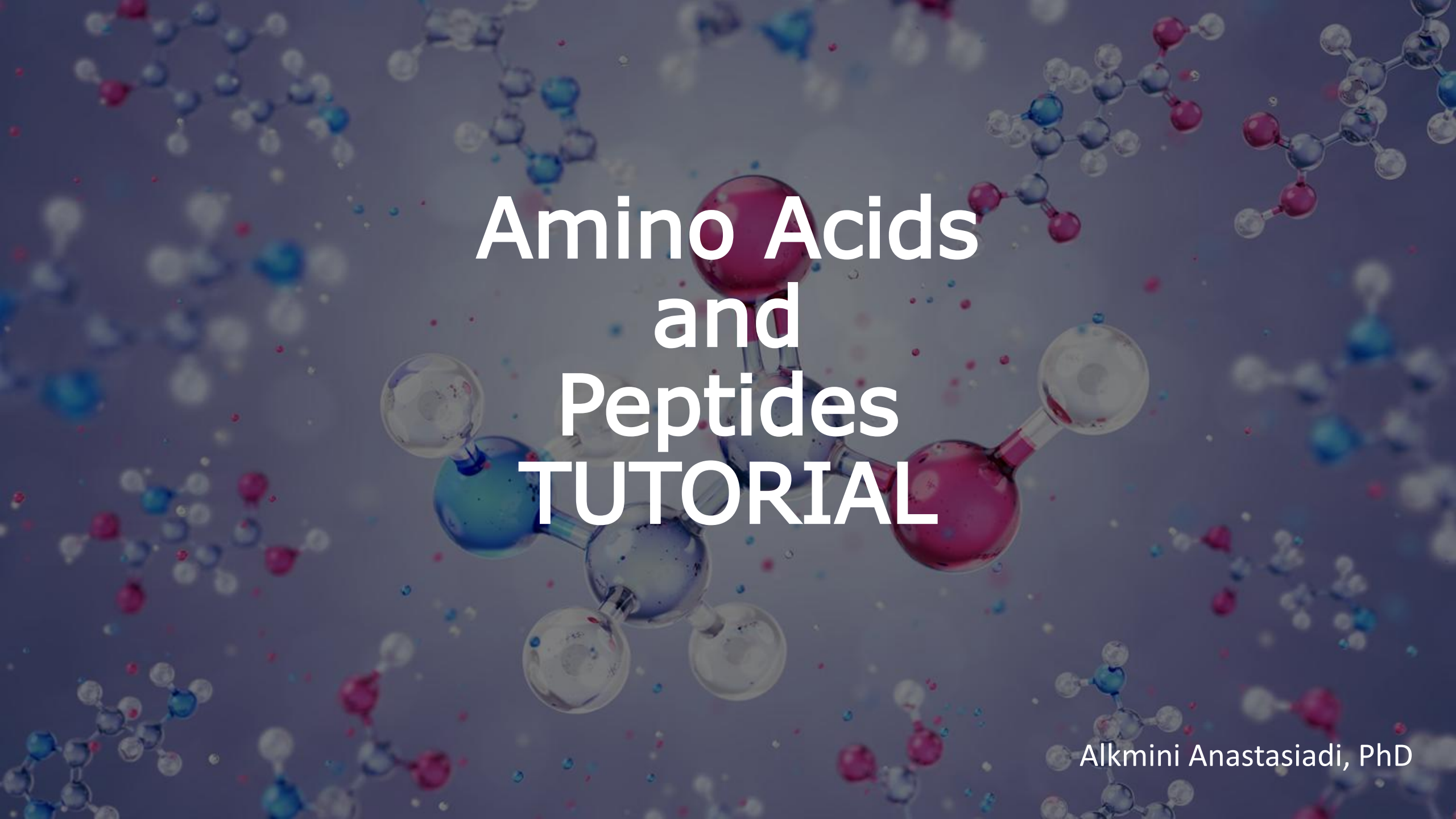


The background is a dark blue-grey gradient filled with numerous molecular models. These models consist of small spheres (atoms) in white, blue, and red, connected by thin lines (bonds). Some models are sharp and in focus, while others are blurred, creating a sense of depth. In the center, there is a larger, more detailed model of an amino acid, showing a central carbon atom (grey) bonded to a hydrogen atom (white), an amino group (blue and red), a carboxyl group (red and white), and a variable side chain (blue and white).

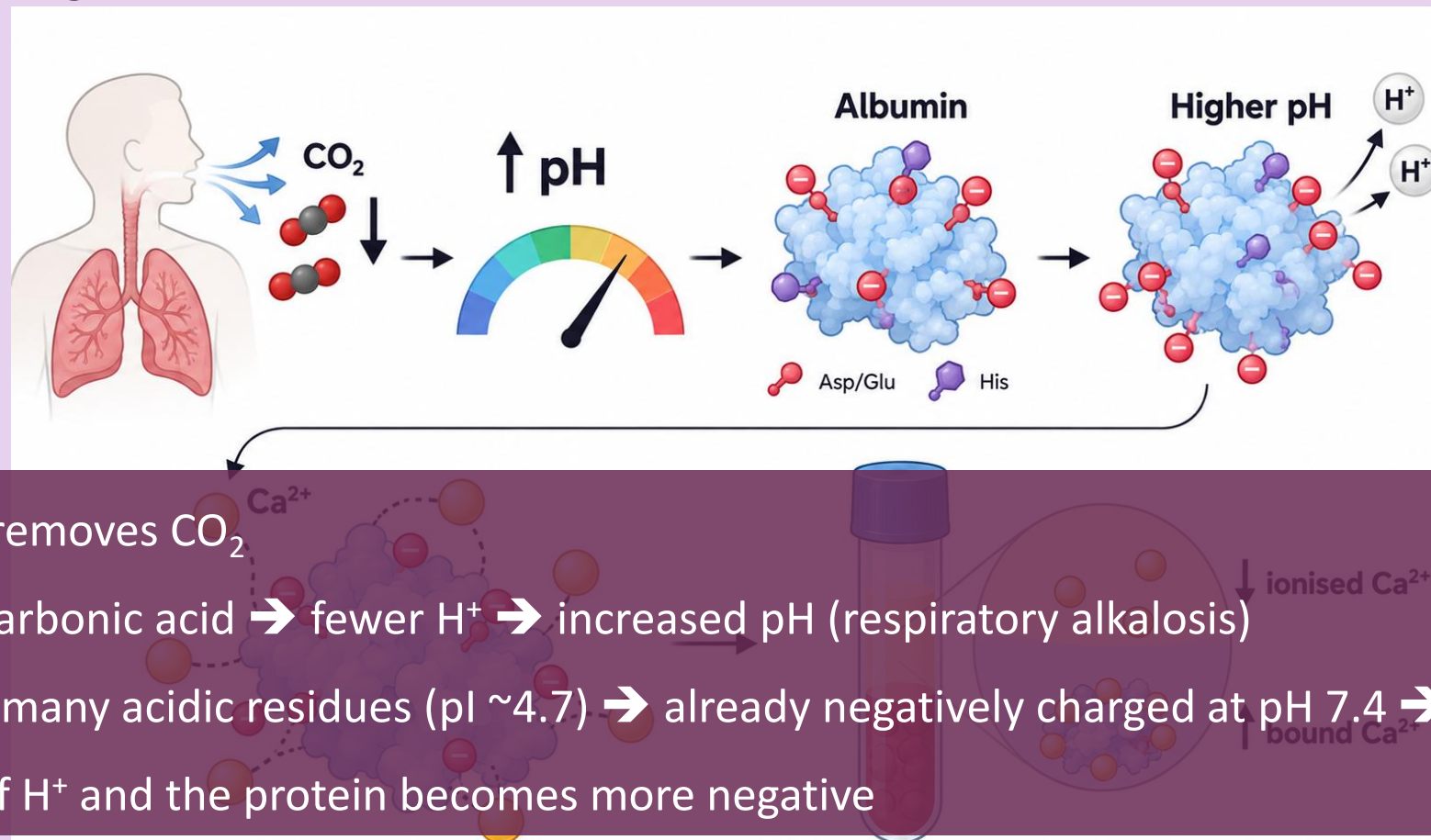
Amino Acids and Peptides TUTORIAL

Alkmini Anastasiadi, PhD

Intrinsic Characteristics of Amino Acids

Acid-Base Properties

A student hyperventilates before an exam and within minutes reports tingling around her mouth and in her finger

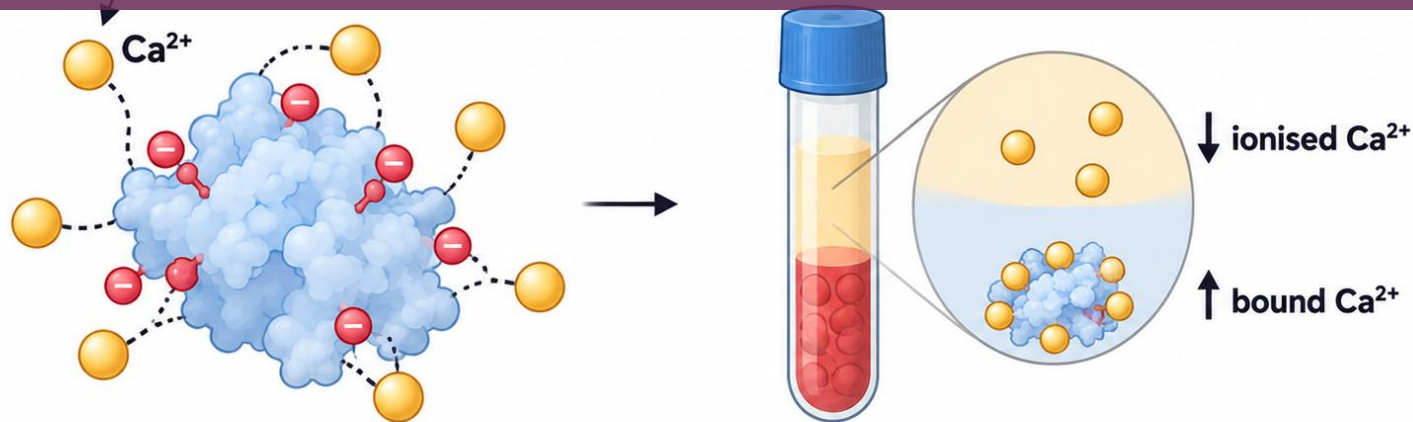


Intrinsic Characteristics of Amino Acids

Acid-Base Properties

A student hyperventilates before an exam and within minutes reports tingling around her mouth and in her finger

4. Calcium binds mainly to carboxylate groups, and in effect H^+ and Ca^{2+} compete for the same sites. When H^+ leaves, Ca^{2+} moves in.
5. Calcium is still there but it is mainly in its bound form (total calcium = normal / ionized Ca^{2+} = lower)
6. Since calcium neutralizes negative charges on the outer surface of nerve membranes and keeps Na^+ channels away from their activation threshold $\rightarrow$ less free $\text{Ca}^{2+} \rightarrow$ hyperexcitable neurons $\rightarrow$ tingling



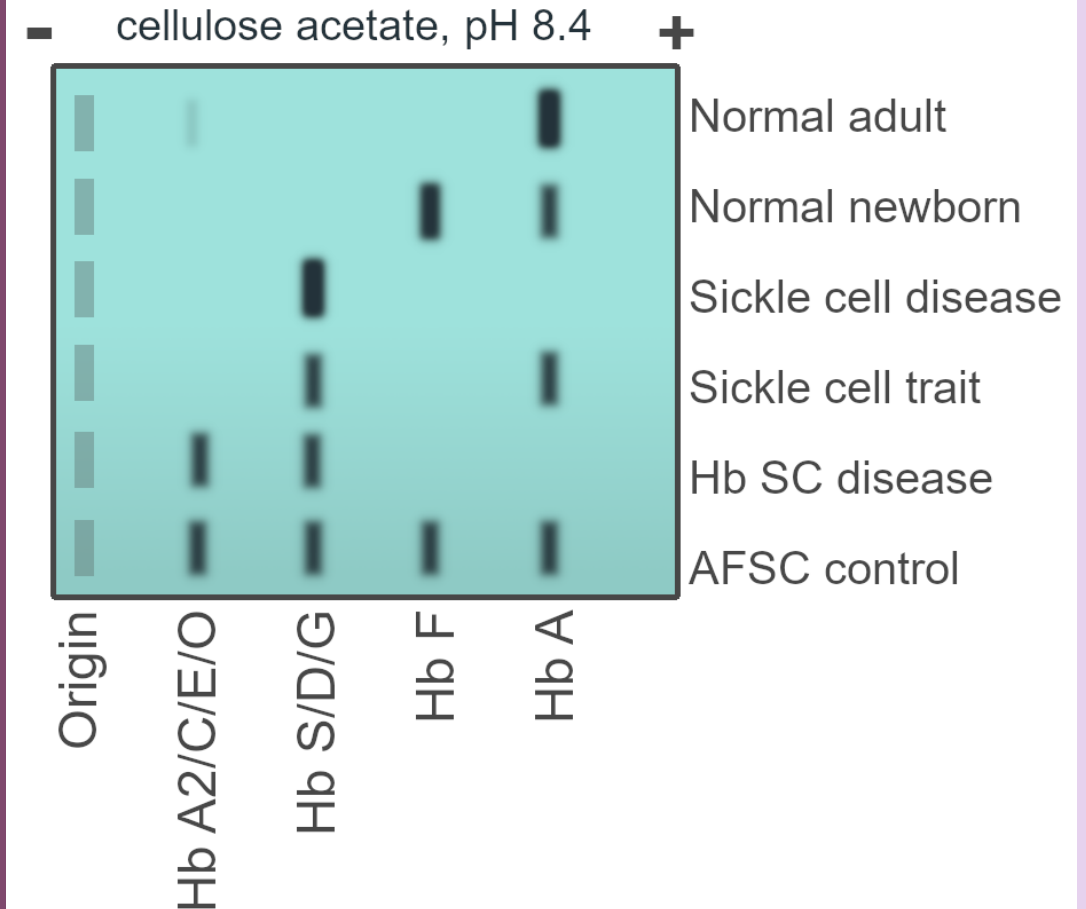
Intrinsic Characteristics of Amino Acids

Acid-Base Properties

Can we “take advantage” of these properties for diagnostic purposes?

- All the common hemoglobins are tetramers of almost identical size (about 64 kDa), so size does not separate them → they differ in their net charge
- Alkaline electrophoresis → pH ~ 8.4 = above the pI of all common hemoglobins → **all Hb types are negatively charged**
- We apply an electric field → each protein migrates according to its net charge towards the anode (+) → the further the pH from the pI, the larger the charge and the faster the movement

Hemoglobin electrophoresis

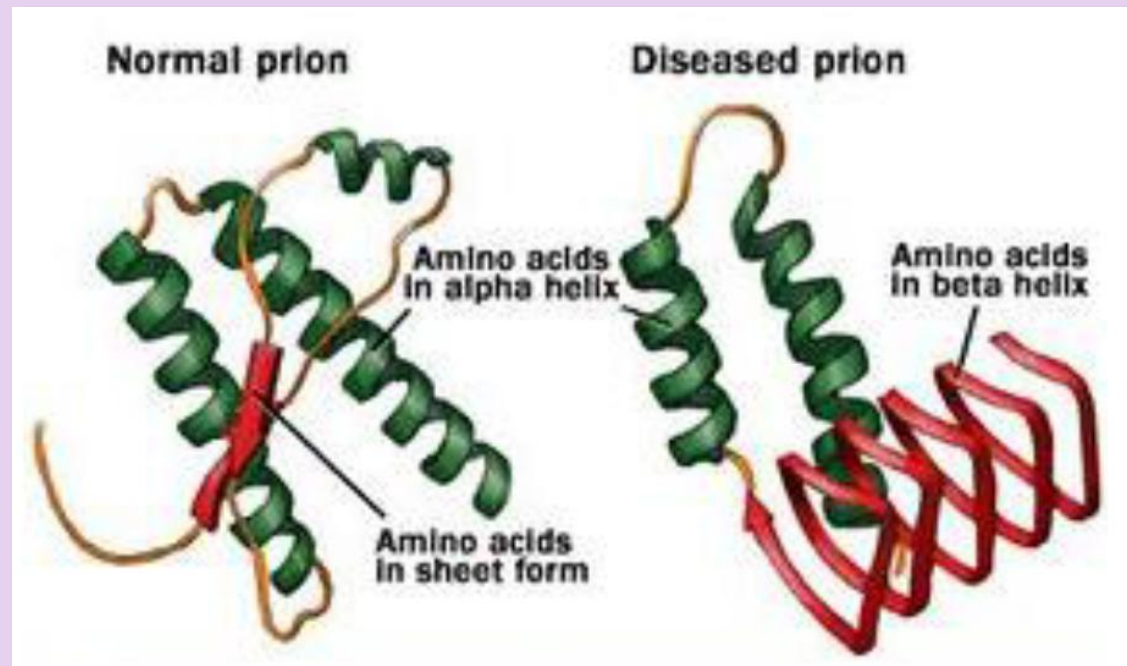


Protein Structure

Secondary Structure

Can a change in secondary structure lead to pathology?

- Normal cellular prion protein PrP^c is on the surface of neurons, anchored to the membrane
→ Its folded domain = mostly α -helices and a really short β -strand region
- Pathological prion protein PrP^{Sc} has the exact same amino acid sequence but an extended region of β -sheets

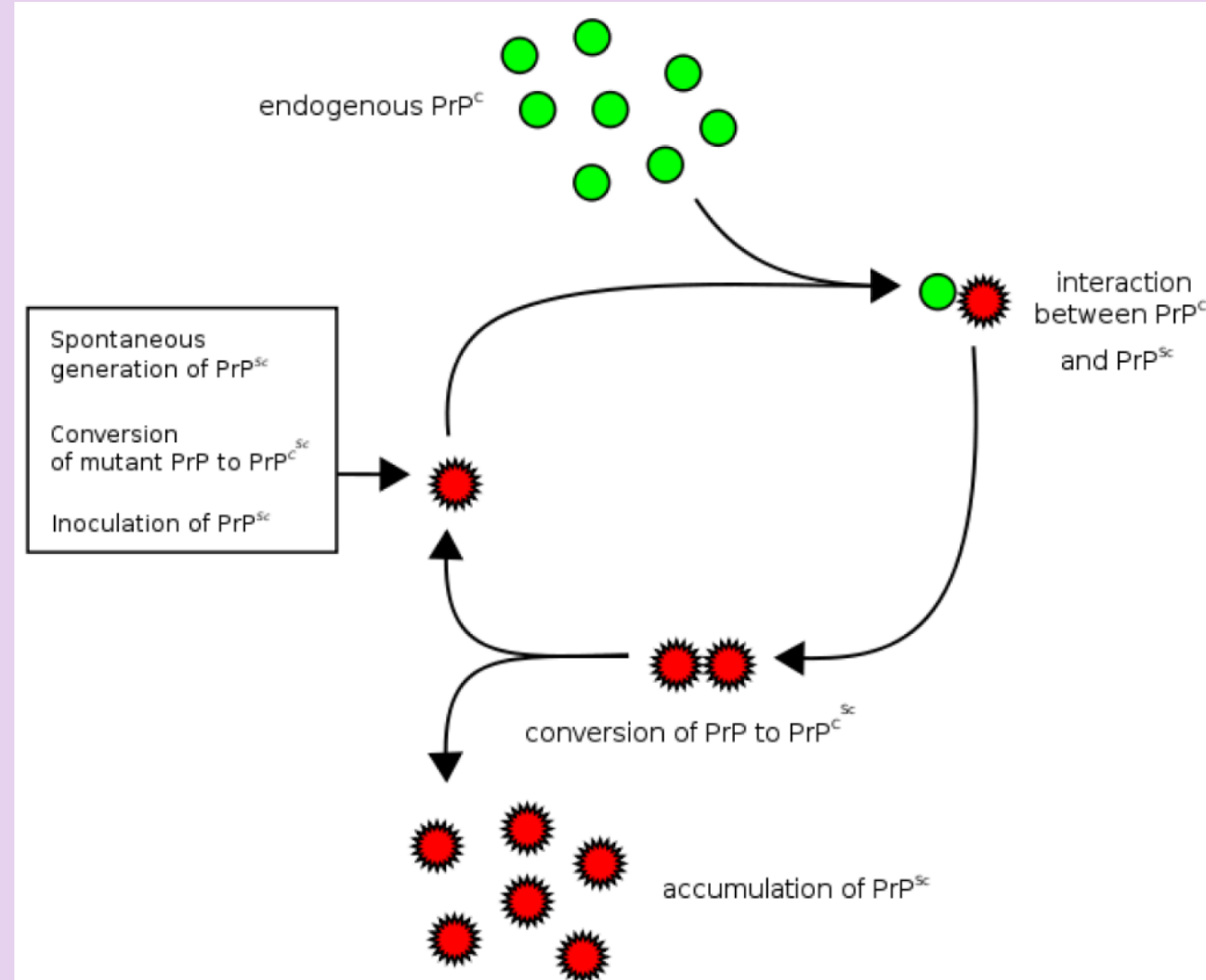


Protein Structure

Secondary Structure

Can a change in secondary structure lead to pathology?

- The β -sheet edge of the pathological protein (PrP^{Sc}) pairs with the normal PrP^{C} and **forces it into the same shape**
- We have an exponential increase in pathological molecules
- They form oligomers and aggregates that lead to neurodegeneration = **Creutzfeldt–Jakob disease** (CJD)



Protein Structure

Secondary Structure

Can a change in secondary structure lead to pathology?

- The reason for the initial appearance of PrP^{Sc} :
 - Random misfolding, usually in old age ($\sim 85\%$)
 - Mutations predisposes PrP^{c} to switch to PrP^{Sc} more easily ($\sim 10\text{-}15\%$). Again, the sequence between PrP^{c} and PrP^{Sc} is the same
 - Acquired: mainly from food (Bovine spongiform encephalopathy aka mad cow disease $\rightarrow$ CJD)

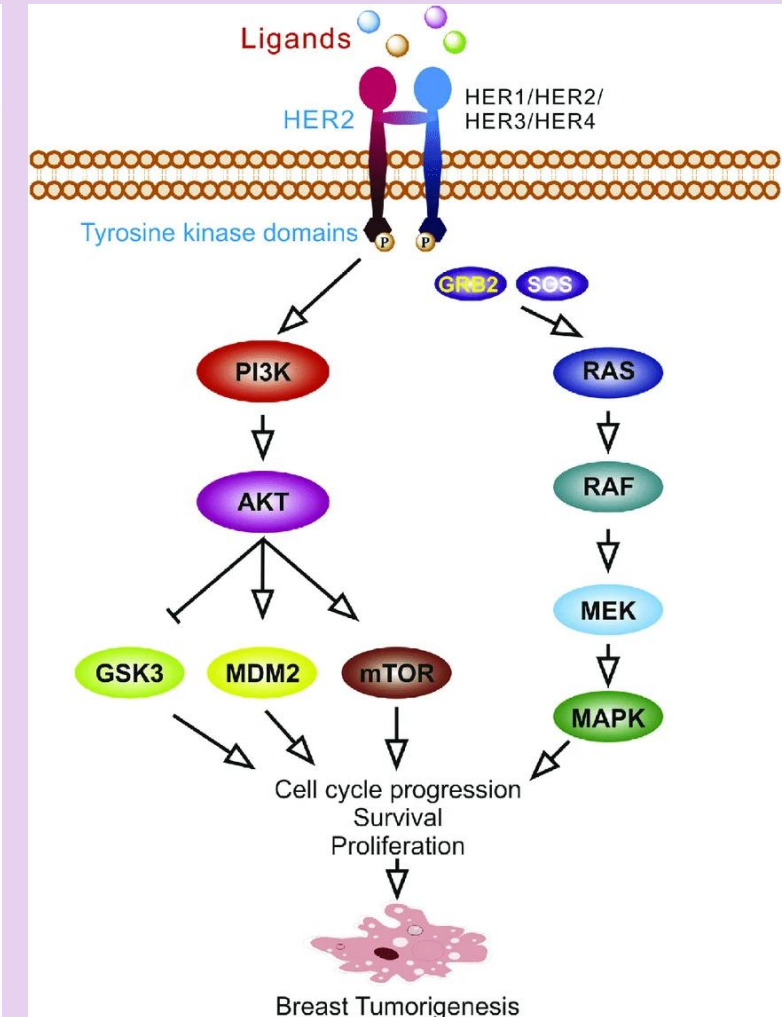
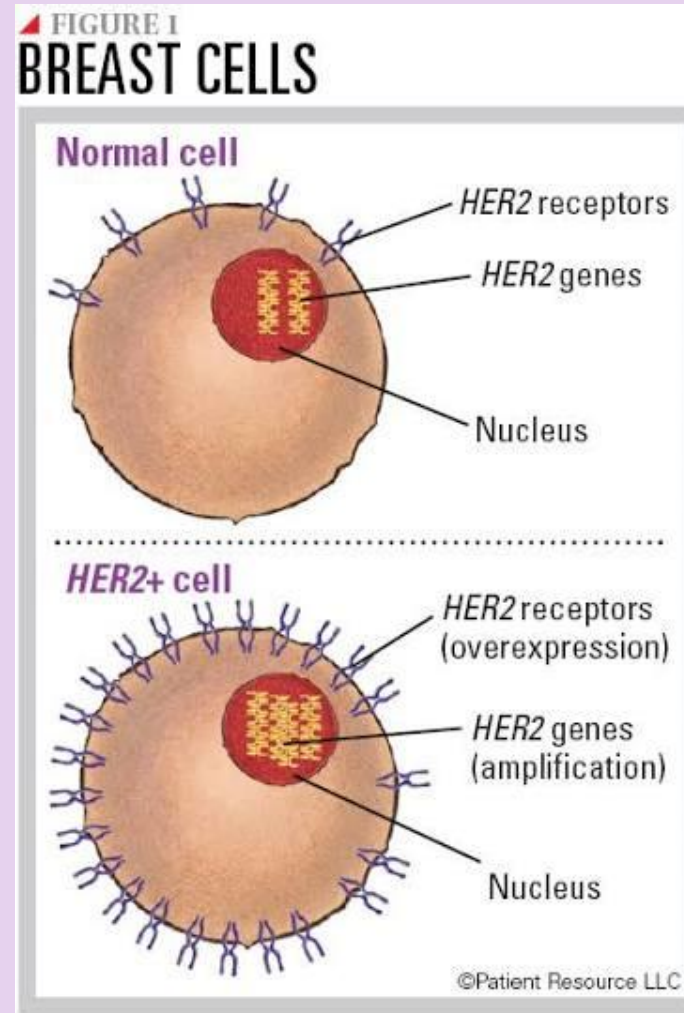


Protein Structure

Quaternary Structure

Can we therapeutically target the quaternary structure?

- In some types of breast cancer → overexpression of HER2 receptors
- HER2 belongs to a family of receptors that when a ligand binds to them they form dimers and start a signaling cascade → cell cycle progression, cell survival, cell proliferation
- When in abundance → continuous signaling → tumorigenesis



Protein Structure

Quaternary Structure

Can we therapeutically target the quaternary structure?

- Trastuzumab and Pertuzumab → antibodies that target different regions that do not allow the dimerization of HER2 with other HER receptors → anti-HER2 targeted therapy

