

~1976



[https://en.wikipedia.org/wiki/Apple\\_I](https://en.wikipedia.org/wiki/Apple_I)



<https://en.wikipedia.org/wiki/Kraftwerk>

*Computer World* (German: *Computerwelt*) is the eighth studio album by German electronic music band Kraftwerk, released on 10 May 1981. The album deals with the themes of the rise of computers within society.

[https://en.wikipedia.org/wiki/Computer\\_World](https://en.wikipedia.org/wiki/Computer_World)



## Redesigning life

The promise of synthetic biology



It was hard for any listener not to fall under his spell. He spoke slowly and precisely in a lingering South African accent, his sentences long and perfectly constructed and often ending with a joke. Insights into the nature of the cell would alternate with his playful inventions, like Occam's broom — “to sweep under the carpet what you must to leave your hypotheses consistent” — or Avocado’s number, “the number of atoms in a guacamole.”

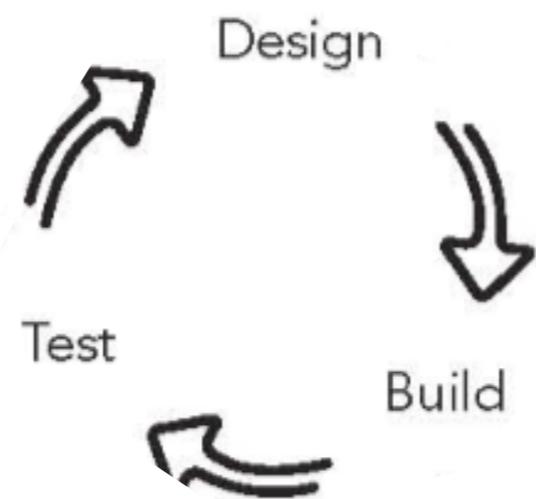
The New York Times

## Sydney Brenner, a Decipherer of the Genetic Code, Is Dead at 92

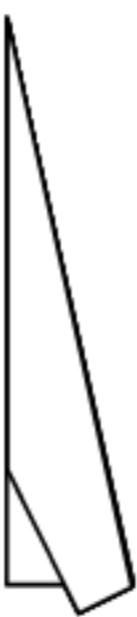
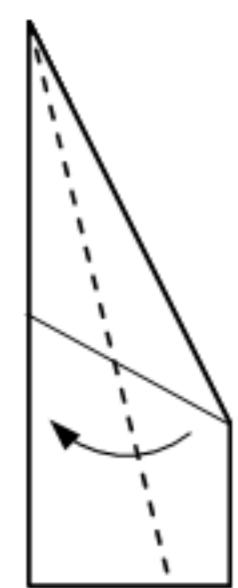
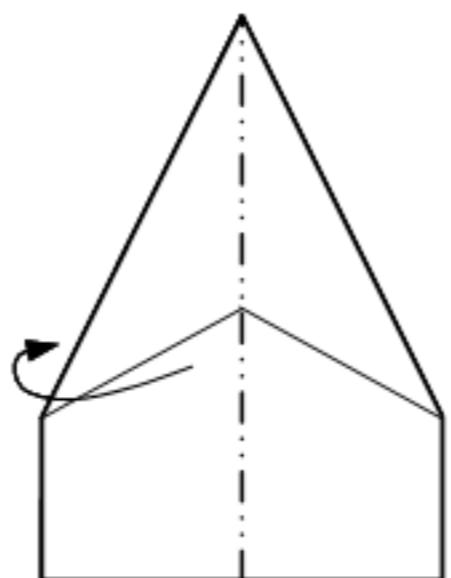
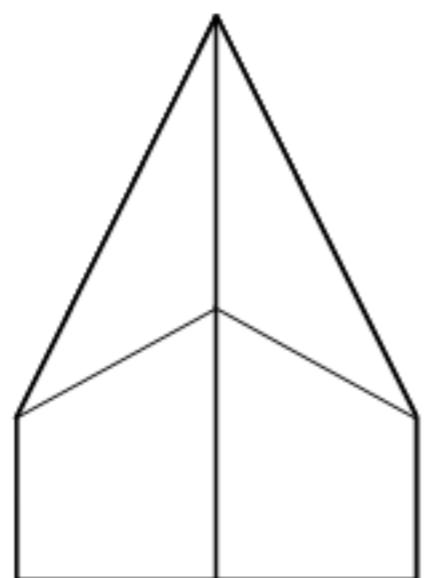
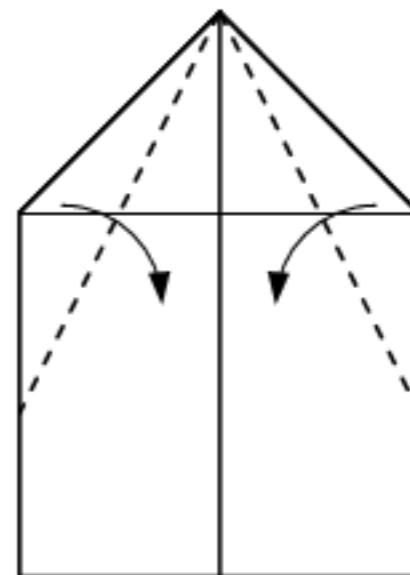
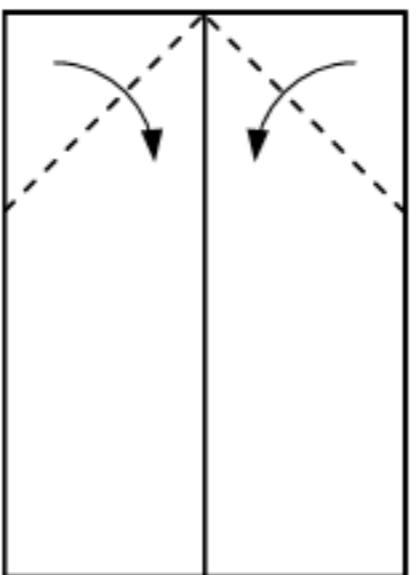
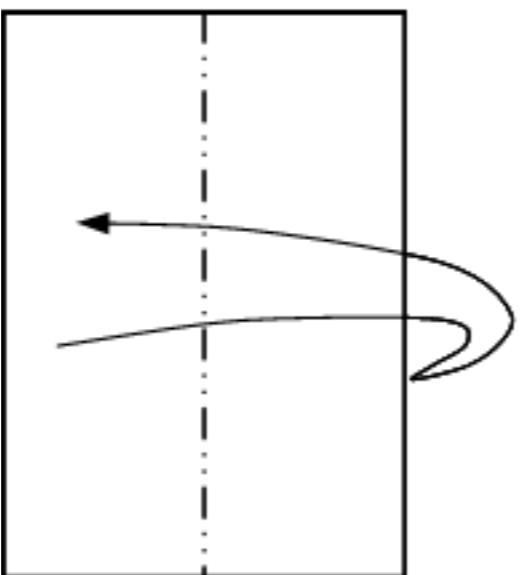


# Design, build, & test week

(model) (make) (measure)



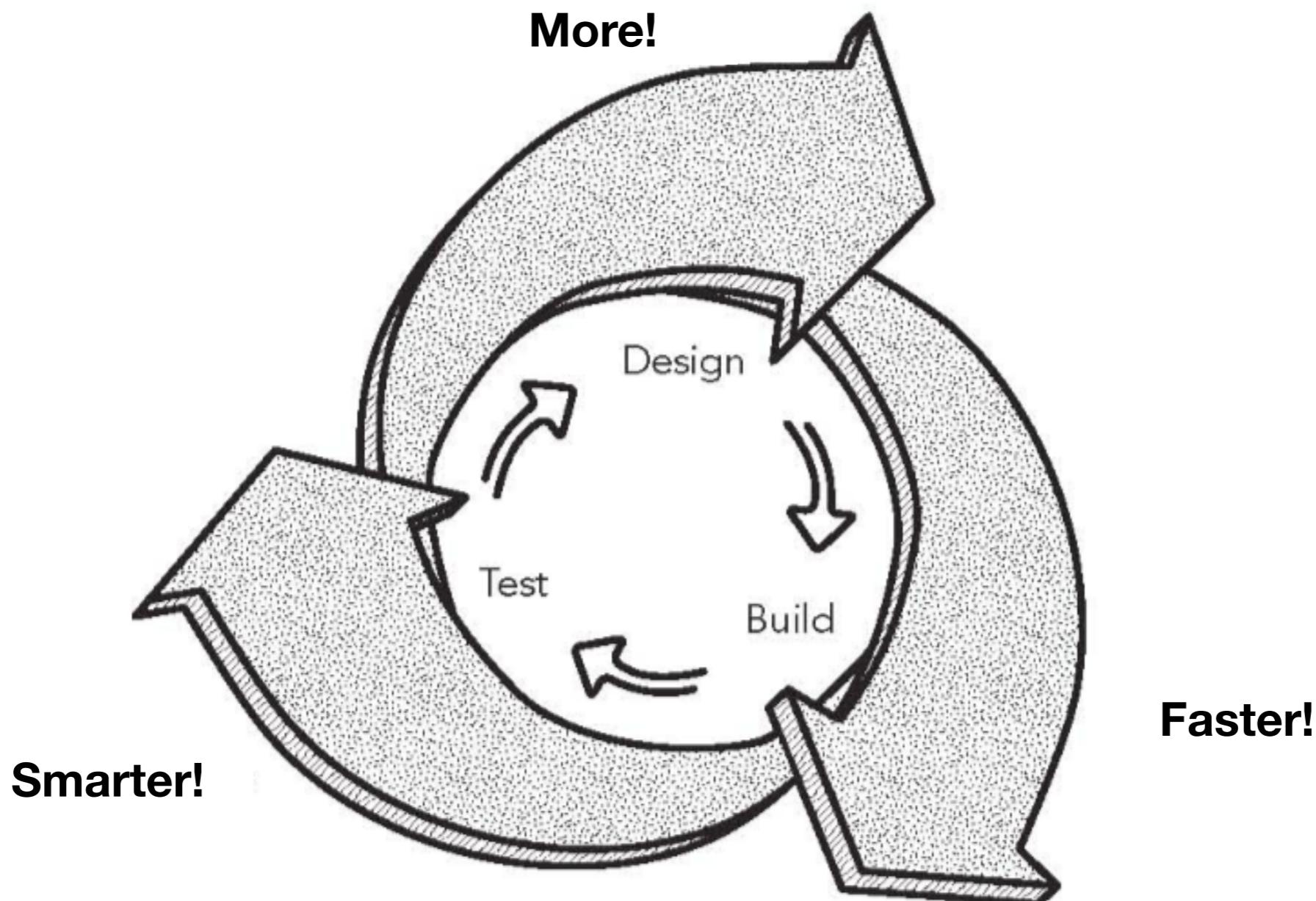
*Graphic adapted from "Synthetic Aesthetics" MIT Press (2014)*



What happens when you  
can't see and feel, etc?

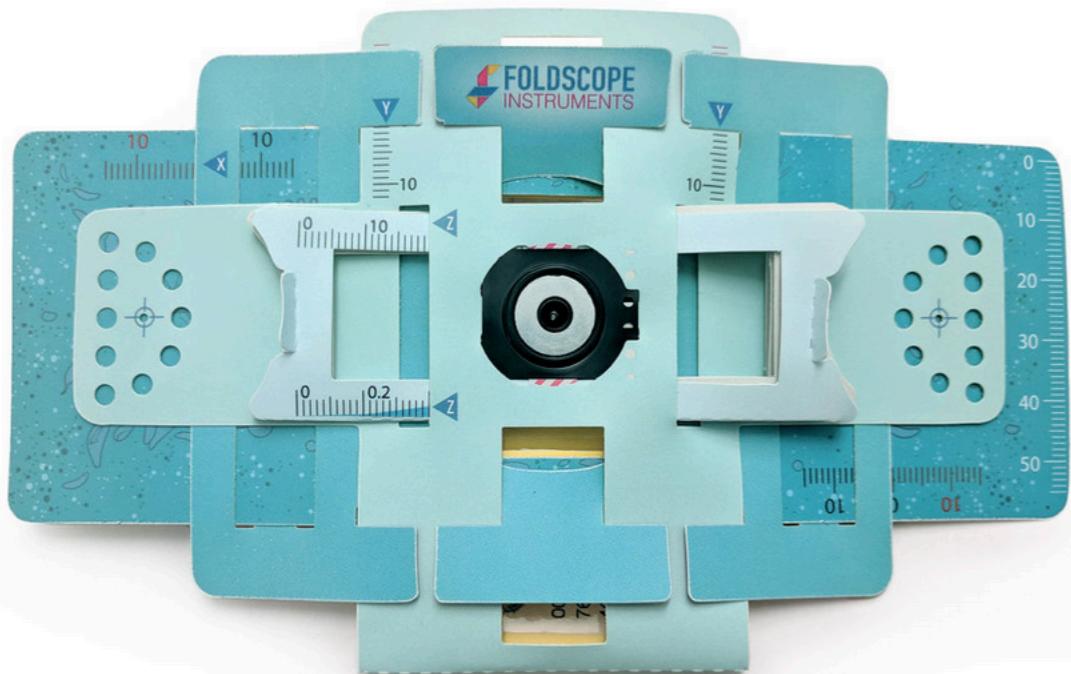
# Design, build, & test week

(model) (make) (measure)



*Graphic adapted from "Synthetic Aesthetics" MIT Press (2014)*

# Engineer for biology to see better...



## THE PAPER MICROSCOPE

Foldscope is the ultra-affordable, paper microscope that you assemble yourself. Designed to be inexpensive, durable, and to give optical quality similar to conventional research microscopes (magnification of 140X and 2 micron resolution), Foldscope brings hands-on microscopy to new places!

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#knowyourself  
#tools  
#backtonature  
#BioEquality

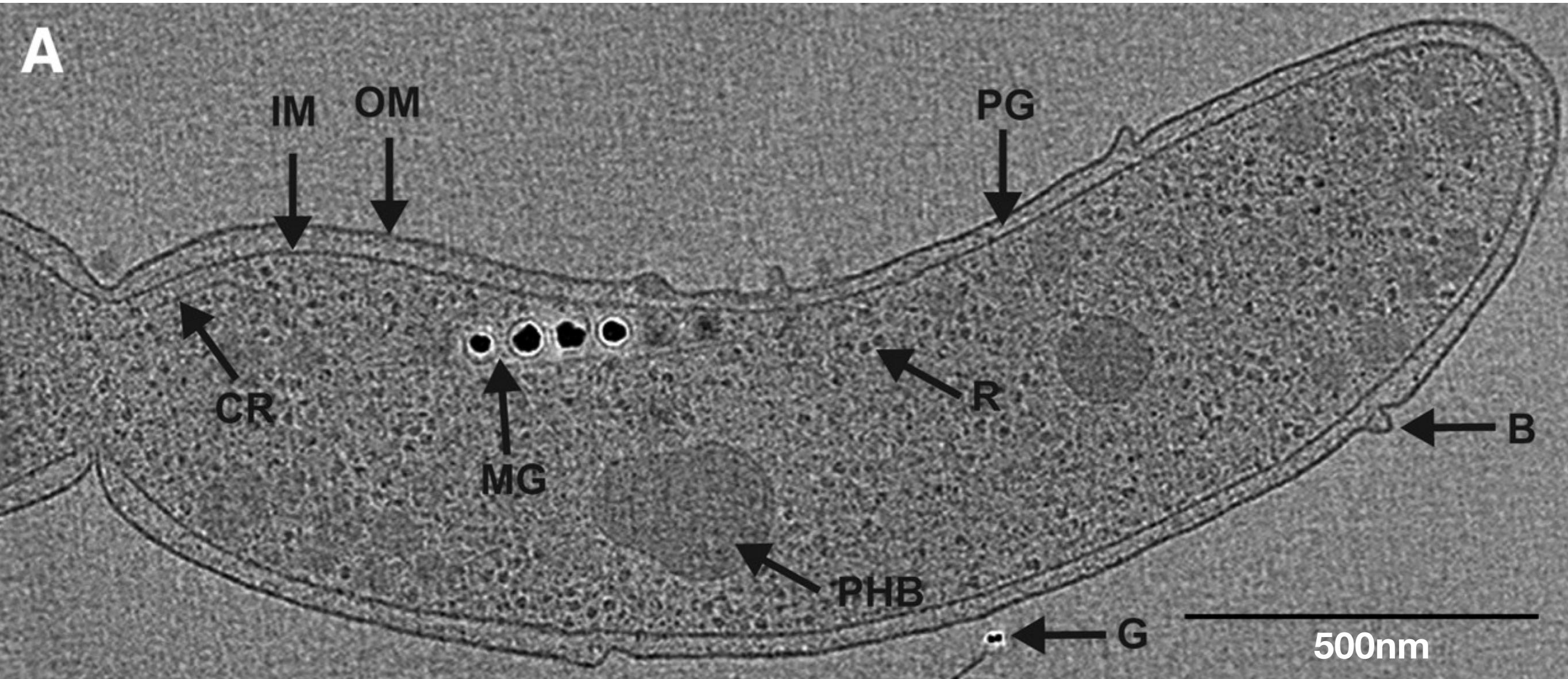
# Engineer for biology to see better...



<https://youtu.be/pbGRZZwX9Q8>

<https://jensenlab.caltech.edu/movies/>

# Engineer for biology to see better...



OK... but what about the molecules  
that make the cells themselves...



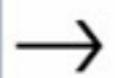
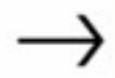
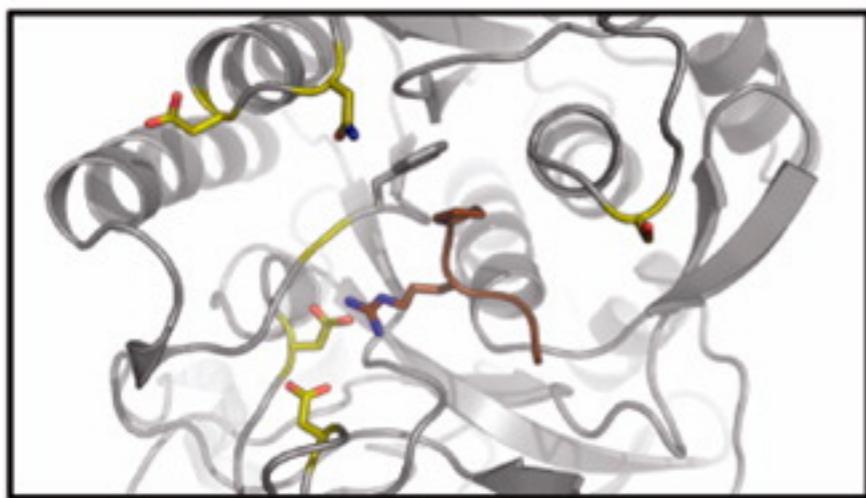
“An ideal oral enzyme therapeutic (OET) for celiac disease would have the following traits:

- (1) optimal activity at the pH of the stomach after a meal (in the range of 2–4);(7)
- (2) resistance to common digestive proteases;
- (3) facile recombinant production in a soluble form; and
- (4) specificity for the common proline–glutamine (PQ) motif found in immunogenic  $\alpha$ -gliadin oligopeptides.(6, 8)”

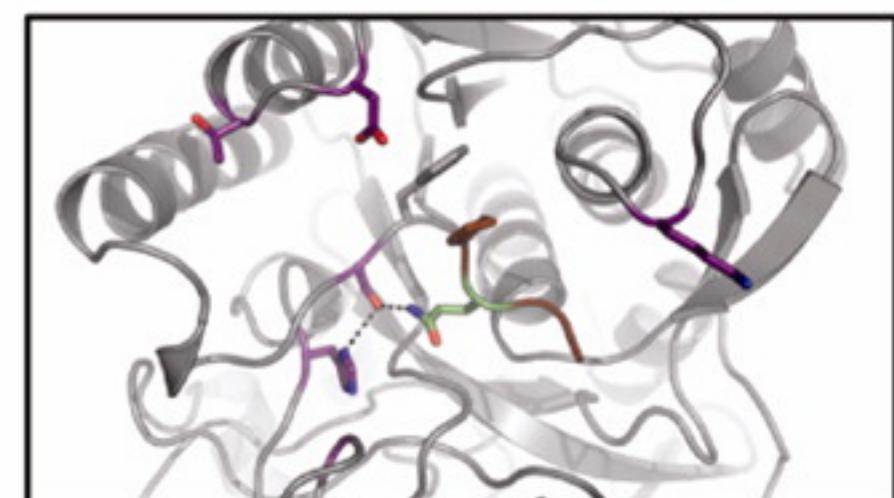
**Gordon, Sydney R., et al. "[Computational design of an  \$\alpha\$ -gliadin peptidase.](#)"**  
*Journal of the American Chemical Society* 134.50 (2012): 20513-20520.

# 7 mutations provide solution...

Native Enzyme



Engineered Enzyme



..xxPRxx..  $k_{cat}/K_M = 132 \text{ M}^{-1} \text{s}^{-1}$

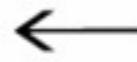


Native Motif



..xxPRxx.. no activity

..xxPQxx..  $k_{cat}/K_M = 5 \text{ M}^{-1} \text{s}^{-1}$



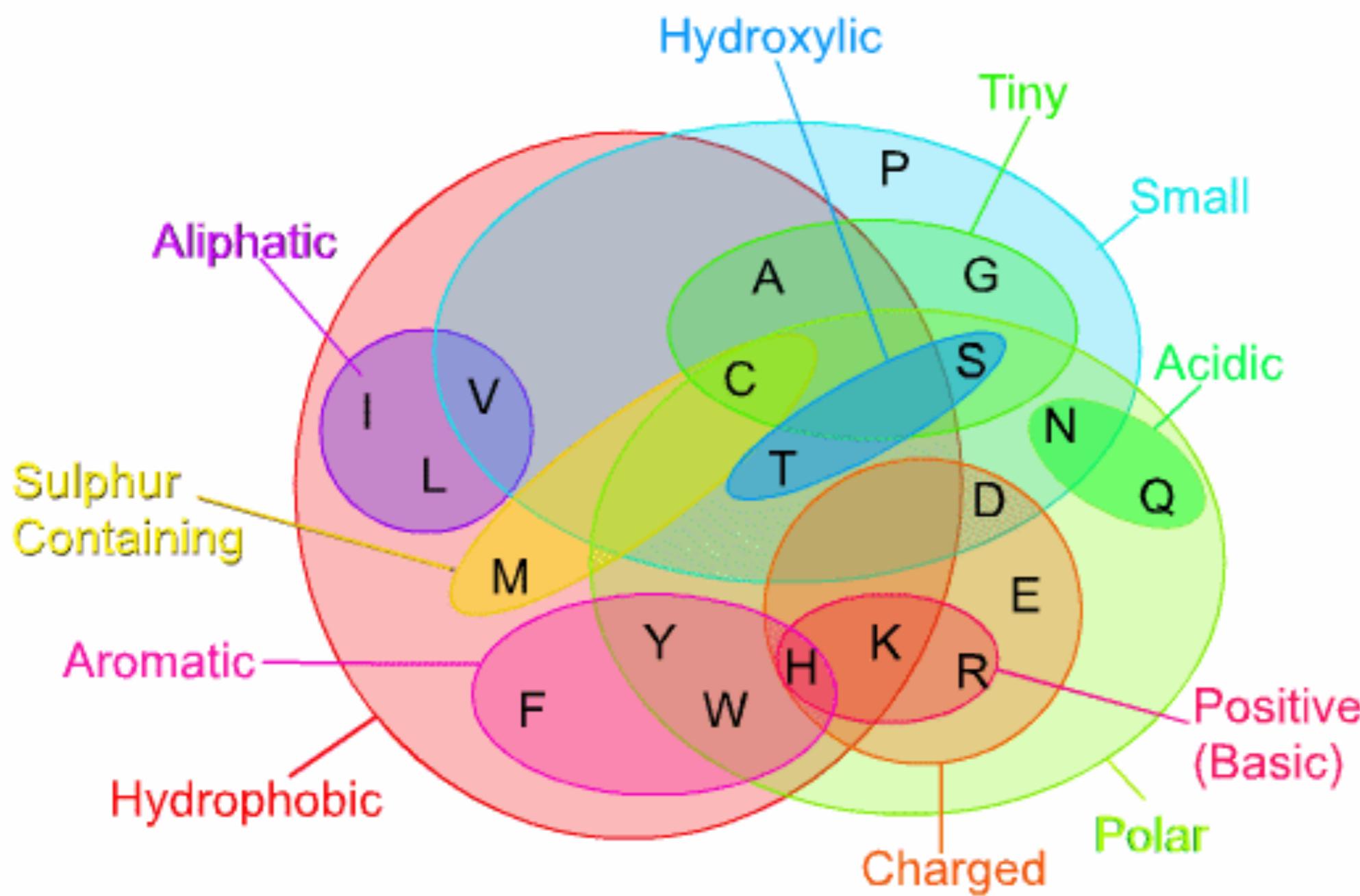
$\alpha$ -gliadin Motif



..xxPQxx..  $k_{cat}/K_M = 569 \text{ M}^{-1} \text{s}^{-1}$

V119D, S262K, N291D, D293T, G319S, D358G, D368H

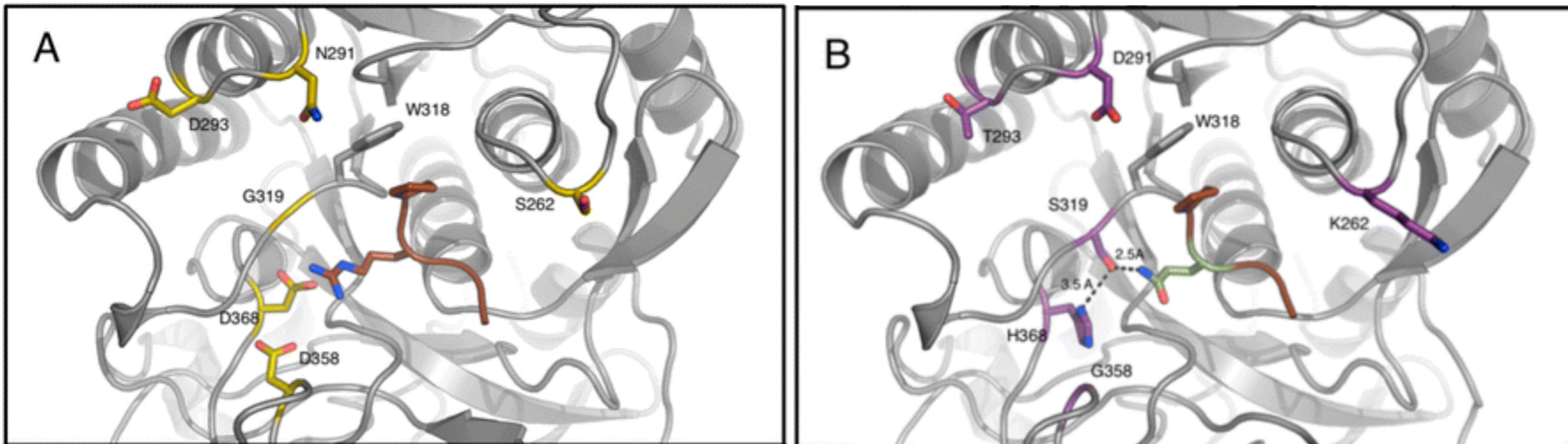
Gordon, Sydney R., et al. "[Computational design of an  \$\alpha\$ -gliadin peptidase.](#)"  
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## Amino Acids

- A** alanine (ala)
- R** arginine (arg)
- N** asparagine (asn)
- D** aspartic acid (asp)
- C** cysteine (cys)
- Q** glutamine (gln)
- E** glutamic acid (glu)
- G** glycine (gly)
- H** histidine (his)
- I** isoleucine (ile)
- L** leucine (leu)
- K** lysine (lys)
- M** methionine (met)
- F** phenylalanine (phe)
- P** proline (pro)
- S** serine (ser)
- T** threonine (thr)
- W** tryptophan (trp)
- Y** tyrosine (tyr)

# “Eats” collagen (PR) v. “Eats” gluten (PQ)



V119D, S262K, N291D, D293T, G319S, D358G, D368H

- V119D (not shown) I in propeptide domain, does not affect catalytic activity
- S262K (S73K) I Likely introduces interaction other residues outside catalytic site
- N291D (N102D)I Likely introduces interaction other residues outside catalytic site
- D293T (D104T) I Likely introduces interaction other residues outside catalytic site
- G319S (G130S) I New H bond w/ Q at P1 position
- D358G (D169G) I New H bond w/ Q at P1 position
- D368H (D179H) I New H bond w/ Q at P1 position

Gordon, Sydney R., et al. "[Computational design of an  \$\alpha\$ -gliadin peptidase](#)."  
*Journal of the American Chemical Society* 134.50 (2012): 20513-20520.

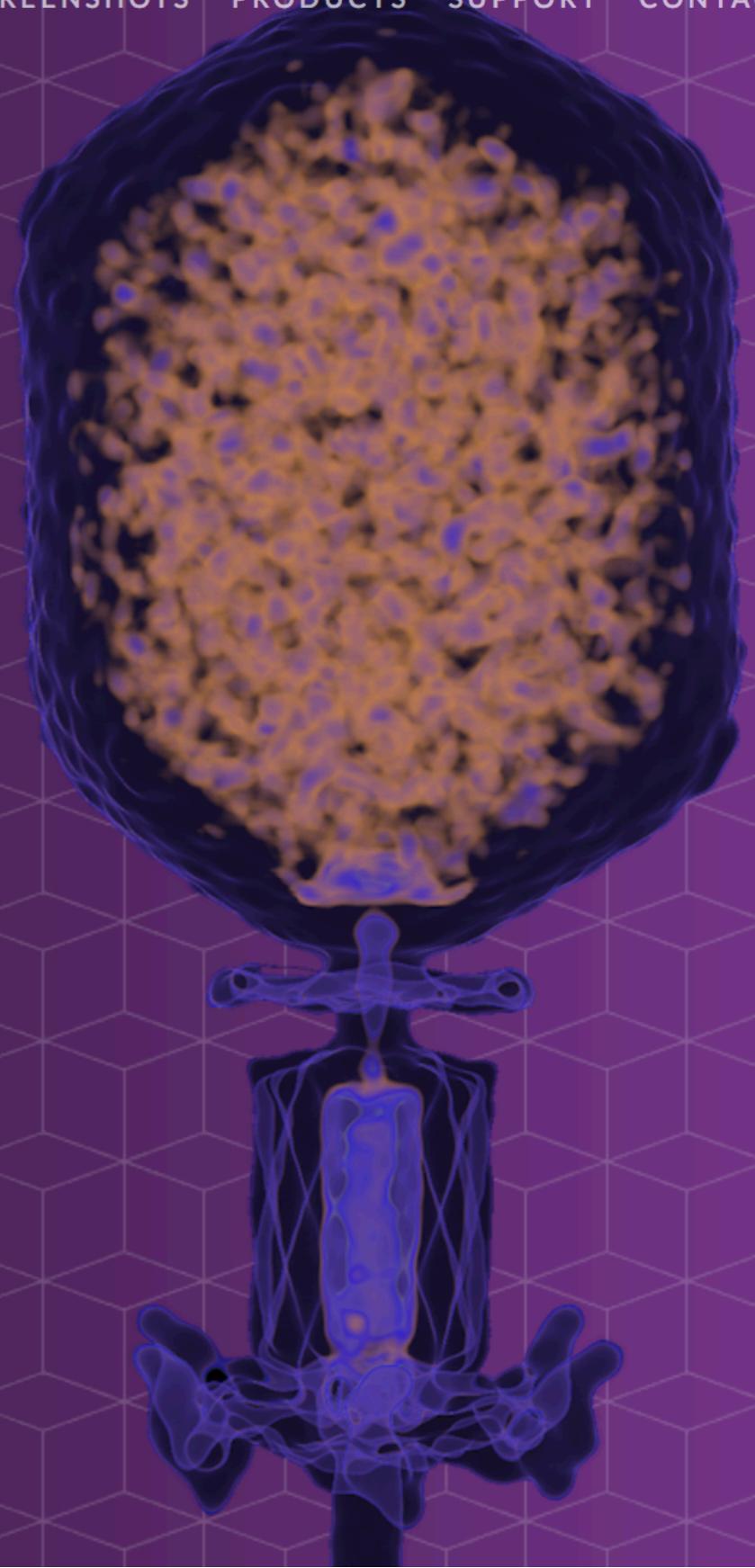
PyMOL is a user-sponsored molecular visualization system on an open-source foundation, maintained and distributed by Schrödinger.

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RELEASE HIGHLIGHTS



# To summarize Ingrid's workflow...

Using modeling & simulation tools (PyMol & Rosetta) to suggest mutants that better bind desired substrate motif (PQLP)

