

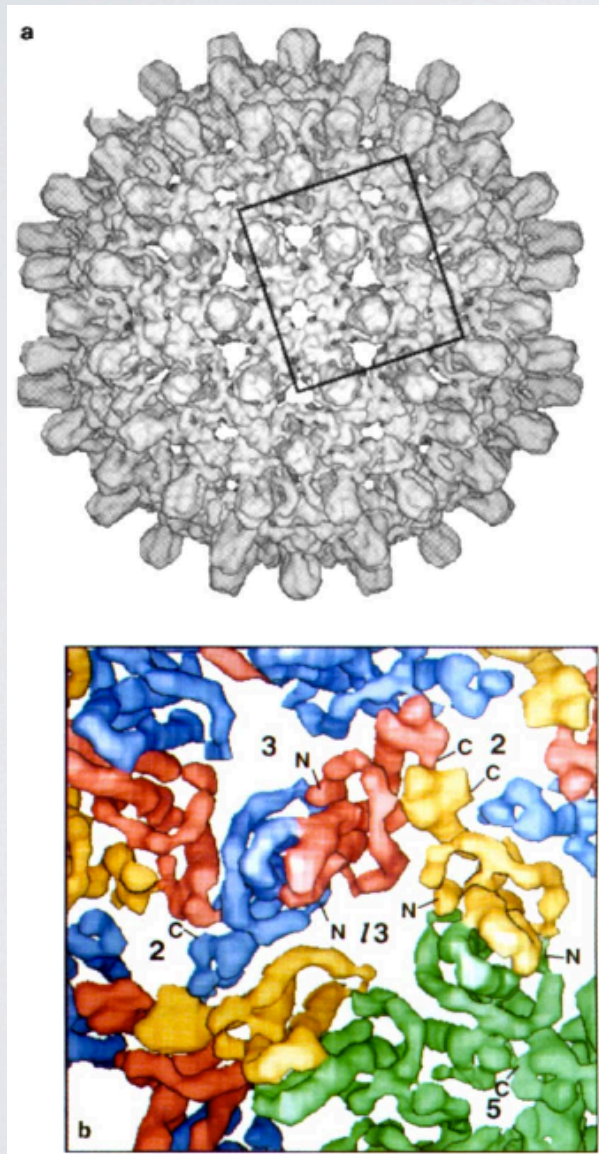
Where do we
go from here?





EM, circa 2004

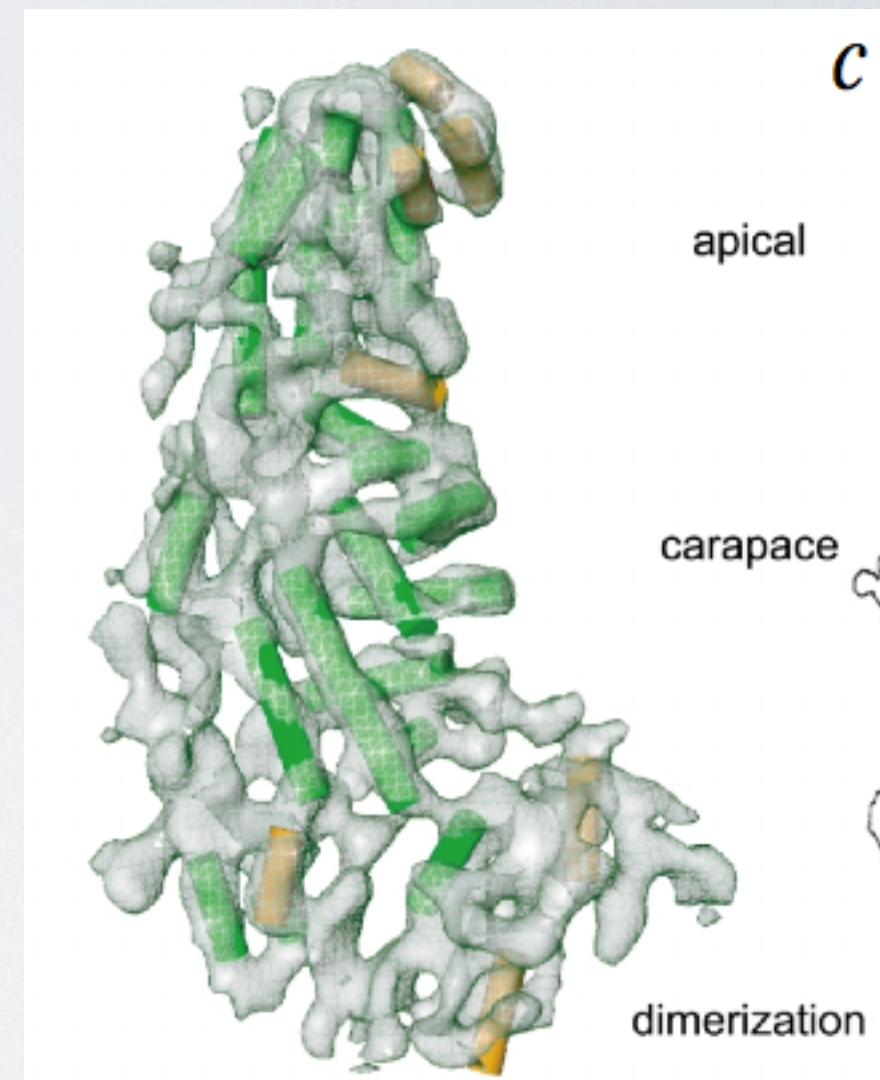
Handful of sub-nanometer structures
(symmetric viruses)



Bottcher, Wynne,
Crowther, Nature 1997



Conway et al., Nature 1997

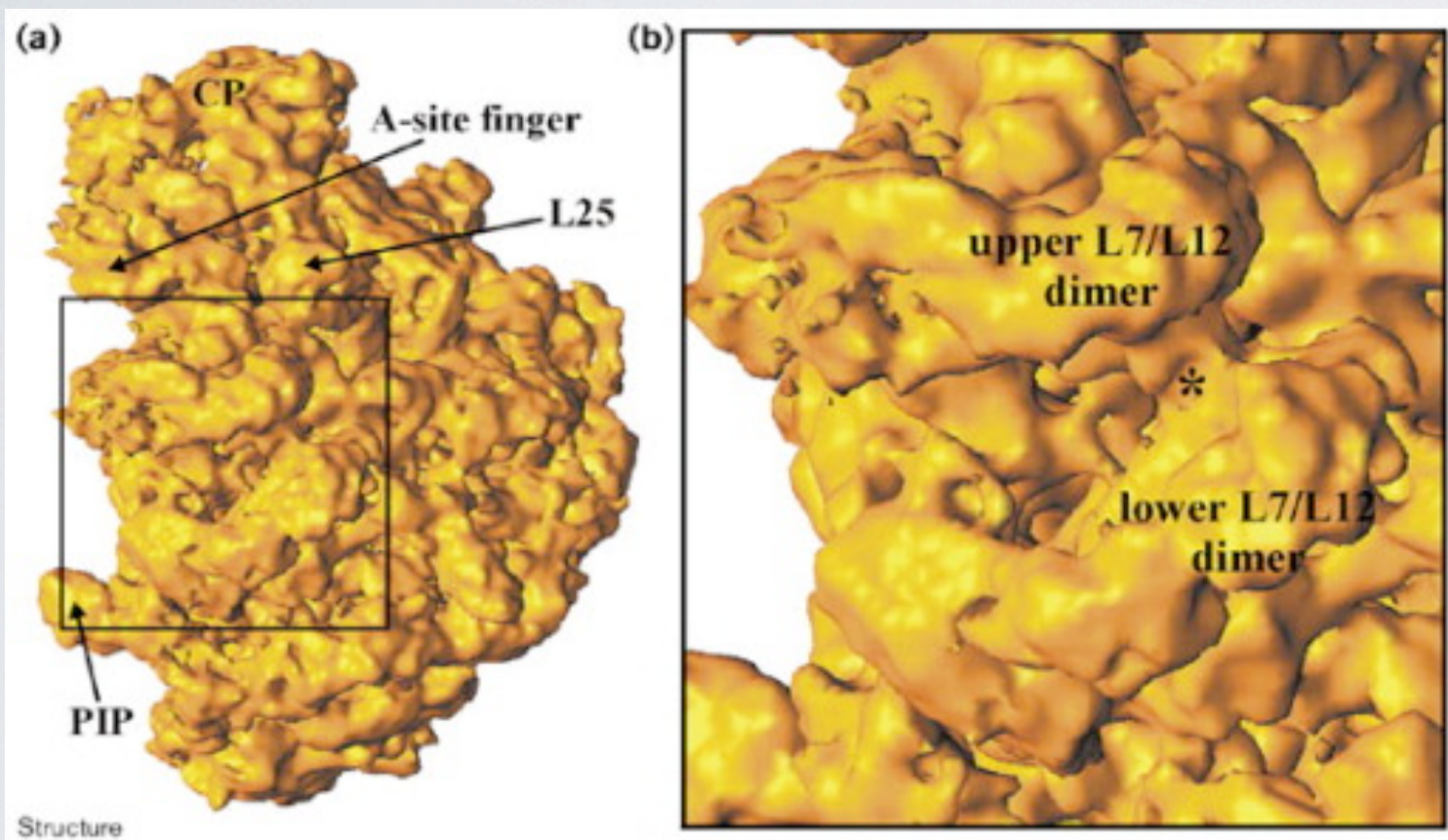


Zhou et al., Nature 2001

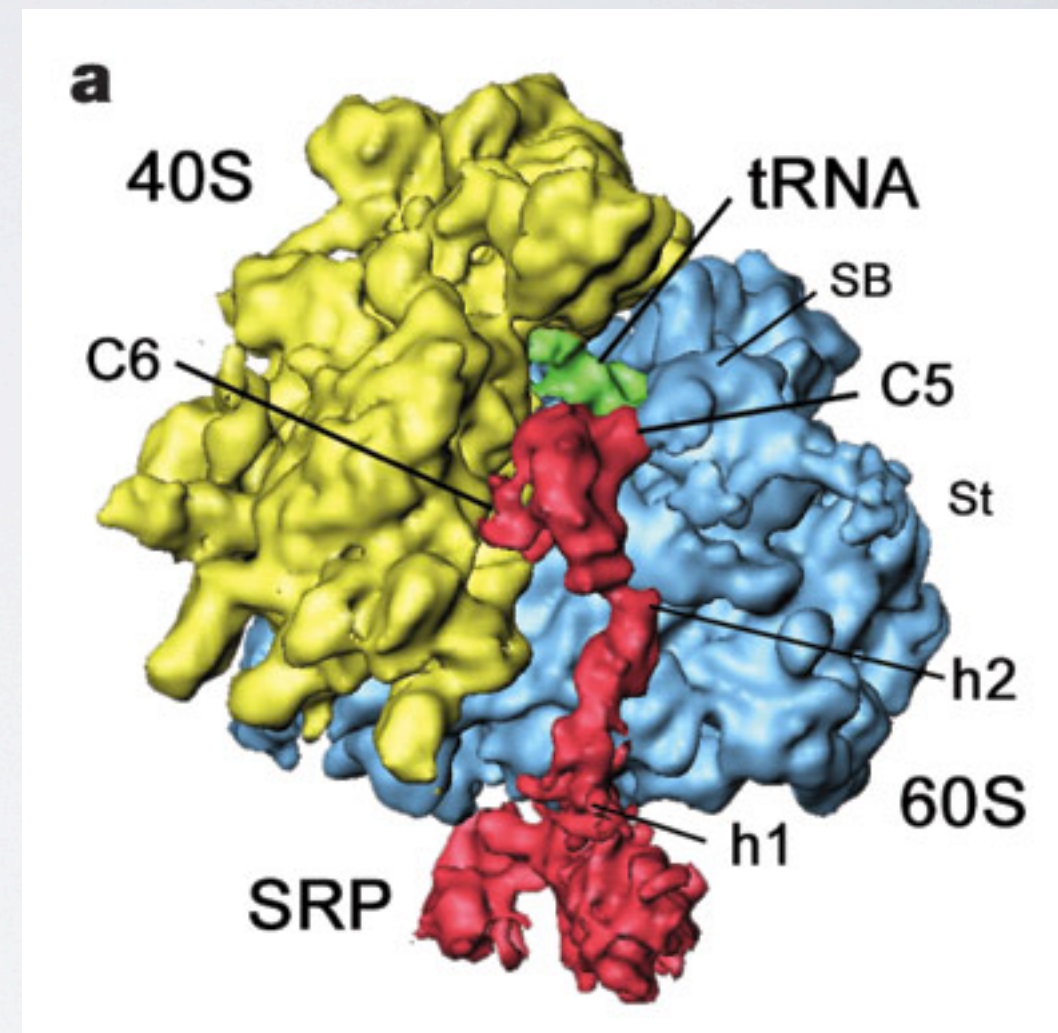


EM, circa 2004

Ribosome $\sim 10\text{-}12\text{\AA}$



Matadeen et al., Structure 1999



Halic et al., Nature 2004

EM, circa 2004

Hey, I saw your blob in
Journal X! Cool blob!



EM, circa 2004



Hey, I saw your blob in Journal X! Cool blob!

Thanks, I spent 3 years working on that blob!



EM, circa 2004

I noticed part of your blob looks... wrong...



EM, circa 2004

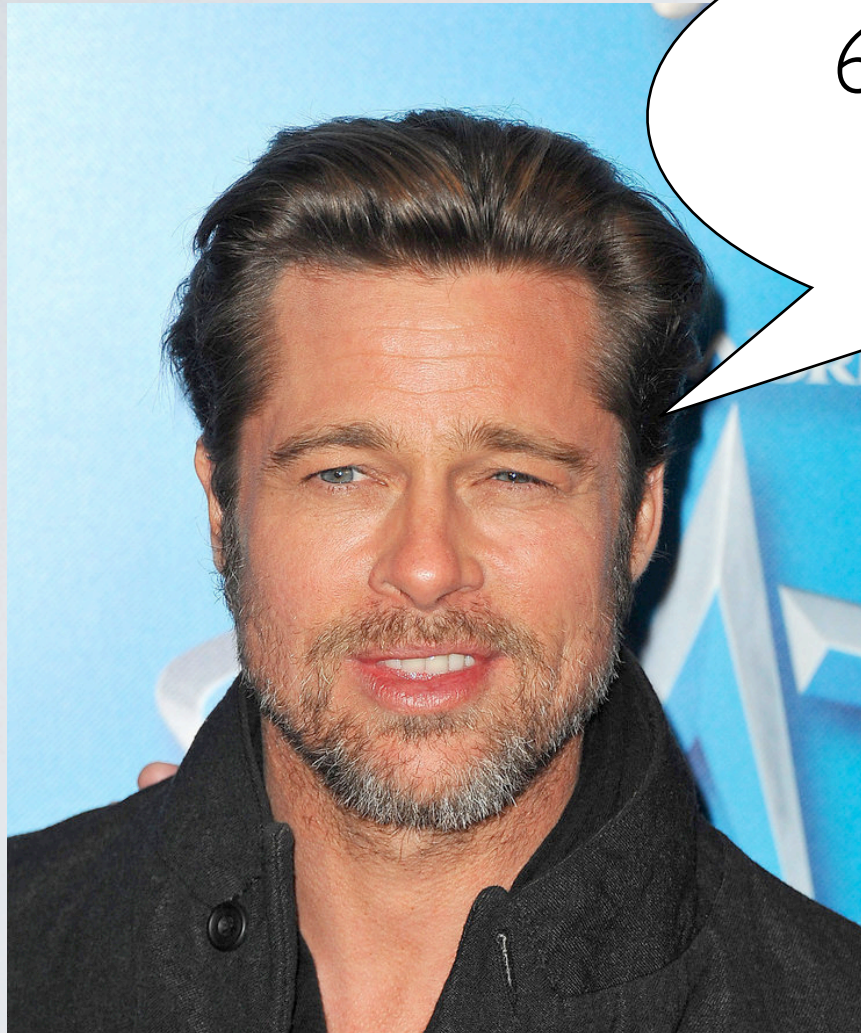


I noticed part of your blob looks... wrong...

Oh it probably is... but who cares? It's just a blob!

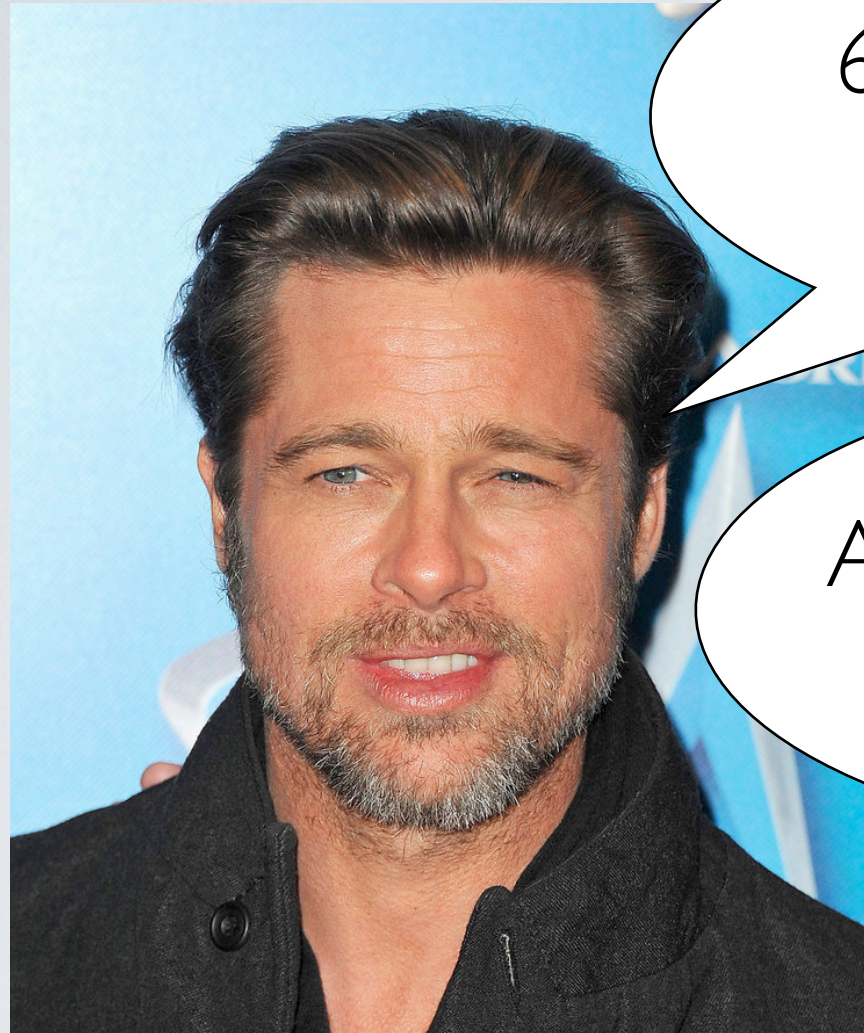


EM, present day



6Å resolution! I see
helical pitch!

EM, present day



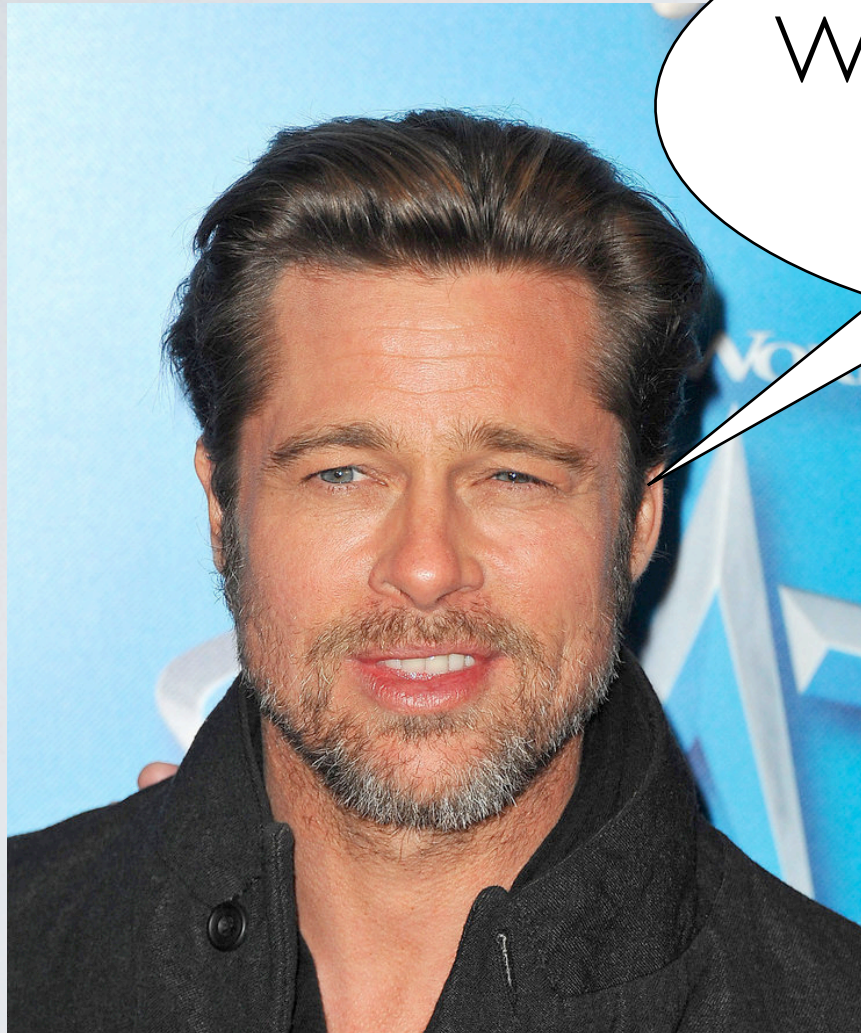
6Å resolution! I see
helical pitch!



Already solved it, I see
side chains!

EM, present day

Well I've got this other complex...



EM, present day

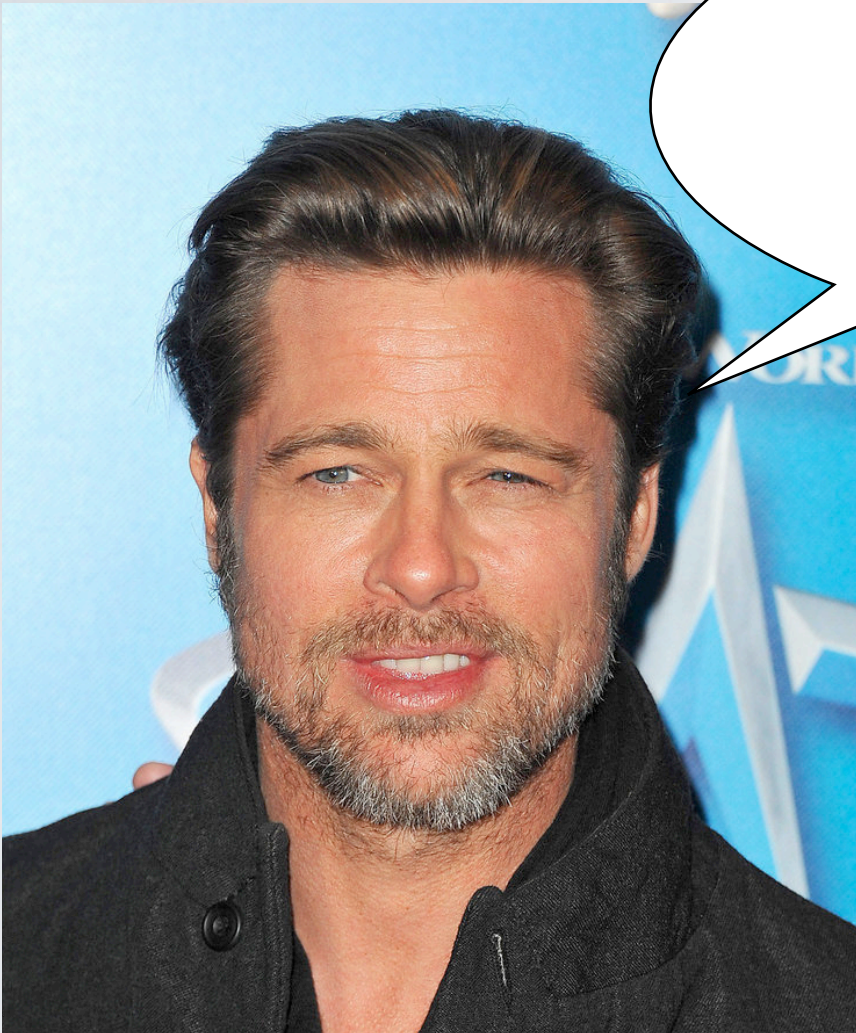


Well I've got this other complex...



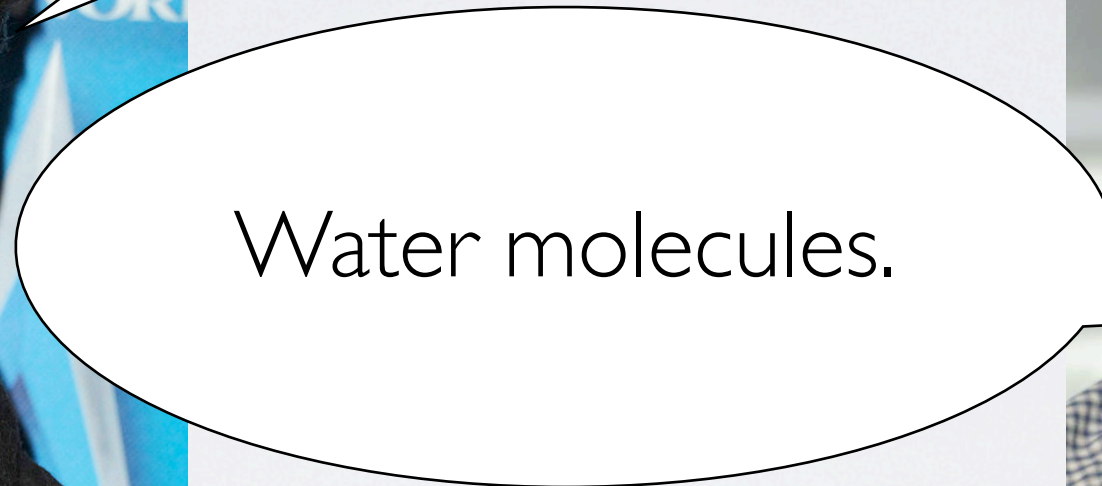
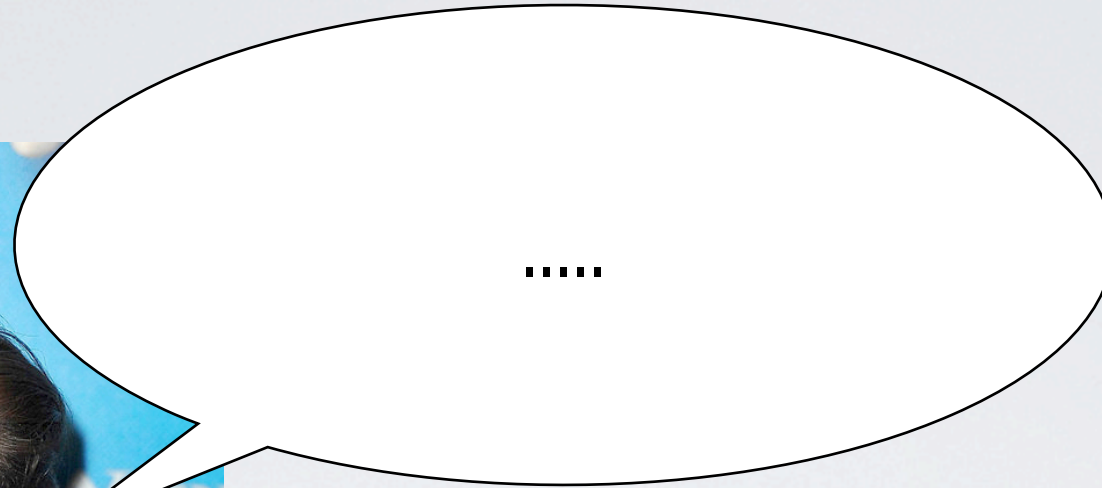
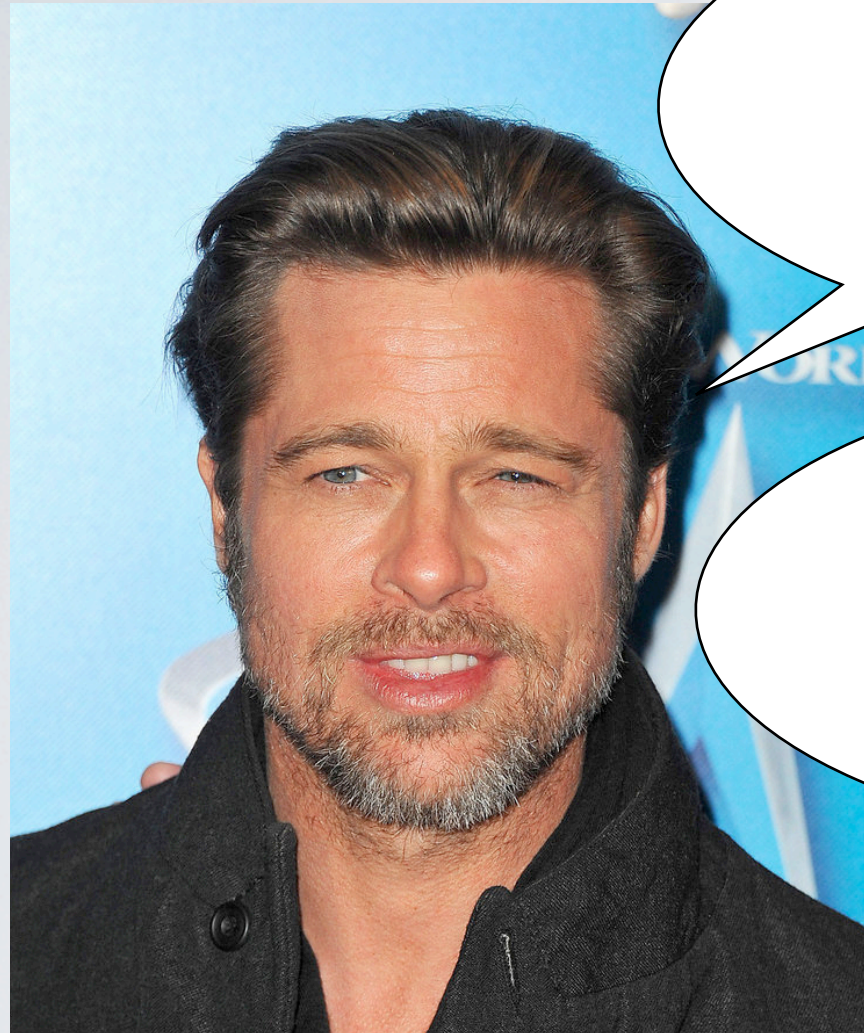
Done. 3Å.

EM, present day

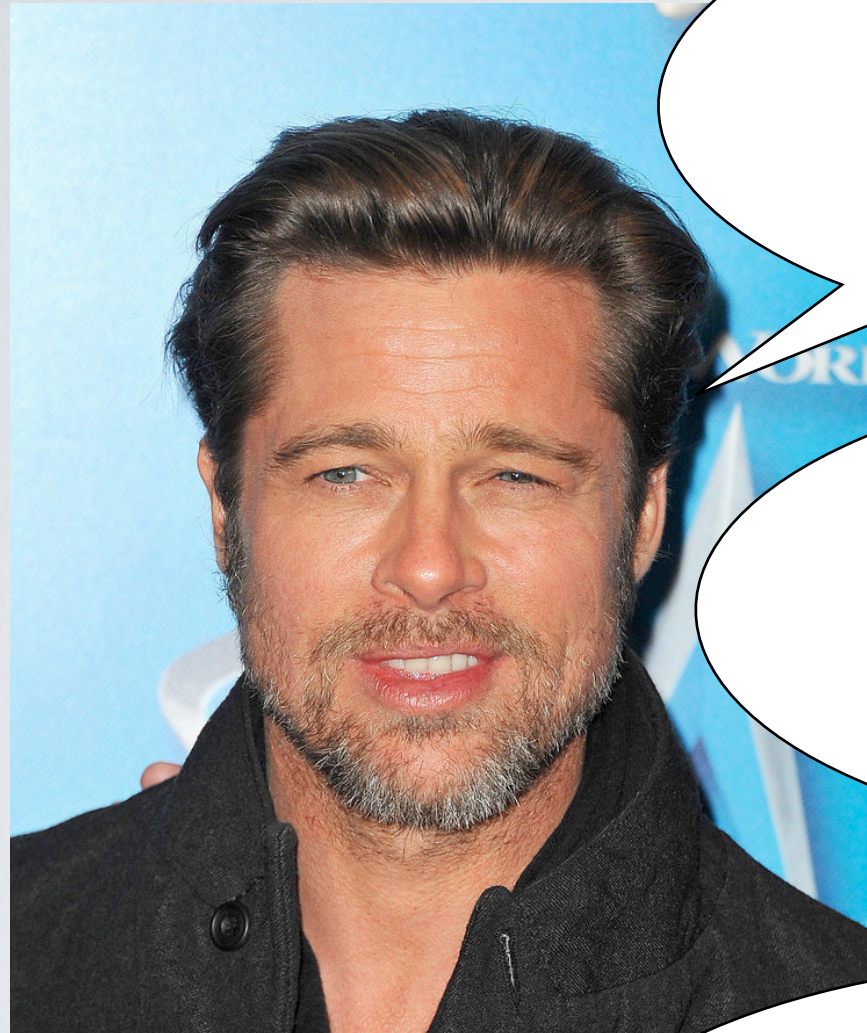


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EM, present day



EM, present day



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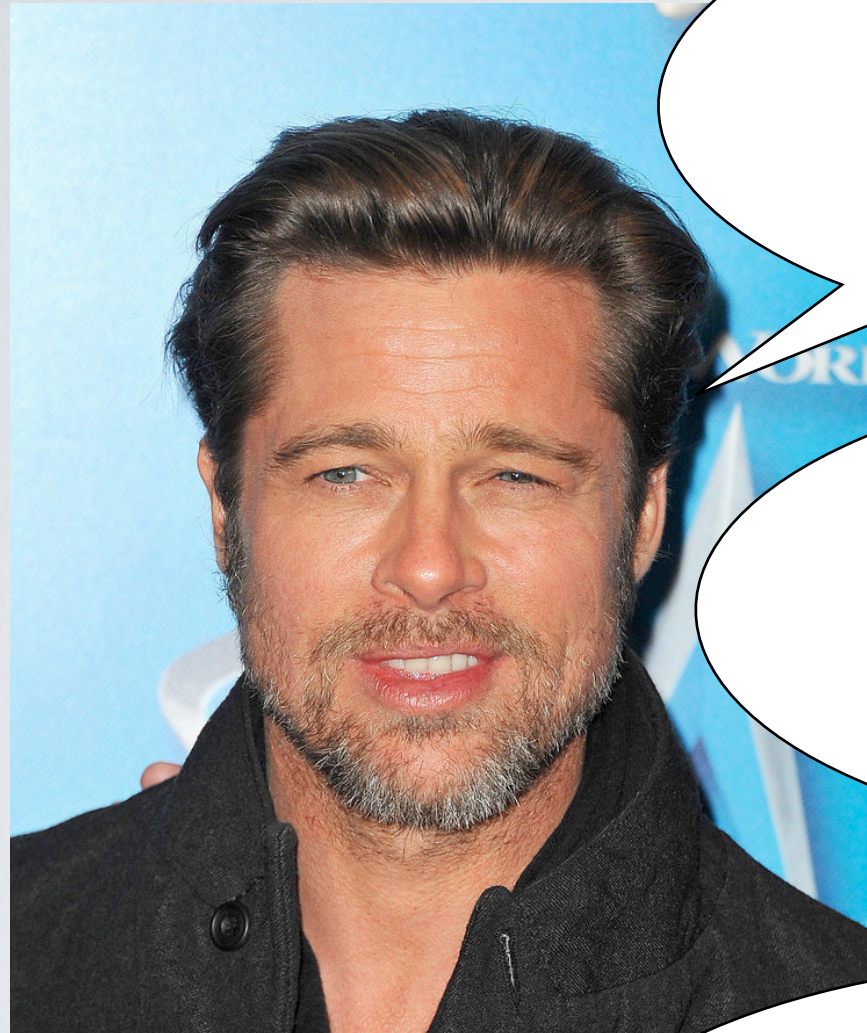
Water molecules.



Water molecules.



EM, present day



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Water molecules.



Water molecules.



Competition!

Inheriting the “secrecy culture” of the crystallography community

Huge influx of non-experts wanting to solve structures quickly - validation?

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Inheriting the “secrecy culture” of the crystallography community

Huge influx of non-experts wanting to solve structures quickly - validation?

Are we there yet?

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assuming crystallography resolution is “there”

For crystal structures $> 200\text{kD}$:

31% are worse than 3\AA resolution

60% are worse than 2.5\AA resolution

We can solve larger structures to better resolution ($\sim 1/2$ of above structures are between $200\text{-}300\text{kD}$)

Certainties (Death & Taxes+)

- Higher resolutions (better instruments, better algorithms), for both single particle & tomography
- Sample Prep/ Freezing conditions will be optimized
- High throughput will increase, more structures faster
- Modeling tools will improve
- Lower resolution structures will be harder to get published
- More users, fewer experts
- High profile structures will be solved incorrectly (journals are not yet requiring all necessary validations)

Uncertainties

- Will the EM surge last? Just lots of low-hanging fruit at the moment?
- Will we be able to break 2Å barrier?
- When will a new technology replace EM?
- Will we ever arrive at a true “gold standard” for validation?
- Can we make journals require validation criteria?
- How do we continue to buy & support expensive EM equipment?

Negative Stain? Crosslinking?

- Is negative stain useful? Do we care about 30Å resolution?
- Is negative stain work publishable? Does everyone expect 3Å cryo structures, regardless of complex?
- Does crosslinking affect resolution?



MONOPOLY

BRAND

Instrumentation?
Data collection software?
Data processing software?

Where do we go from here?

- Panelists:
 - Justin Kollman - University of Washington (2 months)
 - Frank DiMaio - University of Washington (6 months)
 - Dan Southworth - University of Michigan (3 years)
 - David Veessler - University of Washington (-1 months)
 - Elizabeth Villa - University of San Diego, CA (5 months)