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# Folded

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# Primary Protein Structure

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[https://upload.wikimedia.org/wikipedia/commons/3/38/Protein\\_primary\\_structure.svg](https://upload.wikimedia.org/wikipedia/commons/3/38/Protein_primary_structure.svg)

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# Secondary / Tertiary Protein Structure

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<https://www.boundless.com/biology/textbooks/boundless-biology-textbook/biological-macromolecules-3/proteins-56/protein-structure-304-11437/>

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# Protein Folding Animation

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[https://www.youtube.com/watch?v=erOP76\\_qLWA](https://www.youtube.com/watch?v=erOP76_qLWA)

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# Chaperones

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The chaperones are responsible for:

- ❖ *de-novo* folding of new proteins.
- ❖ refolding of mature proteins.
- ❖ ensuring that terminally abnormal proteins are destroyed.

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I. Chaperonins provide **solitude** for proteins to find the right fold.

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# Moses

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But the most valuable part of Moses' fitting for his lifework was that which he received as a shepherd....In the solitude of the mountains he learned that which all his instruction in the king's palace was unable to impart to him—simple, unwavering faith and a constant trust in the Lord.

—*Counsels to Parents, Teachers and Students*, p. 406

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# Moses

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In the solemn grandeur of the everlasting hills he beheld the majesty of the Most High, and...realized how powerless and insignificant were the gods of Egypt. Everywhere the Creator's name was written....Here his pride and self-sufficiency were swept away...the results of the ease and luxury of Egypt disappeared. Moses became patient, reverent, and humble...yet strong in faith in the mighty God of Jacob.

—Conflict and Courage, p. 86



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## 2. Mis-folded Proteins Cause Disease

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# Protein Folding Energy Diagram

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<https://www.quora.com/Do-misfolded-proteins-have-higher-entropy-than-regularly-folded-proteins>

*Image: F.U. Hartl, A. Bracher, M. Hayer-Hartl. July 2011. Molecular chaperones in protein folding and proteostasis. Nature 475, 324–332; doi:10.1038/nature10317*

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# Mis-folded Proteins Cause Disease

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- ❖ **Sickle Cell Anemia** — point mutation results in replacing Glu for Val in the  $\beta$ -chain in hemoglobin, disrupting folding
- ❖ **Cystic Fibrosis** — mis-folded CF conductance regulator protein (CFRP) due to a single amino acid omission (Phe)
- ❖ **Neurodegenerative Diseases** — protein aggregation ( $A\beta$ , tau, prions,  $\alpha$ -synuclein, etc.)
  - ❖ Alzheimer's
  - ❖ Parkinson's
  - ❖ Huntington's

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# Paul

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- ❖ But Saul was ravaging the church, and entering house after house, he dragged off men and women and committed them to prison. —Acts 8:3
- ❖ But the Lord said to him, “Go, for he is a chosen instrument of mine to carry my name before the Gentiles and kings and the children of Israel. For I will show him how much he must suffer for the sake of my name.” —Acts 9:10

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3. Mis-folded protein cause other proteins to mis-fold.

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# A Bad Report

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And they told him, “We came to the land to which you sent us. It flows with milk and honey, and this is its fruit. **However**, the people who dwell in the land are strong, and the cities are fortified and very large. And besides, we saw the descendants of Anak there. The Amalekites dwell in the land of the Negeb. The Hittites, the Jebusites, and the Amorites dwell in the hill country. And the Canaanites dwell by the sea, and along the Jordan.”

—Numbers 13:27-29

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# Doubt Inspires Doubt

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Then the men who had gone up with him said, **“We are not able to go up against the people, for they are stronger than we are.”** So they brought to the people of Israel a bad report of the land that they had spied out.

—Numbers 13:31-32

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# Hezekiah

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- ❖ Do not let your God in whom you trust deceive you by promising that Jerusalem will not be given into the hand of the king of Assyria. Behold, you have heard what the kings of Assyria have done to all lands, devoting them to destruction. And shall you be delivered?

—2 Kings 19:10-11



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# Hezekiah

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- ❖ Hezekiah received the letter from the hand of the messengers and read it; and Hezekiah went up to the house of the Lord and spread it before the Lord....So now, O Lord our God, save us, please, from his hand, that all the kingdoms of the earth may know that you, O Lord, are God alone.”

—2 Kings 19:14, 19

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# Faith Inspires Faith

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- ❖ **Nothing more quickly inspires faith than the exercise of faith.** The king of Judah had prepared for the coming storm; and now, confident that the prophecy against the Assyrians would be fulfilled, he stayed his soul upon God. “And the people rested themselves upon the words of Hezekiah.” 2 Chronicles 32:8.

—Prophets and Kings, p. 351

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# Inspire Faith

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- ❖ **Every life is a light that brightens and cheers the pathway of others, or a dark and desolating influence that tends toward despair and ruin. We lead others either upward to happiness and immortal life, or downward to sorrow and eternal death. And if by our deeds we strengthen or force into activity the evil powers of those around us, we share their sin.**

—Prophets and Kings, p. 94

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4. Proteins that don't find their "native" state must enter the chaperone again.

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# Abraham

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And it came to pass...that he said to Sarai his wife, “Indeed I know that you are a woman of beautiful countenance. Therefore it will happen, when the Egyptians see you, that they will say, ‘This is his wife’; and they will kill me, but they will let you live. **Please say you are my sister, that it may be well with me for your sake, and that I may live because of you.**”

—Genesis 12:11-13

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# Abraham

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And Abraham journeyed ...and dwelt between Kadesh and Shur, and stayed in Gerar. **Now Abraham said of Sarah his wife, “She is my sister.”** And Abimelech king of Gerar sent and took Sarah.

—Genesis 20:1-2

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# Abraham

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God had called Abraham to be the father of the faithful, and his life was to stand as an example of faith to succeeding generations. **But his faith had not been perfect.** He had shown distrust of God in concealing the fact that Sarah was his wife (*twice*), and again in his marriage with Hagar. **That he might reach the highest standard, God subjected him to another test, the closest which man was ever called to endure.**

—*Patriarchs and Prophets*, p. 147, emphasis added

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# The Closest Test

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He said, “Take your son, your only son Isaac, whom you love, and go to the land of Moriah, and offer him there as a burnt offering on one of the mountains of which I shall tell you.”

—Genesis 22:2



- ❖ **Proteins that don't find their “native” state must enter the chaperone again.**
- ❖ The Lord brings his children over the same ground again and again, increasing the pressure until perfect humility fills the mind, and the character is transformed; then they are victorious over self, and in harmony with Christ and the Spirit of heaven.

—*Review and Herald*, April 10, 1894

- ❖ Chaperonins have a hydrophobic region at the entry point so that proteins that are mis-folded (have hydrophobic groups on the outside and hydrophilic groups on the inside) are attracted to the chaperonin.
- ❖ Jesus: And Jesus answered them, “Those who are well have no need of a physician, but those who are sick. I have not come to call the righteous but sinners to repentance.”

—Luke 5:31-32

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# Why doesn't God give up?

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**“....The nations who have heard your fame will say, ‘It is because the Lord was not able to bring this people into the land that he swore to give to them that he has killed them in the wilderness.’”**

**—Numbers 14:4, 11-20**

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**5. Proteins visit the chaperonin for routine maintenance.**

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## Routine Maintenance

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Each morning consecrate yourself to God for that day. Surrender all your plans to Him, to be carried out or given up as His providence shall indicate. Thus day by day you may be giving your life into the hands of God, and thus your life will be molded more and more after the life of Christ.

—Steps to Christ, p. 70

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# Lessons from Protein Folding

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1. Chaperonins provide a place of solitude for the protein to find the correct fold.
2. Mis-folded proteins cause disease.
3. Mis-folded proteins cause other proteins to mis-fold.
4. Proteins that don't find their native shape, must enter the chaperonin again.
5. Proteins return to the chaperoning for routine maintenance.