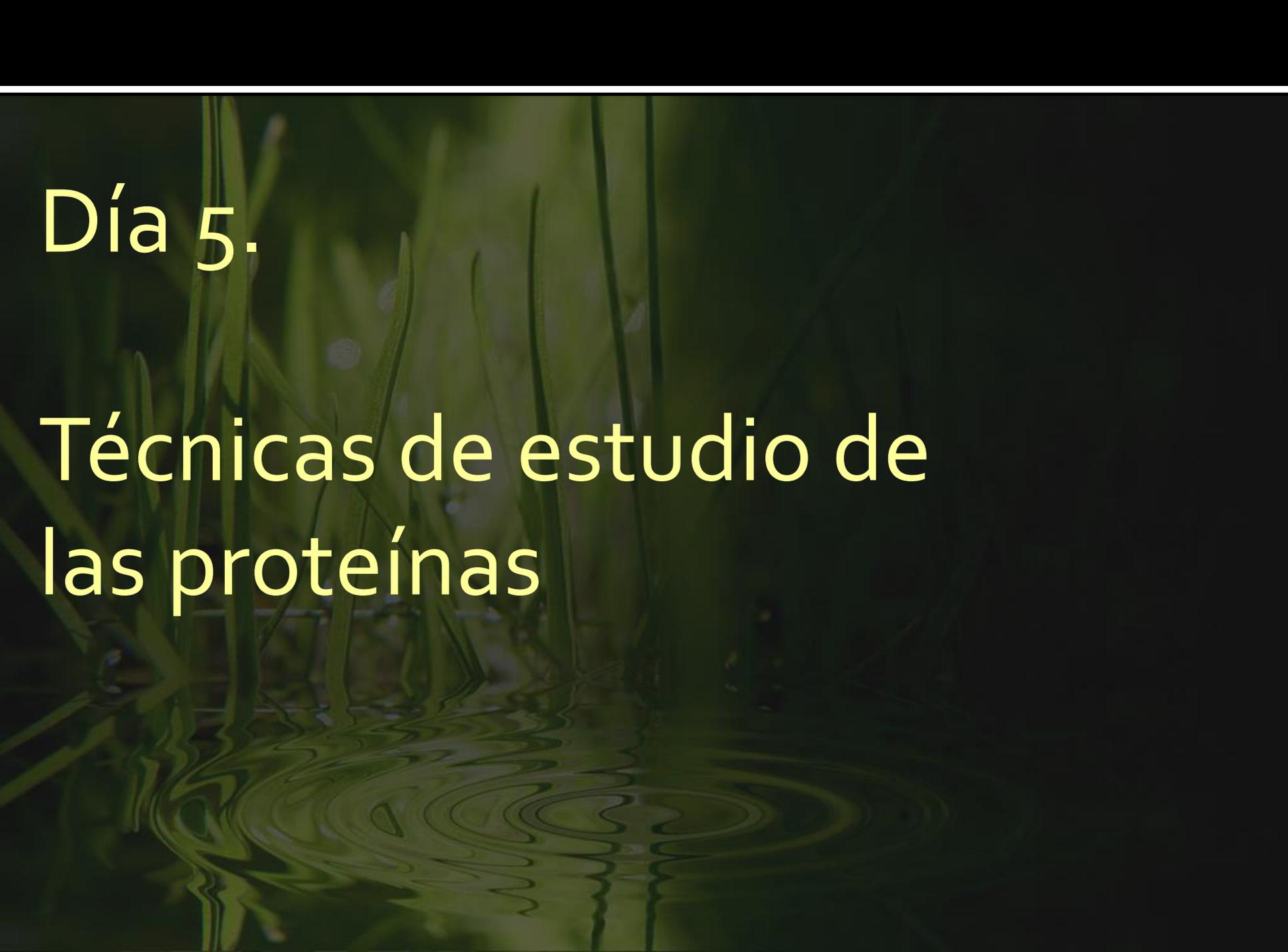
(c) Enzyme complementary to transition state



Que le hace la enzima al substrato?

1. Disminuye el índice de difusibilidad
2. Vuelve a lo grupos más reactivos
3. Induce cambios estructurales en el substrato que lo inestabilizan

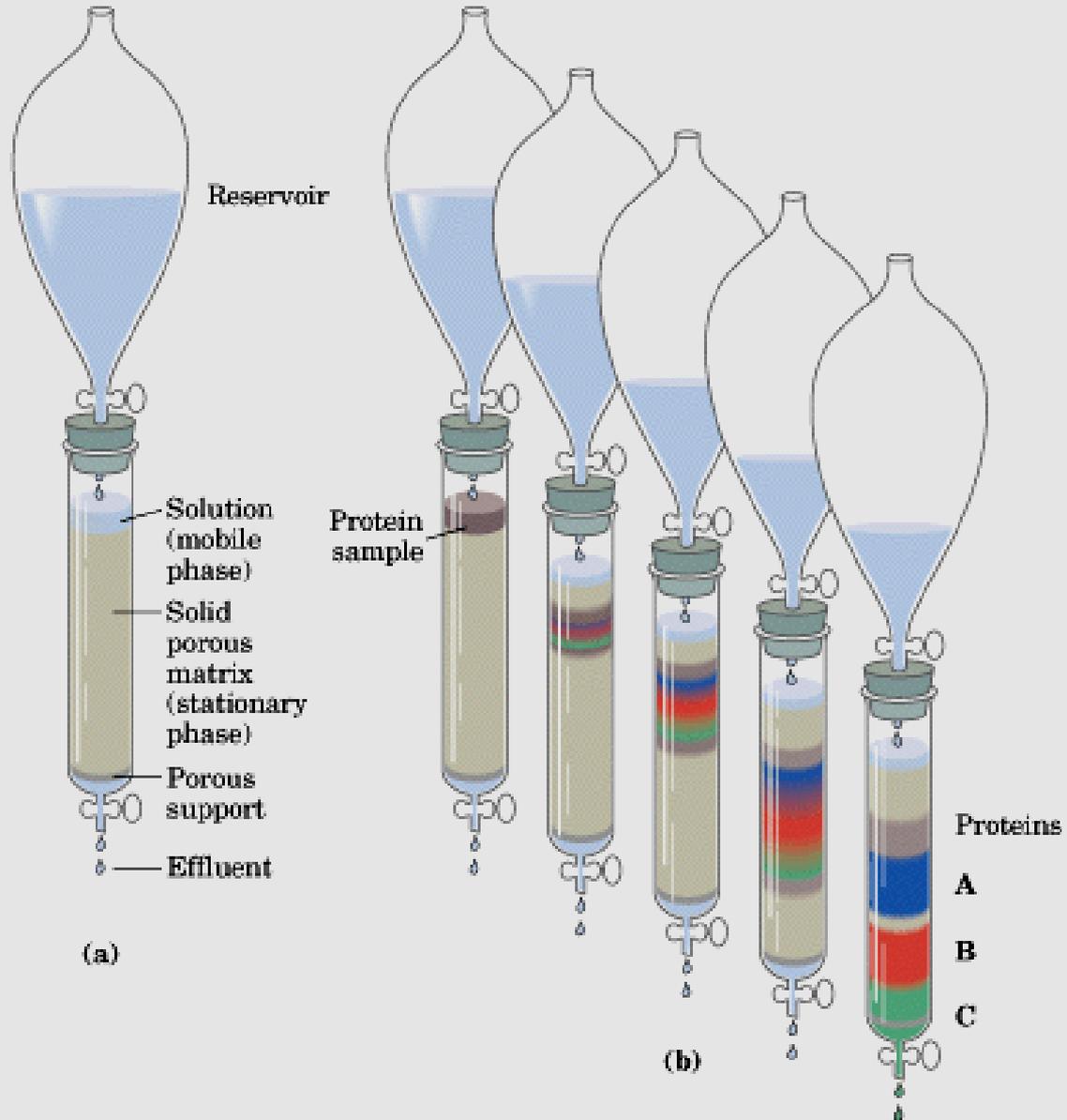


The background of the slide features a dark green, slightly blurred image of tall grass blades. In the lower portion, there are concentric ripples on a dark surface, likely water, reflecting the green light. The overall color palette is monochromatic, ranging from deep black to vibrant green.

Día 5.

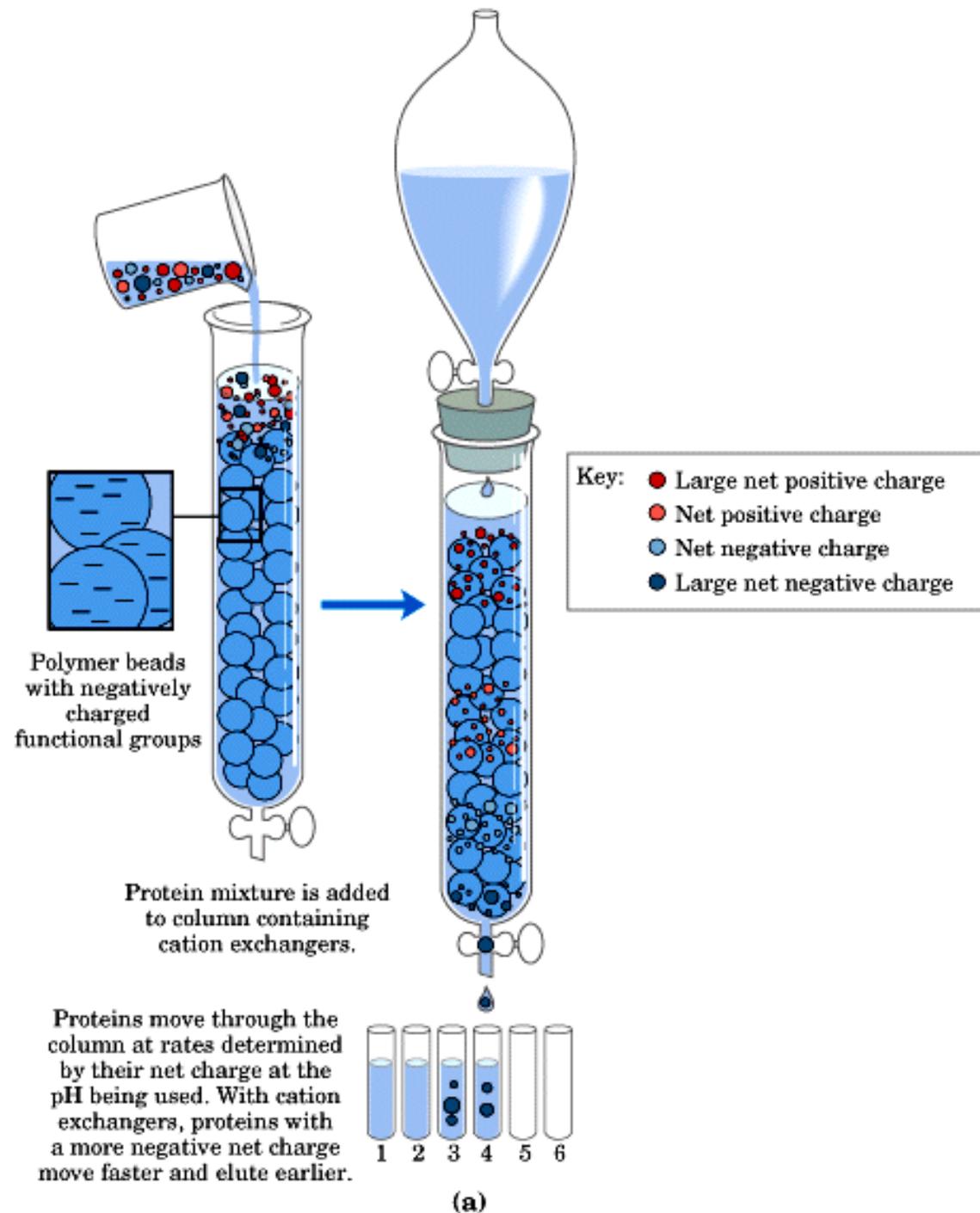
Técnicas de estudio de las proteínas

1) Cromatografía



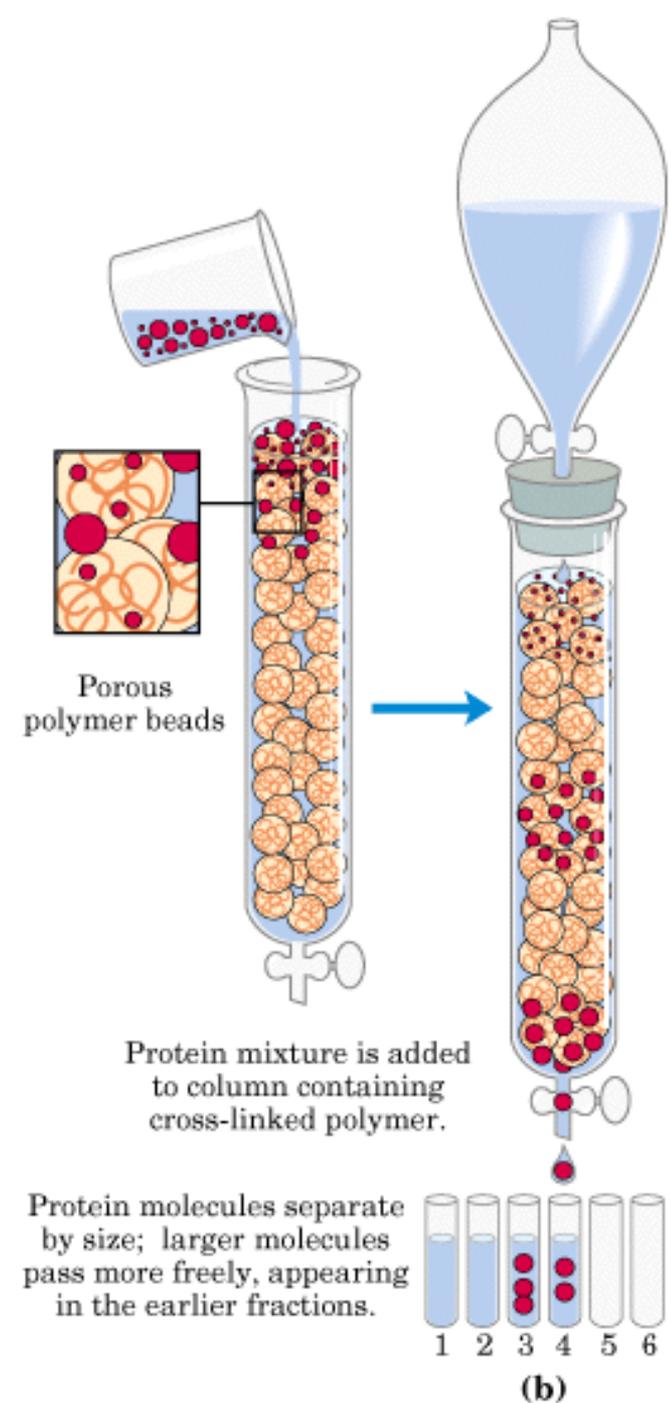
1.1 Cromatografía de intercambio iónico.

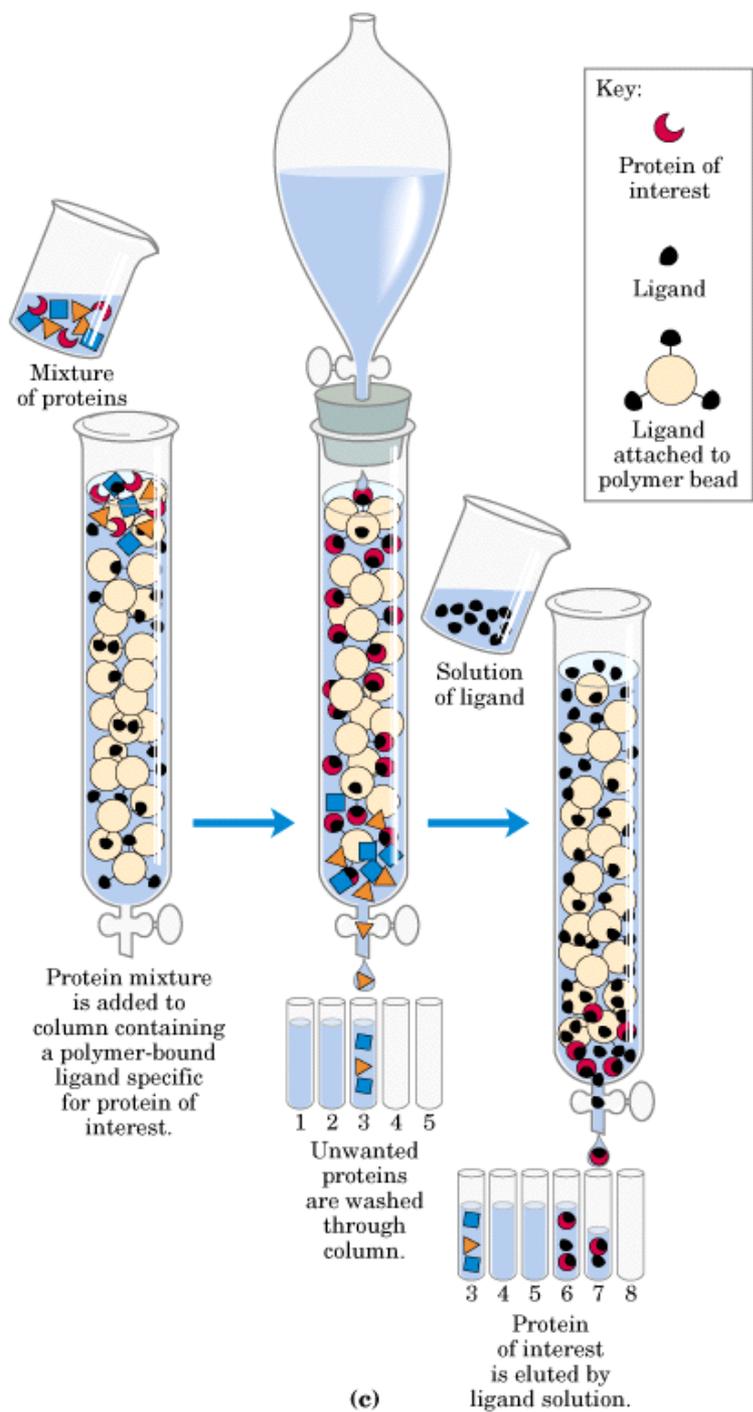
Separa por
cargas



1.2 Cromatografía de exclusión molecular.

Separa por
tamaños

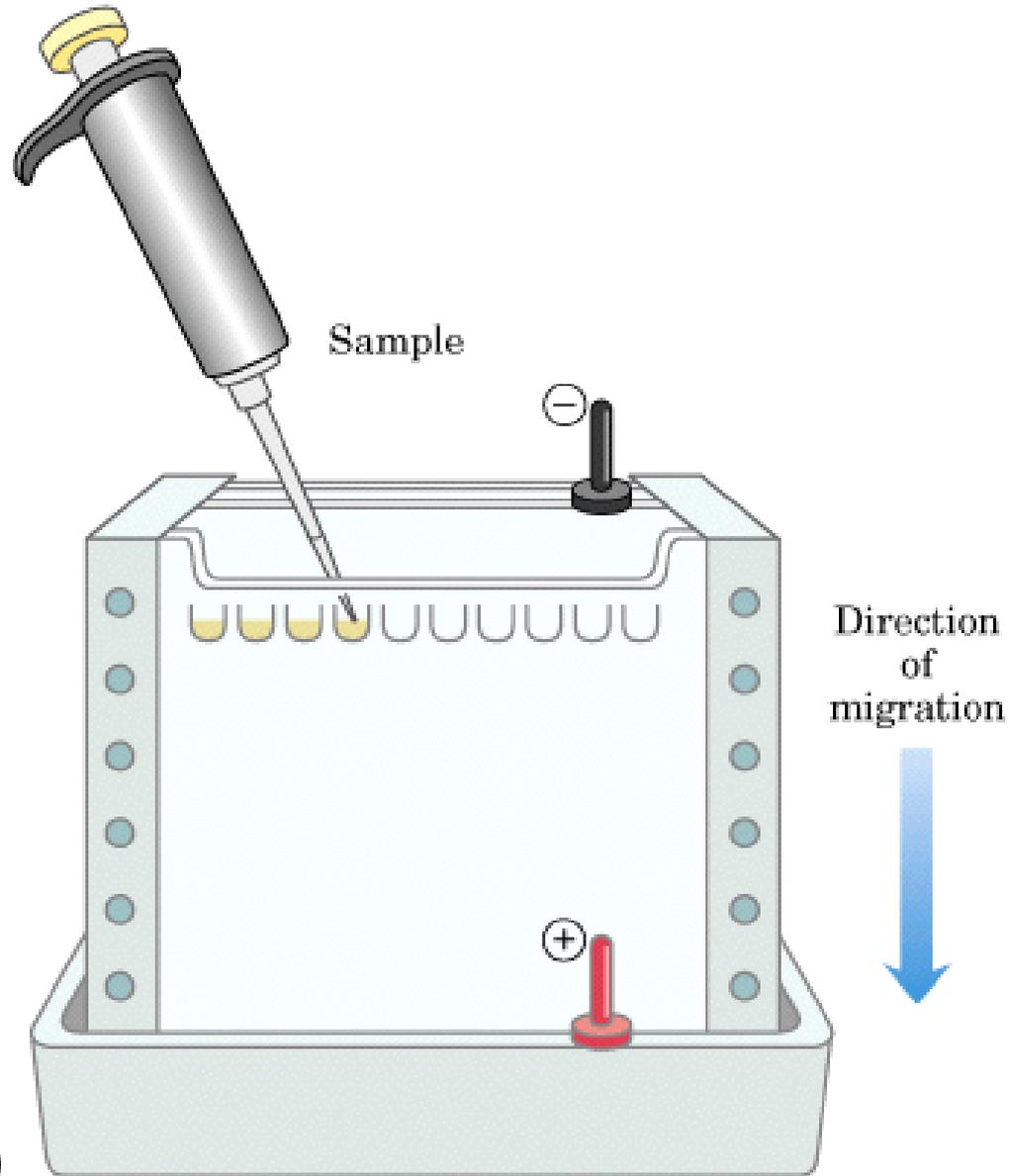


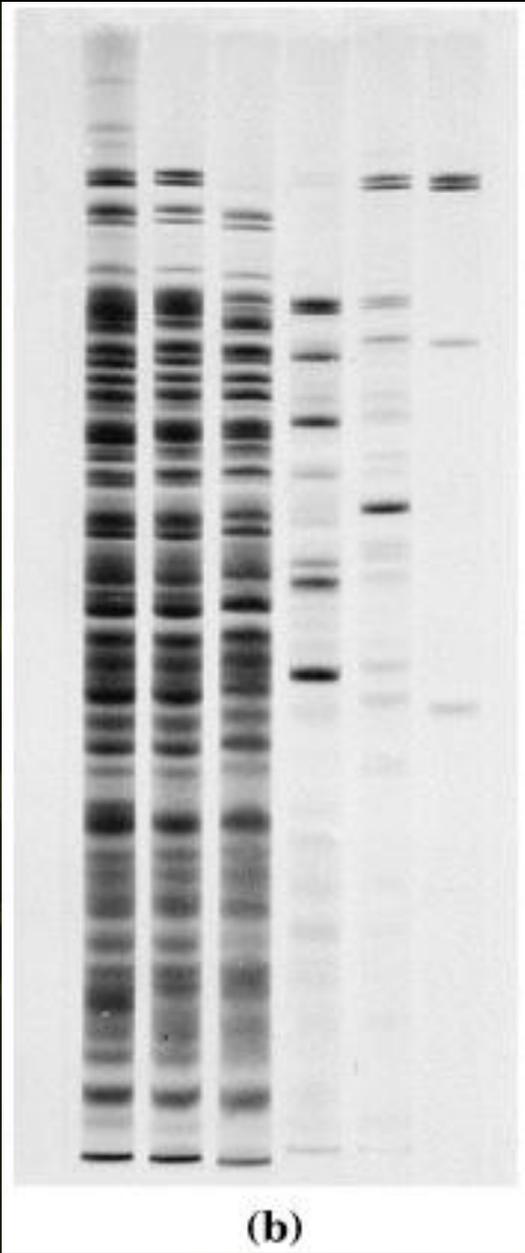


1.3 Cromatografía de afinidad

Separa por
interacciones
específicas

2) Electroforesis





2.1

Electroforesis nativa.

Separa por carga y por tamaño

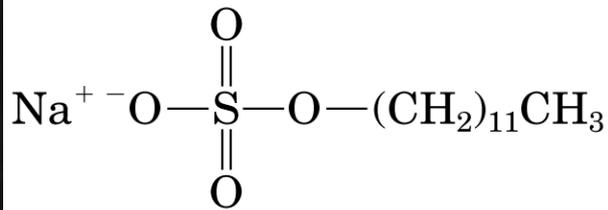
Permite conservar estructuras secundarias, terciarias y cuaternarias y por ende, la función de las proteínas

2.2

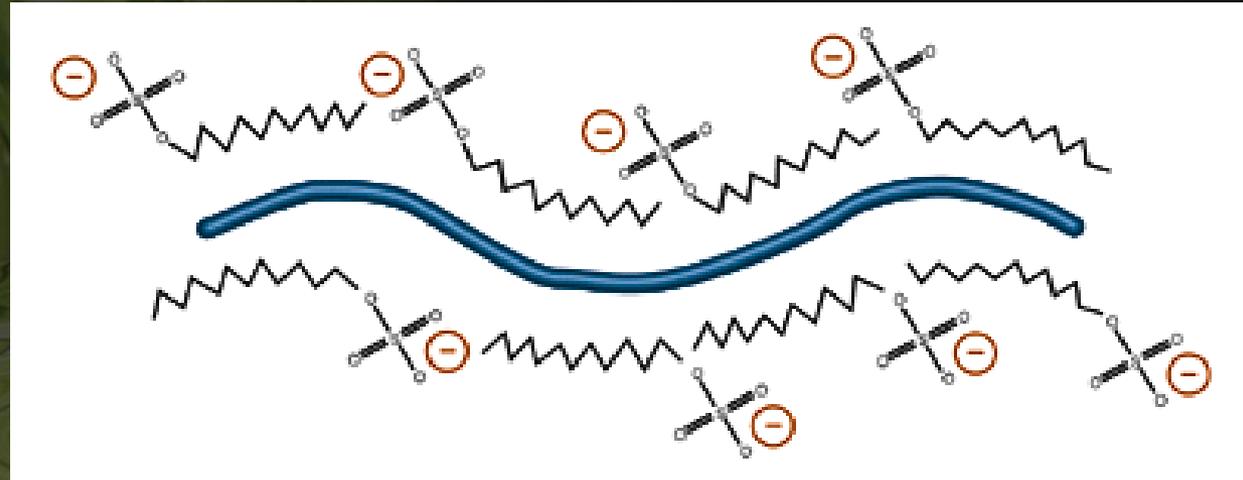
Electroforesis desnaturalizante.

Rompe estructuras secundarias, terciarias y cuaternarias.

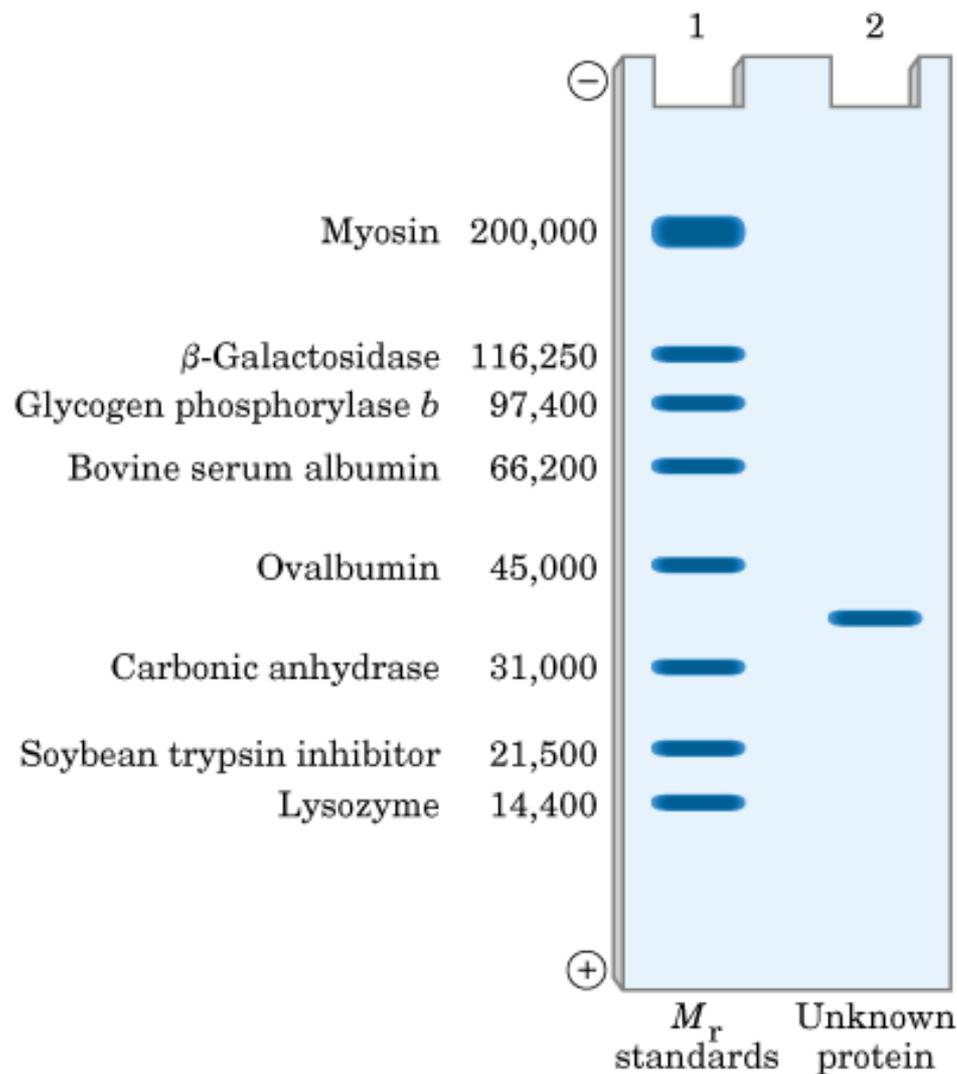
Neutraliza cargas para separar solo por tamaño



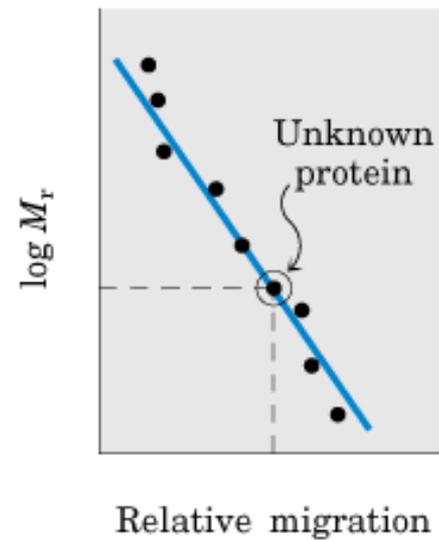
Sodium dodecyl sulfate
(SDS)



Cálculo de peso molecular en muestras problema

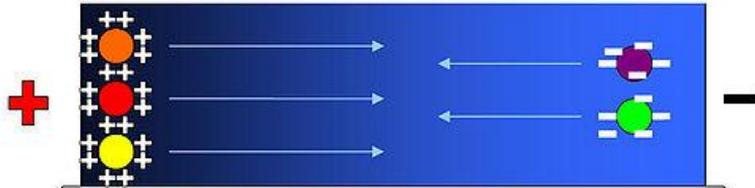


(a)

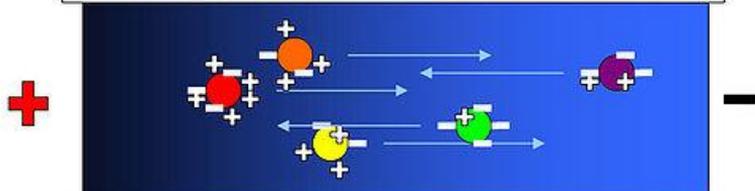


(b)

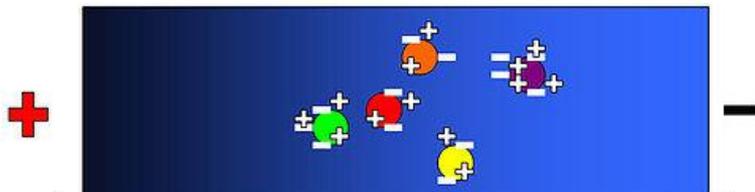
Stable pH gradient



At low pH, most proteins have a positive charge while at high pH, most proteins have a negative charge.



When an electric field is present, the cathode and anode ends pull the proteins to their isoelectric point where each individual protein possesses a neutral charge.

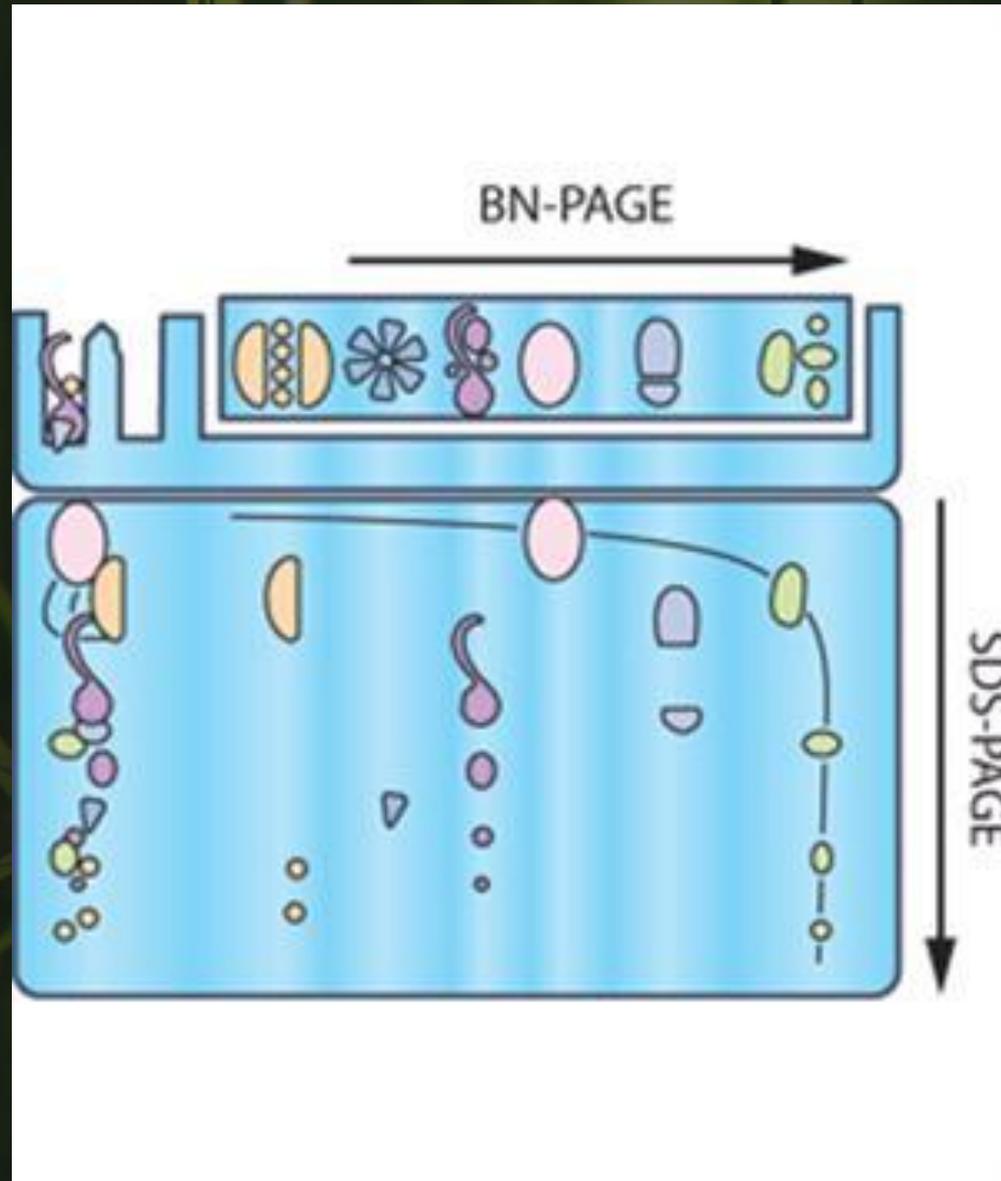


The proteins stopped migrating because they've reached their isoelectric point at a unique pH level.

- Orange circle = Isoelectric point at pH 7.5
- Red circle = Isoelectric point at pH 6.8
- Yellow circle = Isoelectric point at pH 8.5
- Purple circle = Isoelectric point at pH 10.1
- Green circle = Isoelectric point at pH 5.6

2.3 Isoelectroenfoque

Permite separar proteínas según su punto isoelectrico



Electroforesis
bidimensional

3) Espectrometría de masas

3.1 MALDI-TOF

Matrix Attached Lasser Desorption-Ionization
Time Of Flight

Permite descomponer a las proteínas en fragmentos pequeños para determinar su secuencia

3) Espectrometría de masas

3.1 LC-MS/MS-TOF

Liquid Chromatography Masses / Masses
Time Of Flight

Permite descomponer a las proteínas en fragmentos pequeños para determinar su secuencia de acuerdo a la masa de sus componentes.



