

Nobel lecture

Early cryo-electron microscopy

Jacques Dubochet

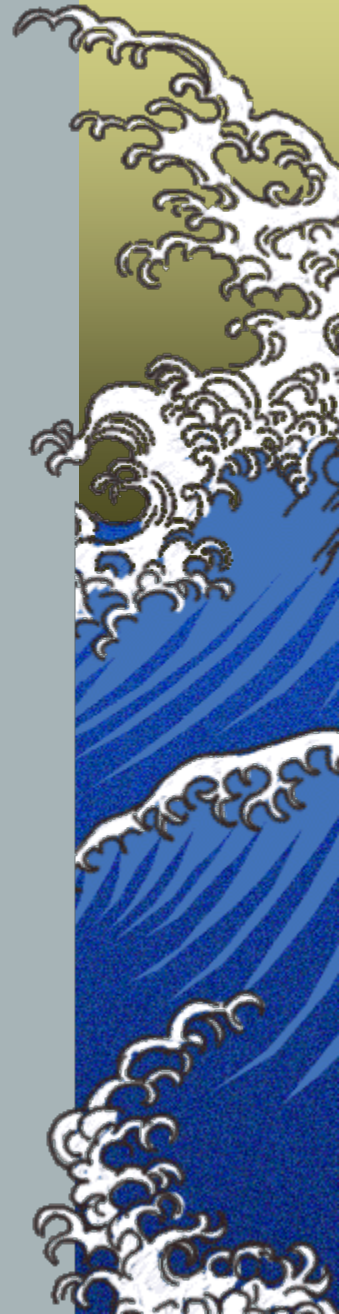
Thank you



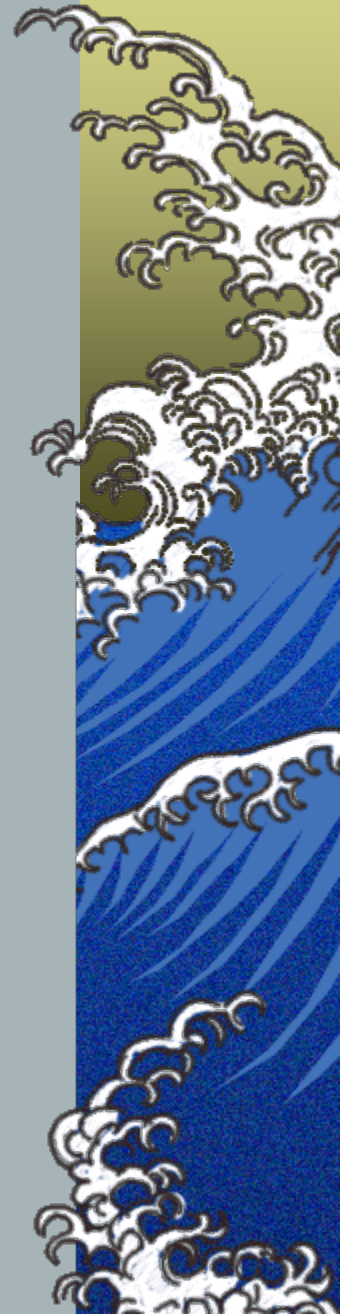
Edouard Kellenberger



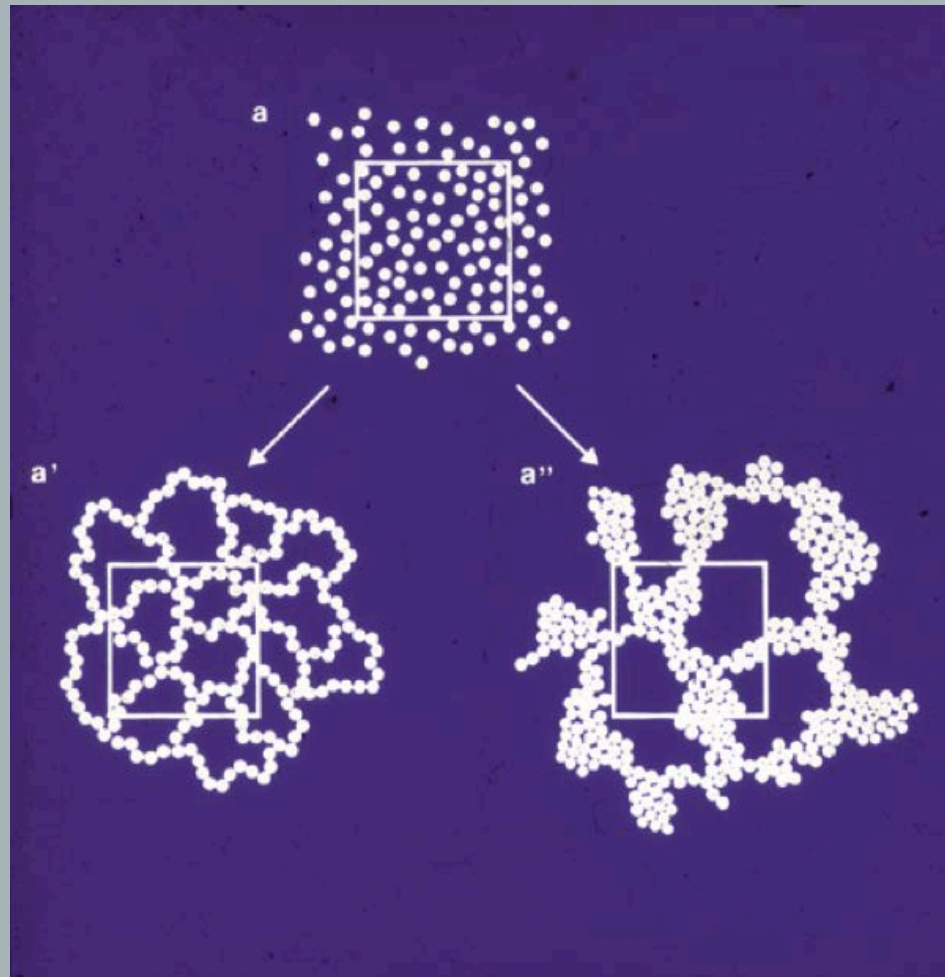
Sir John Kendrew



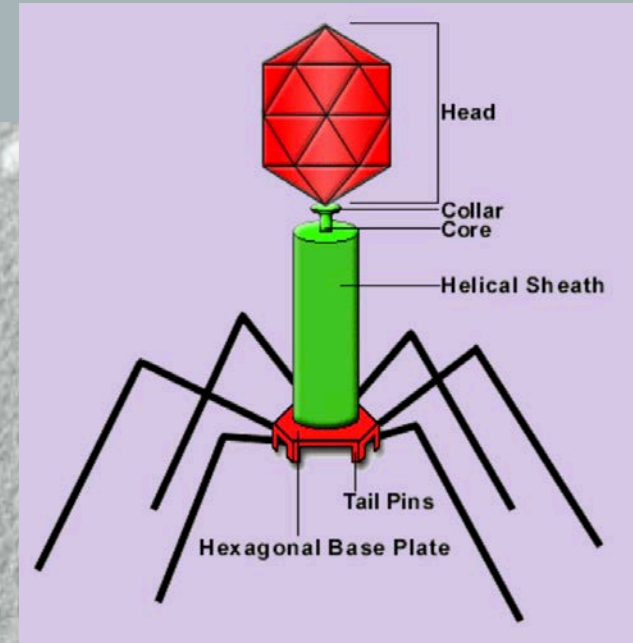
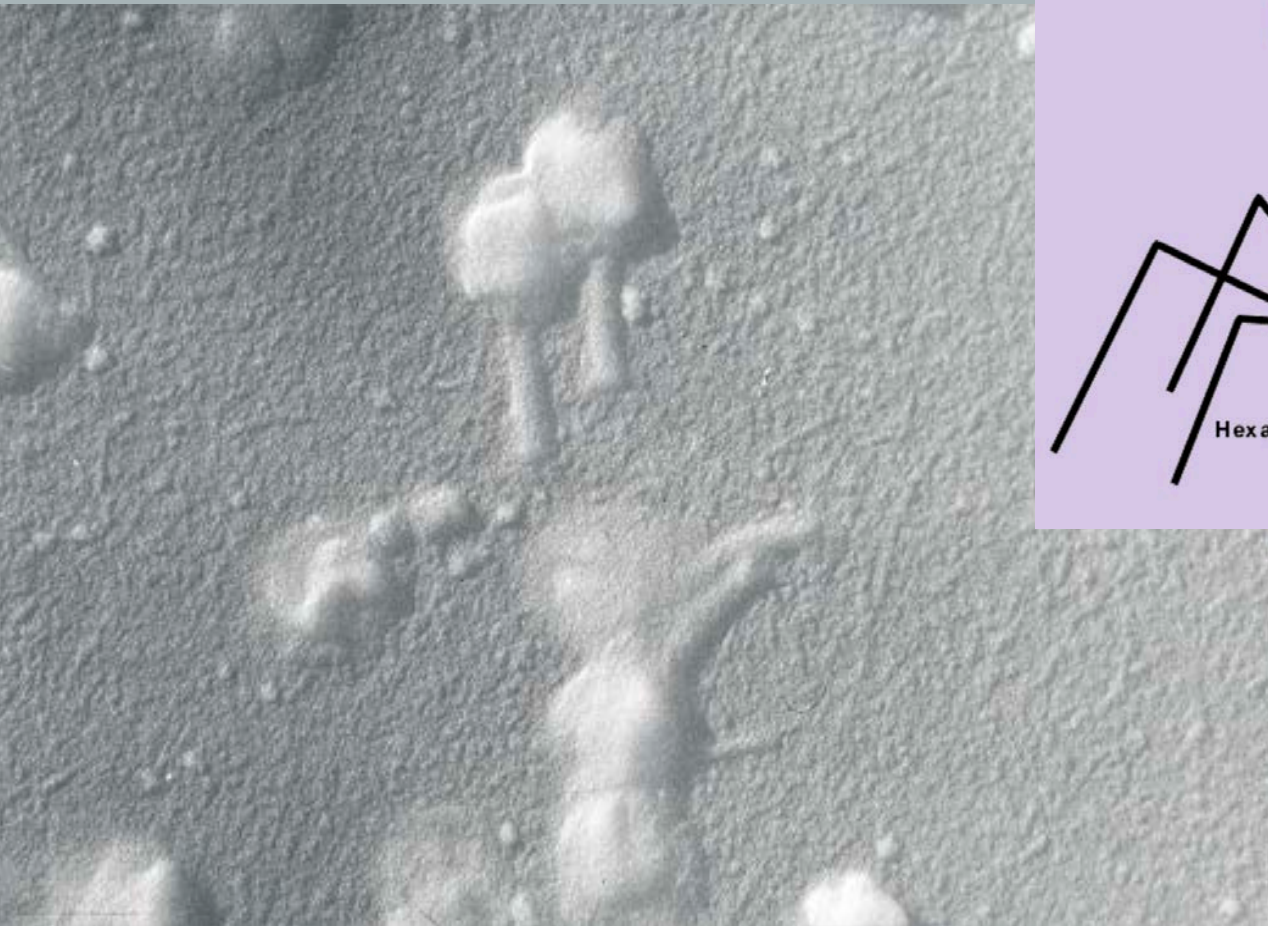
Why cryo-EM?

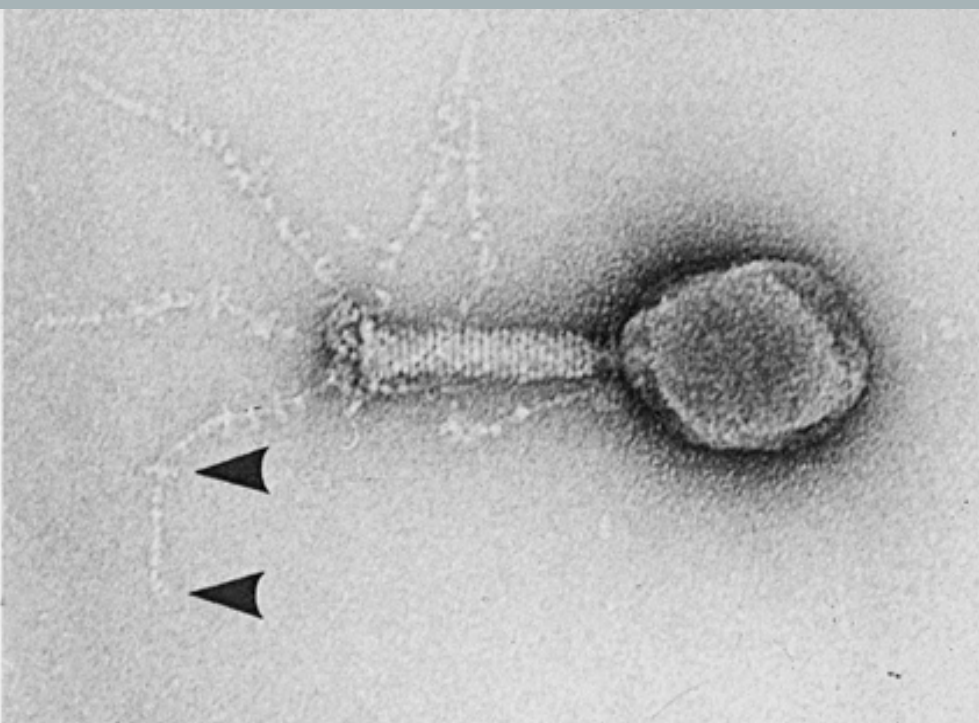


Aggregation



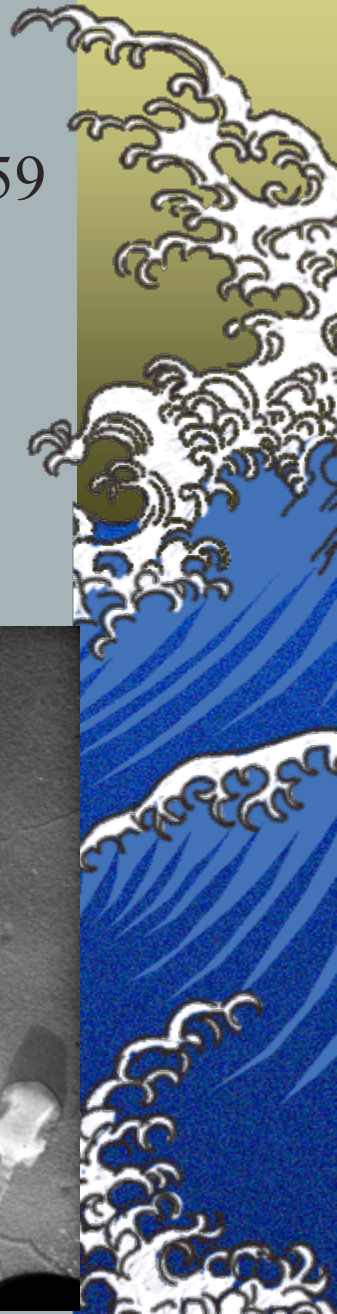
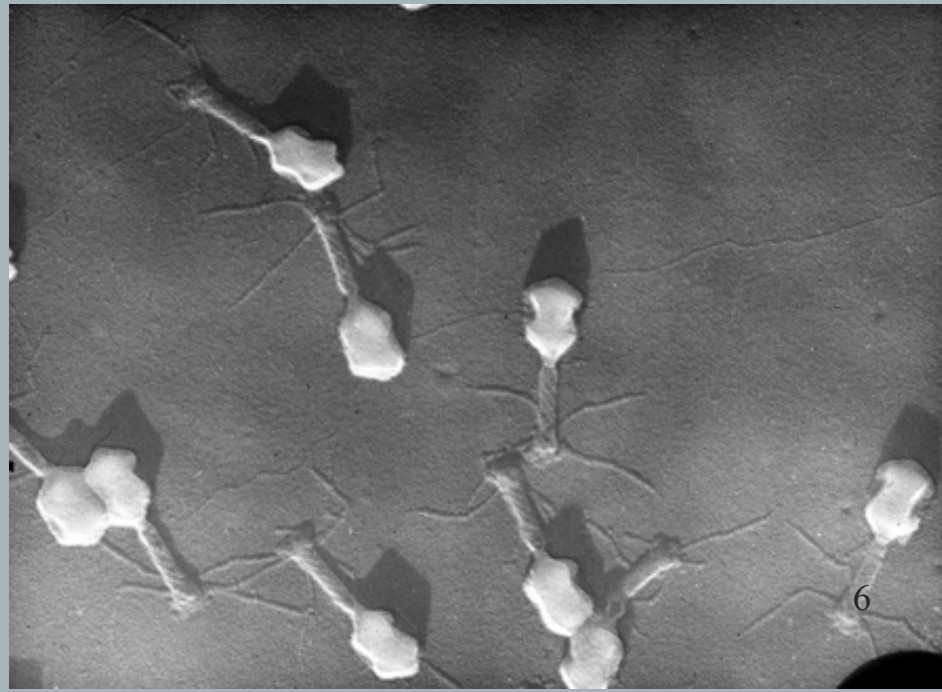
The bad shape of a T4 bacteriophage



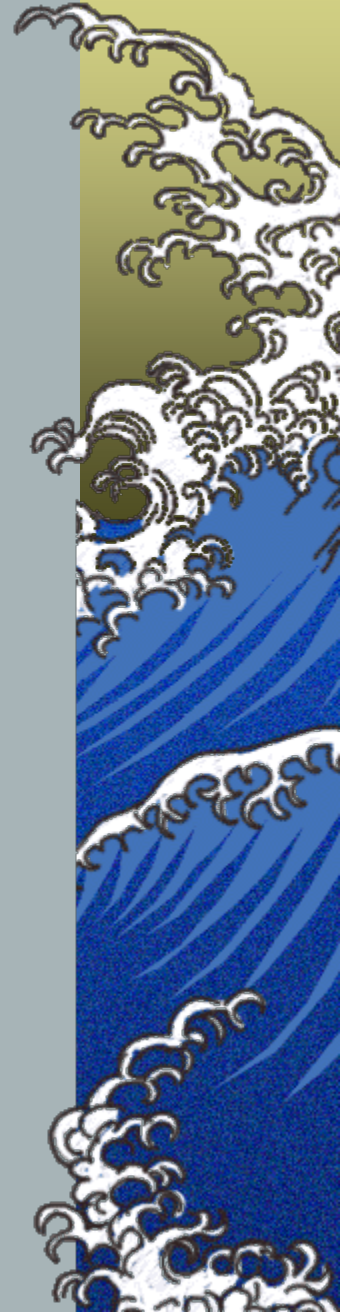


Negative staining
Brenner & Horne, 1959

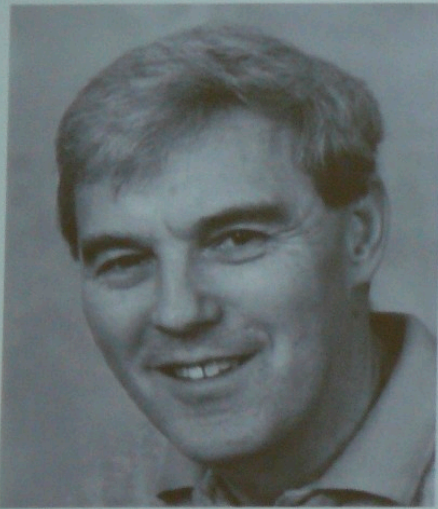
Freeze-drying



Nigel Unwin

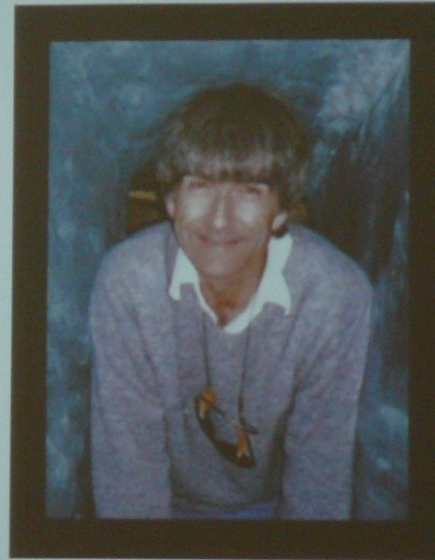


Pioneers of electron crystallography

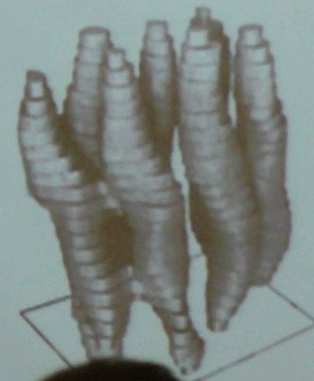


Richard Henderson (MRC)

analysed the first atomic model of bR by electron crystallography in 1990



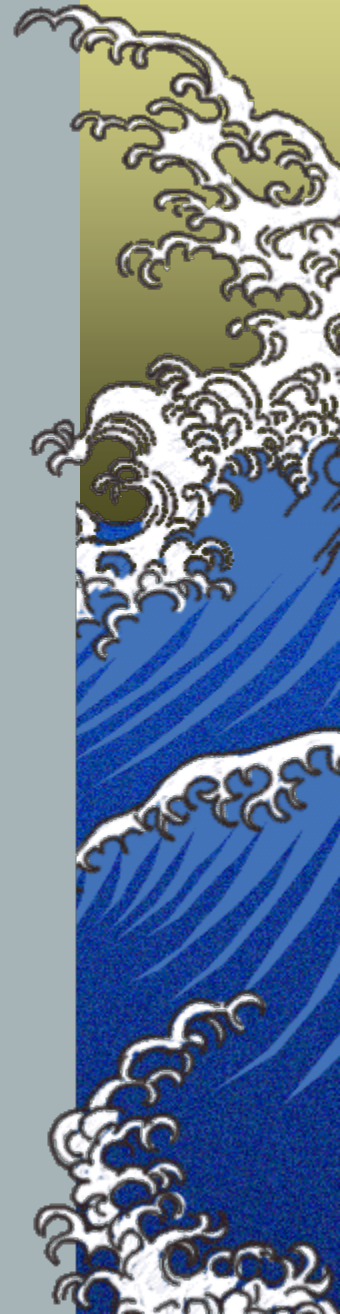
Nigel Unwin (MRC)

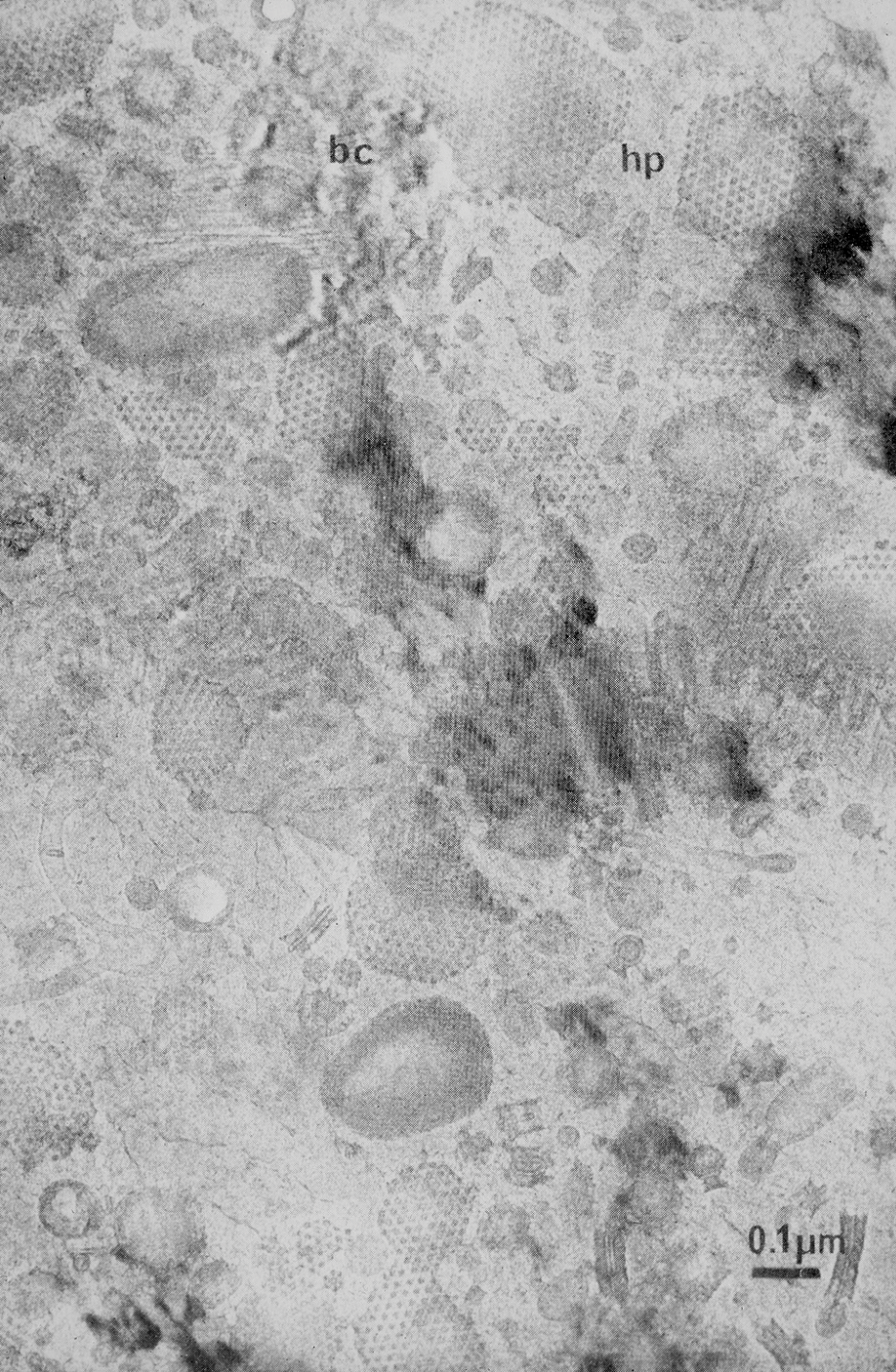


3D model of bacteriorhodopsin

Henderson, R and Unwin, PNT
Nature 257, 28-32, 1975

Bob Glaeser





Taylor, K.A. and R.M. Glaeser,
*Electron microscopy of frozen
hydrated biological specimens.*
J. Ultrastruct. Res., 1976.
55(3): p. 448-56.



1978 EMBL

(European Molecular Biology Laboratory)

A Project:

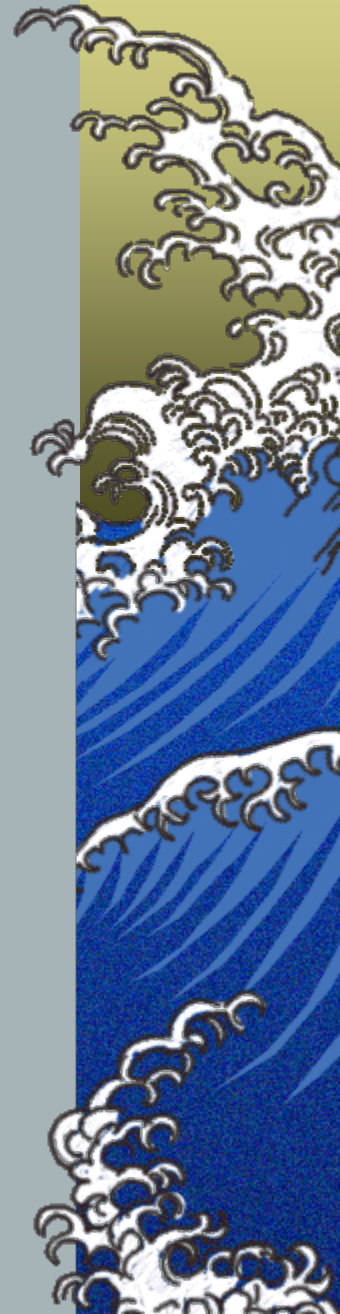
How to deal with water in cryo-electron microscopy?



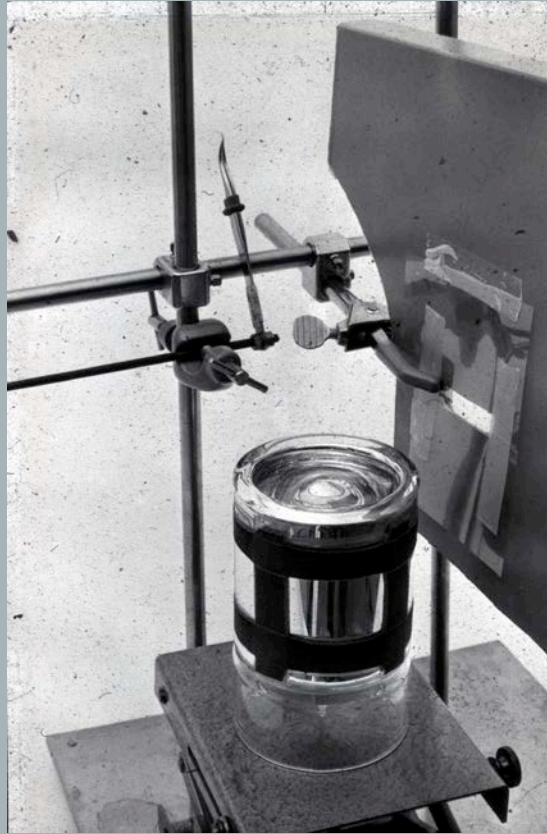
A Problem



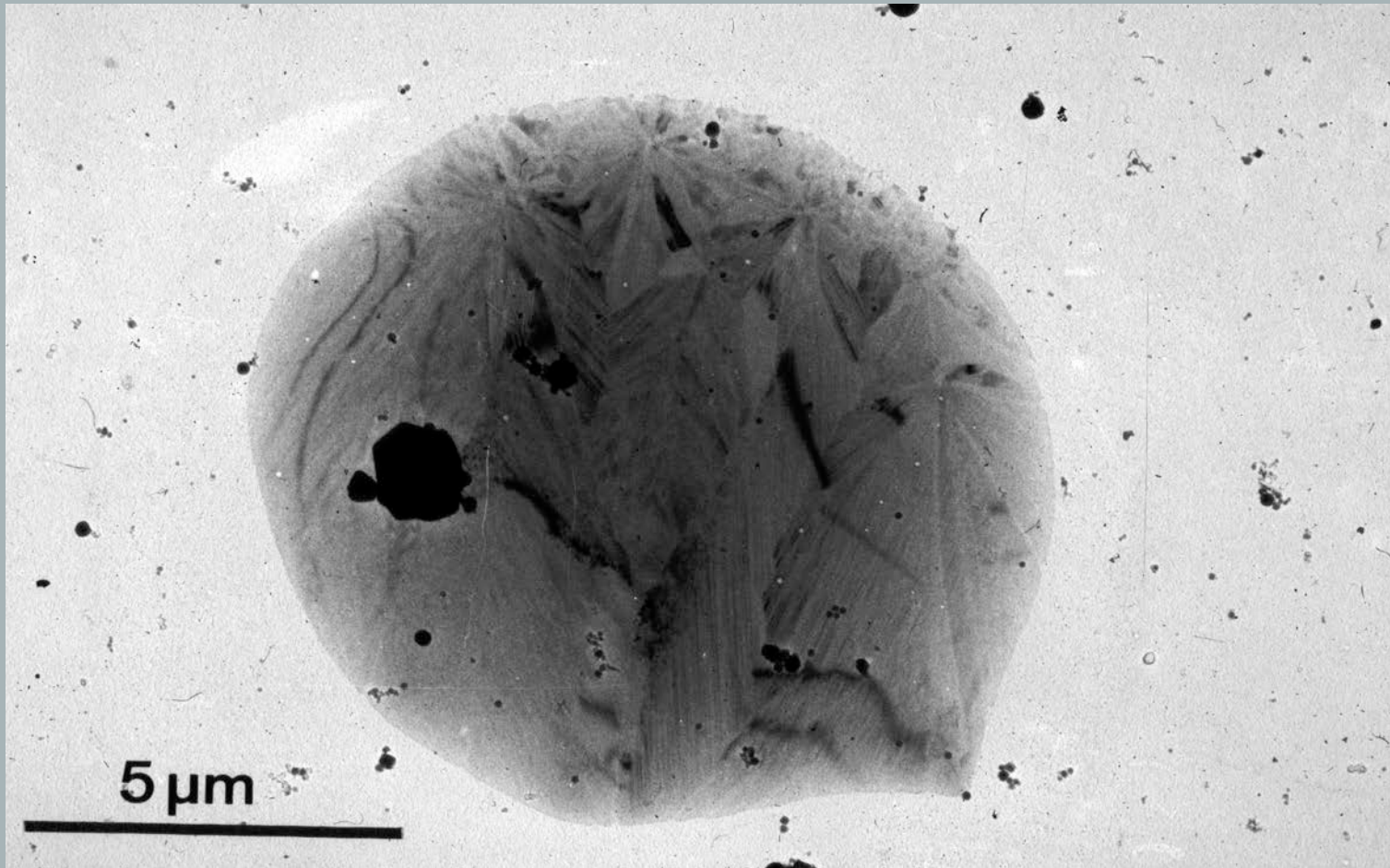
Ice is not like
liquid water



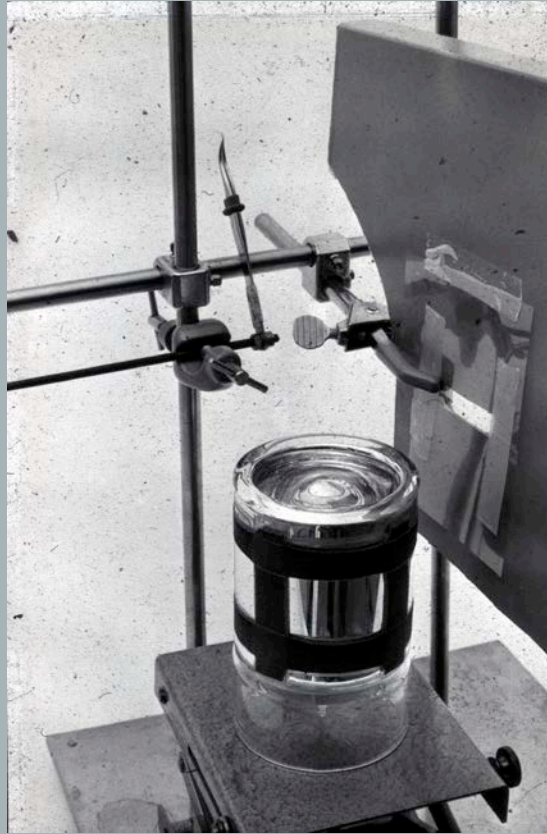
High Tech



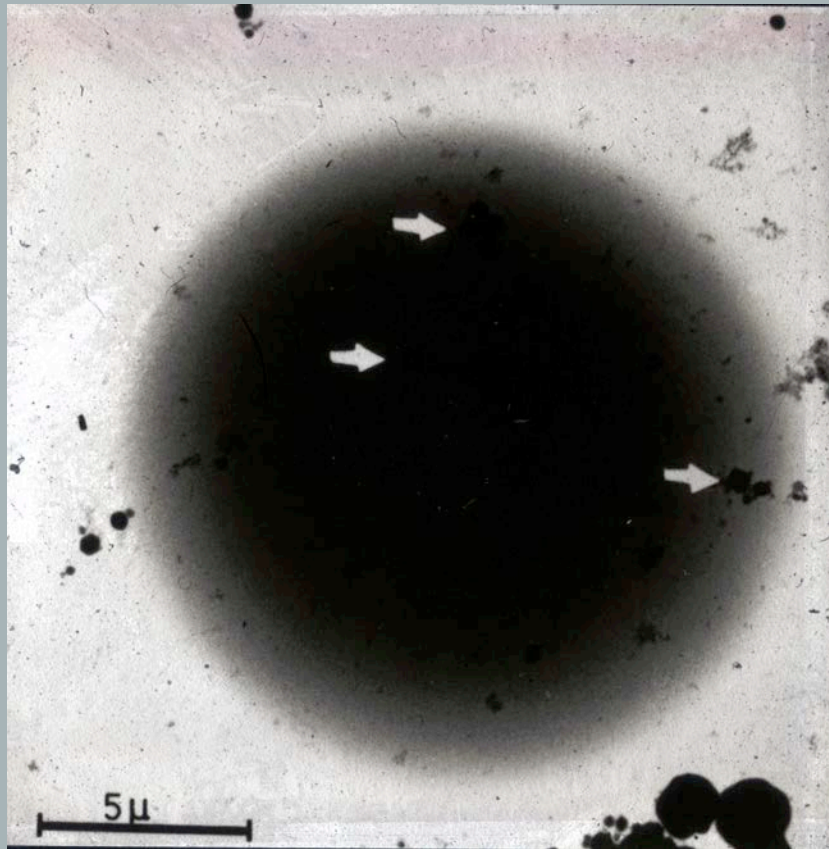
Ice at EMBL



High Tech



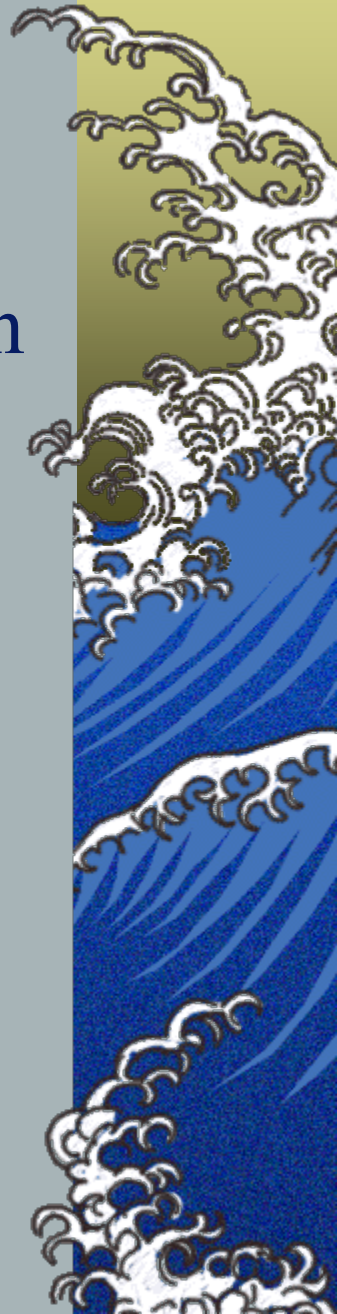
Vitreous Water



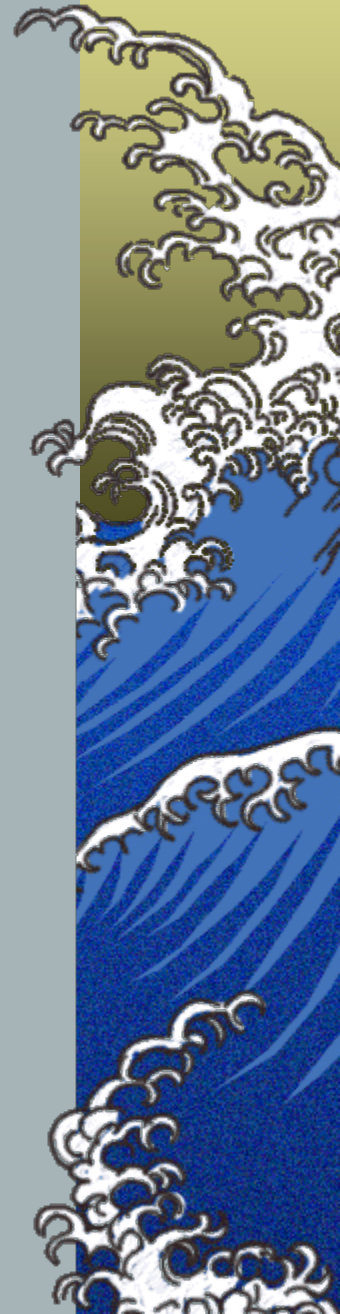
Alasdair McDowall



The “vitrification” man



This was the first *Aha!*



The trouble with
vitreous water
is that vitrification
should be impossible





Farther
Basile
Luyet

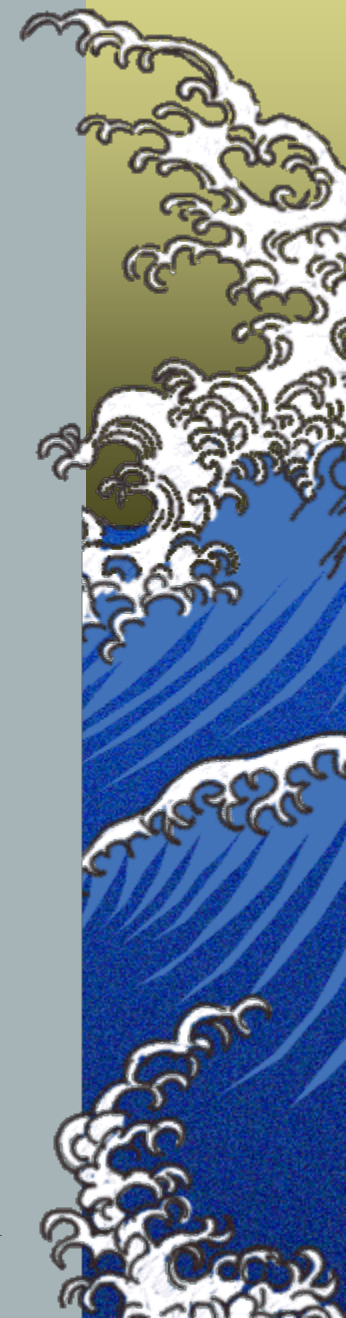
Founder of
cryobiology

Luyet, B. J., & Gehenio, P. M.
(1940). *Life and death at low
temperature*. Normandy,
Missouri: Biodynamica.





Savièse



« You can't bend Nature »

Mayer, E. and P. Brüggeller. 1980. "Complete vitrification in pure liquid water and dilute aqueous solutions." *Nature* 288:569-571.

Dubochet, J., & McDowell, A. W. (1981). Vitrification of pure water for electron microscopy. *J. Microscopy*, 124, RP3-RP4.



Conclusion I

*Vitreous water is not
what we thought ...*

*... but it works so well
for cryo-electron microscopy!*



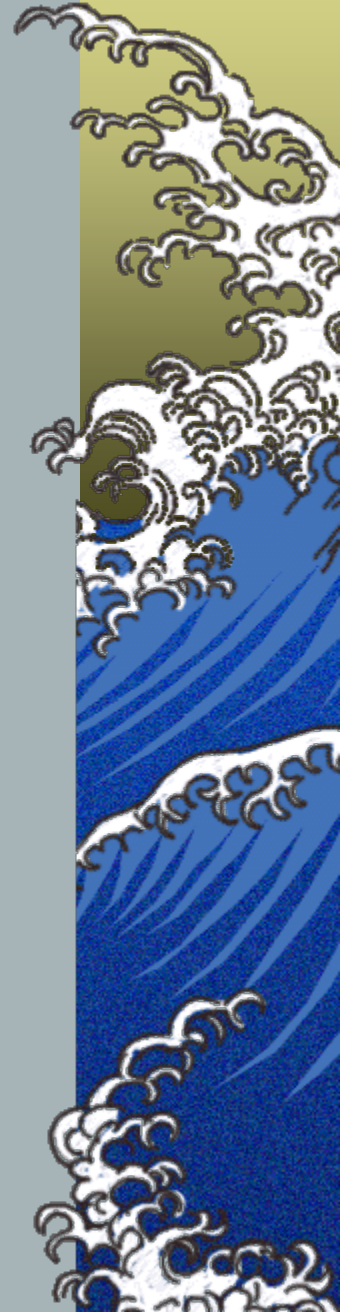
Conclusion II

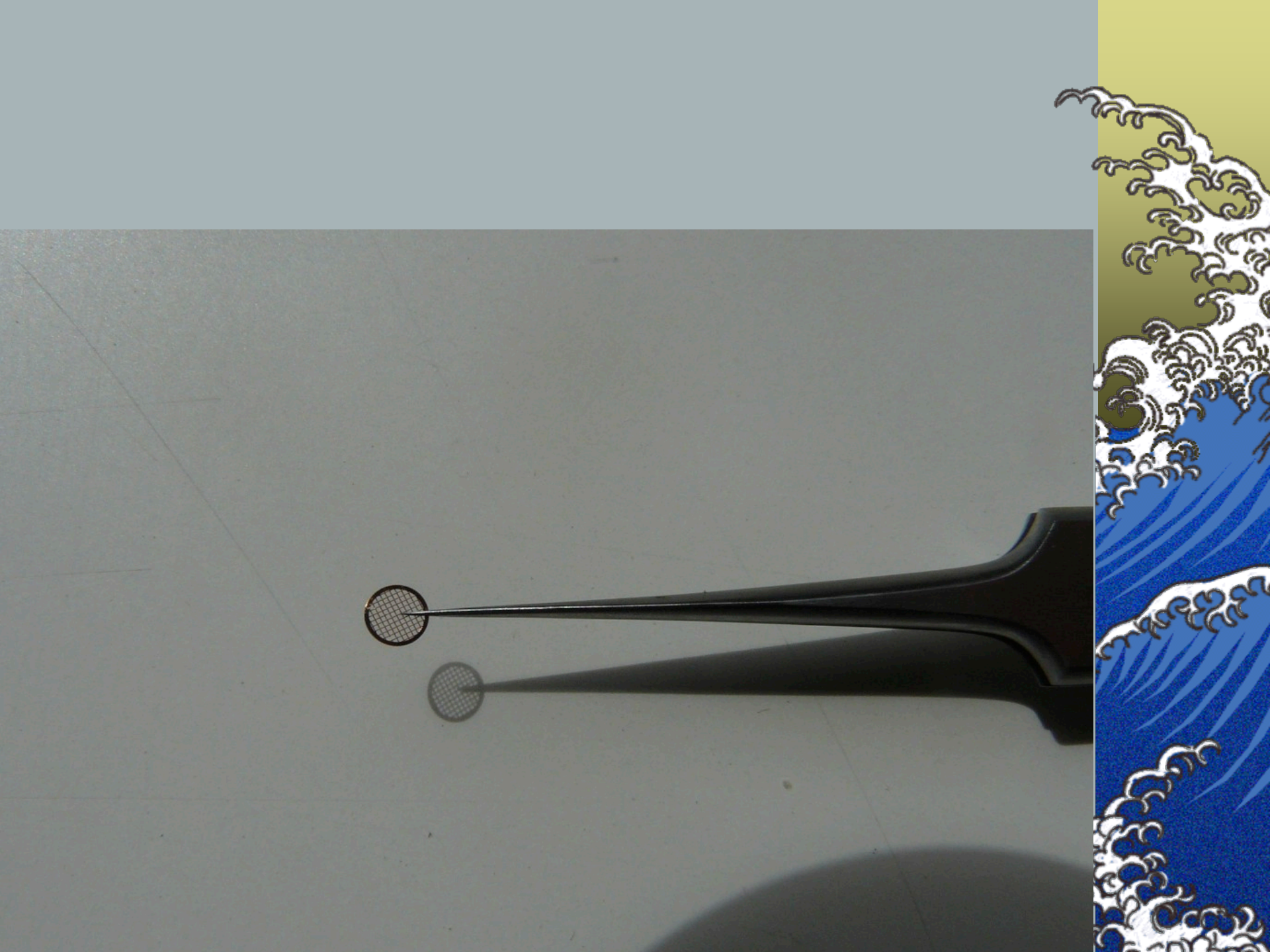
What is water ?

Wait to know more

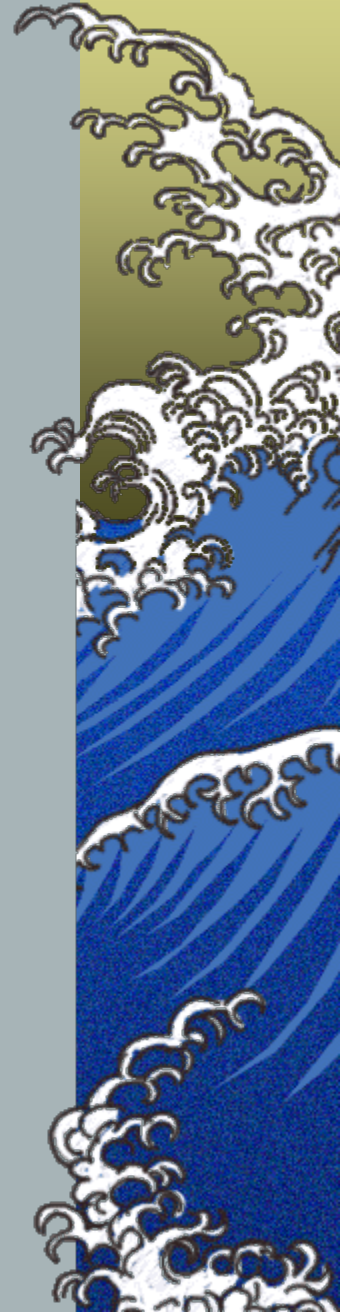
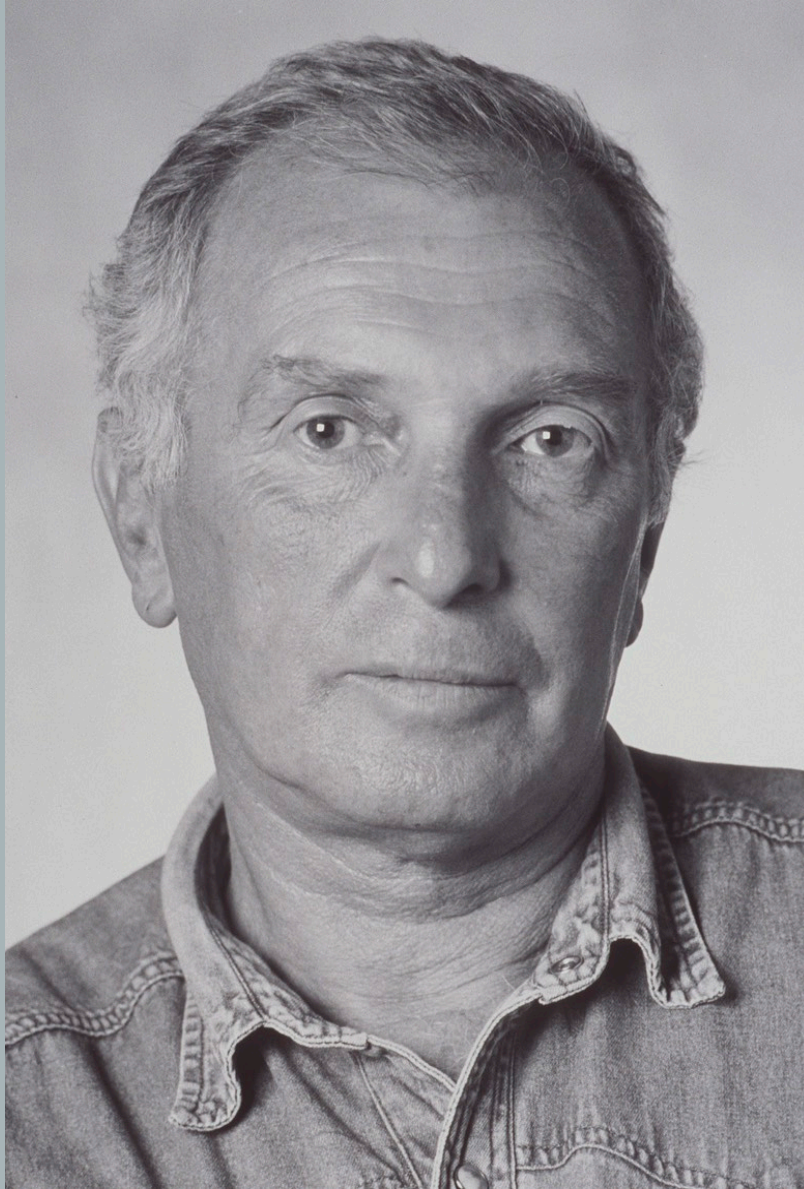


The second *Aha!*





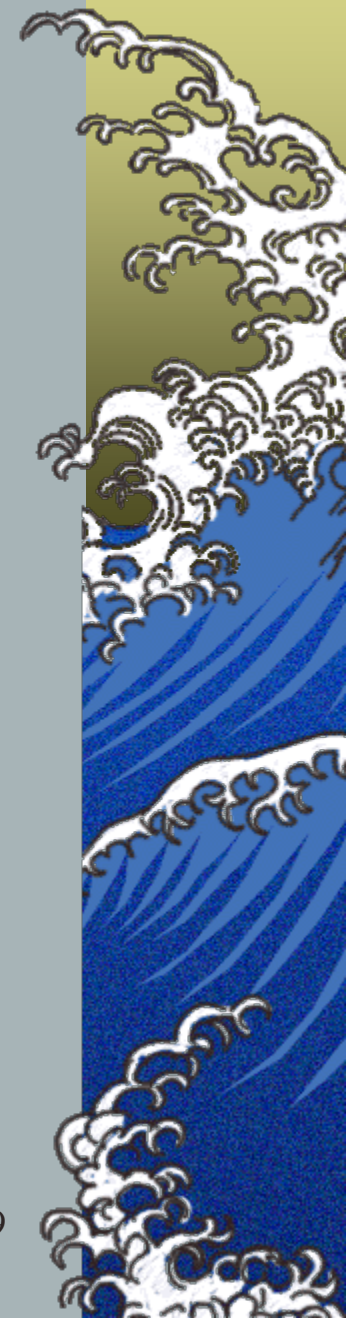
Marc Adrian † 2013



Cryo-em of thin vitrified film

Semliki Forest Virus

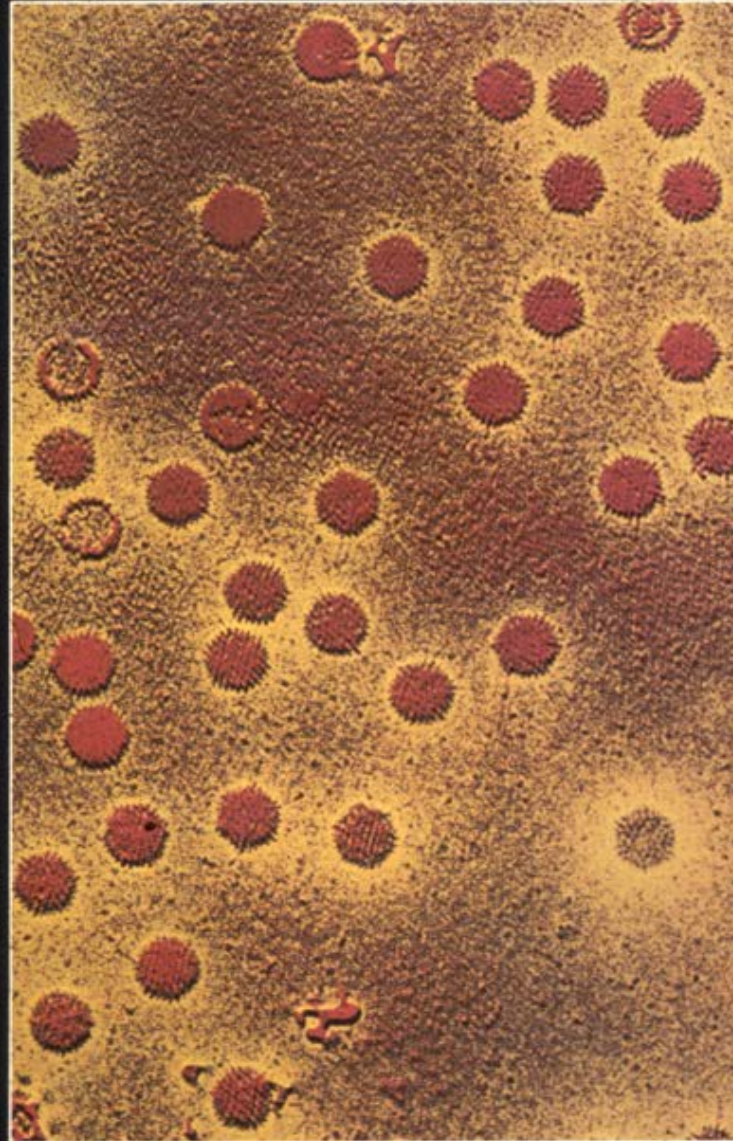
Marc Adrian



nature

INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Vol 308 No 5954 1-7 March 1984 £1.80 \$4.50

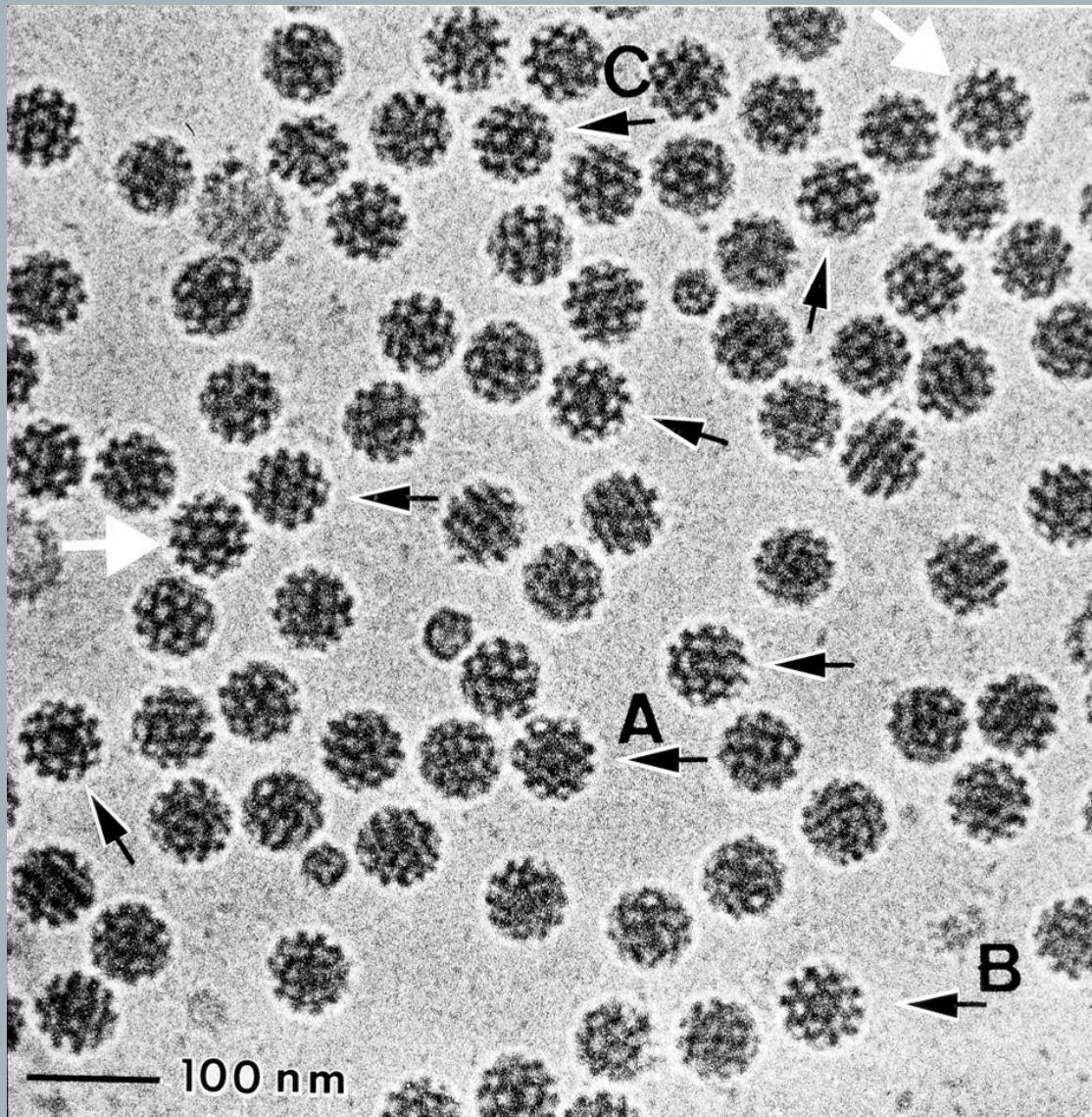


**CRYO-
ELECTRON
MICROSCOPY
OF VIRUSES**

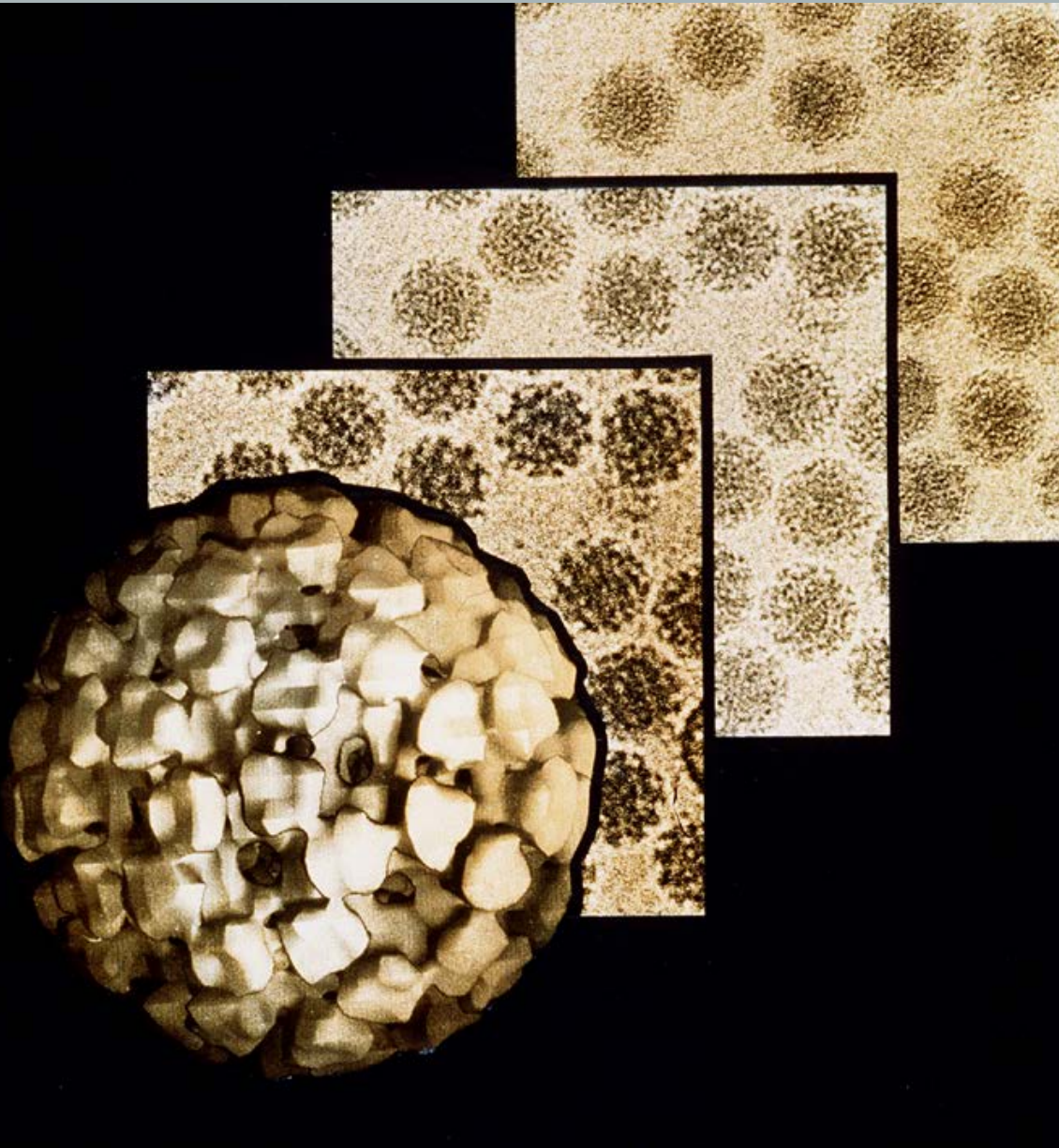


1984

SFV



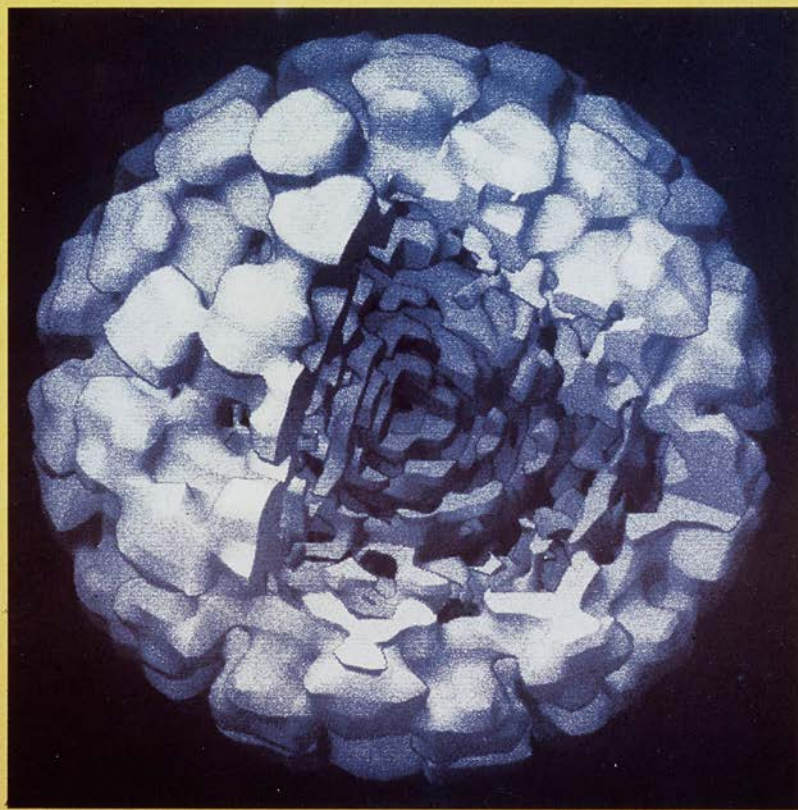
Towards
high resolution
and
3d
reconstruction



nature

INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Volume 320 No 6062 10-16 April 1986 £1.90

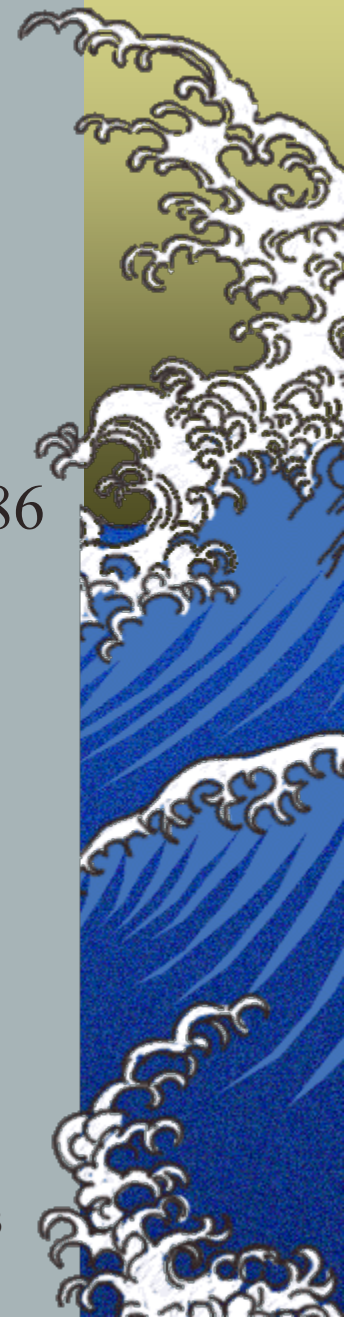


**SEMLIKI FOREST VIRUS
BY CRYO-ELECTRON
MICROSCOPY**

**FASEB
special issue**

1986

33



... then,
from blobology to chemistry

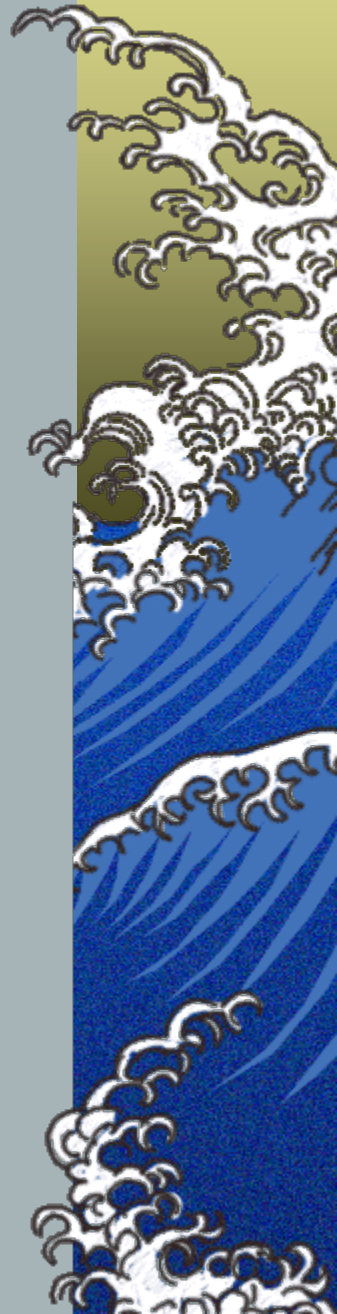


Richard Henderson, Joachim Frank



From 35 to 3.5 Å

▲ *Thirty years*



From 35 to 3.5 Å

- ▶ *Thirty years*
- ▶ *A ten times better resolution*



From 35 to 3.5 Å

- ▶ *Thirty years*
- ▶ *A ten times better resolution*
- ▶ *A thousand times more information*



From 35 to 3.5 Å

- ▶ *Thirty years*
- ▶ *A ten times better resolution*
- ▶ *A thousand times more information*
- ▶ *Seeing atoms*



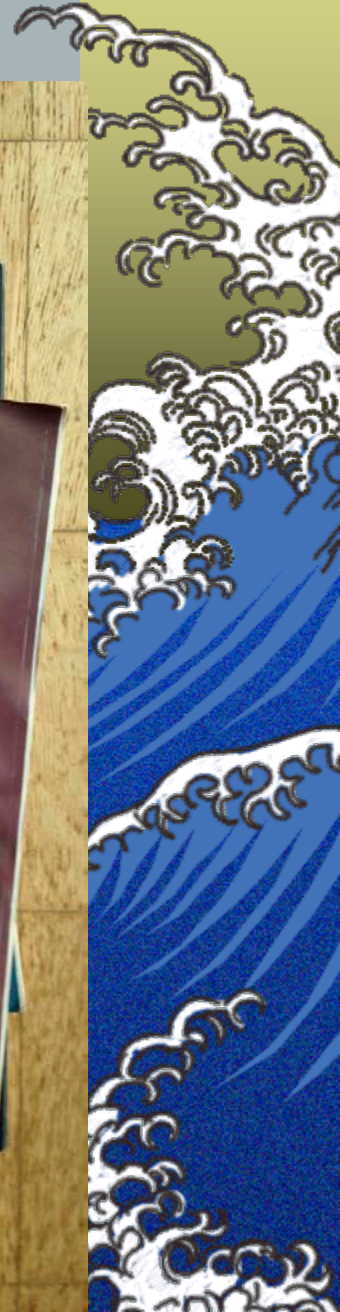
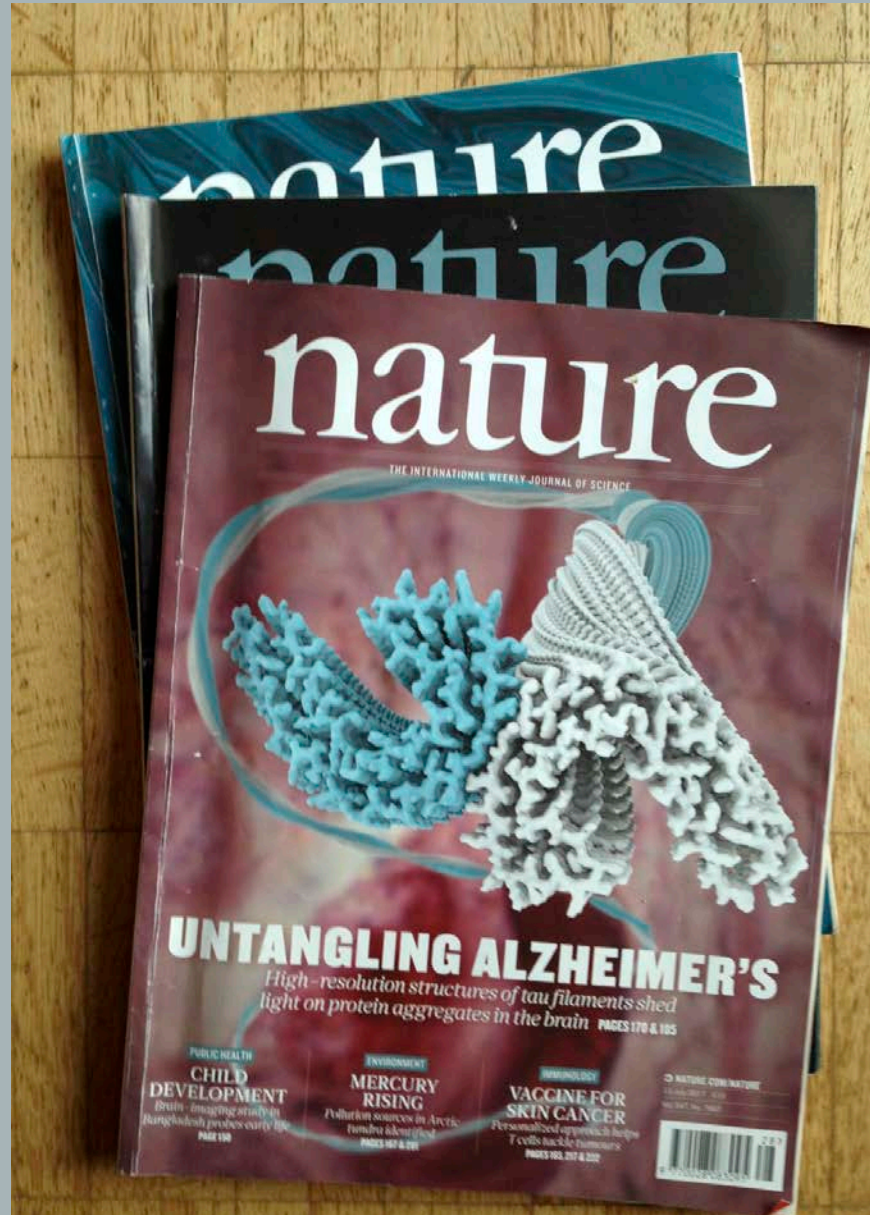
From 35 to 3.5 Å

- ▶ *Thirty years*
- ▶ *A ten times better resolution*
- ▶ *A thousand times more information*
 - ▶ *Seeing atoms*
 - ▶ *Chemistry*

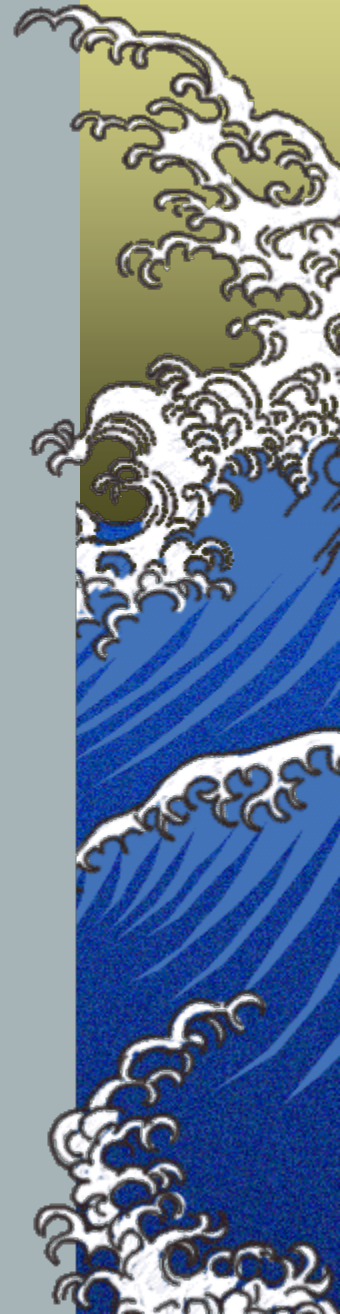
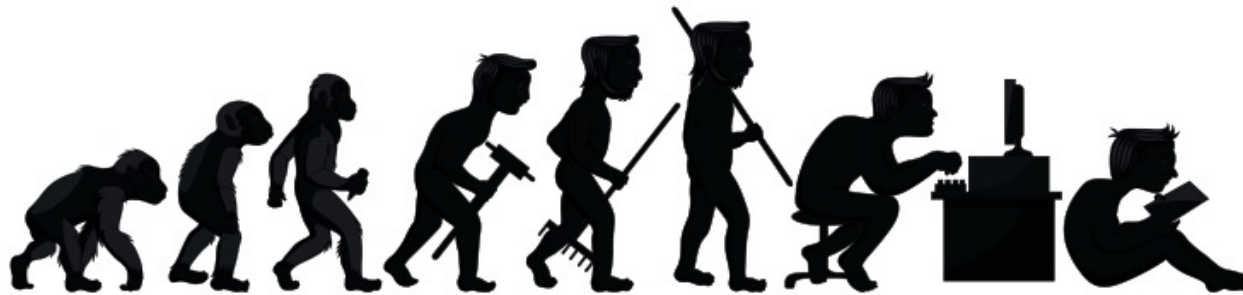


From Chemistry to Medicine

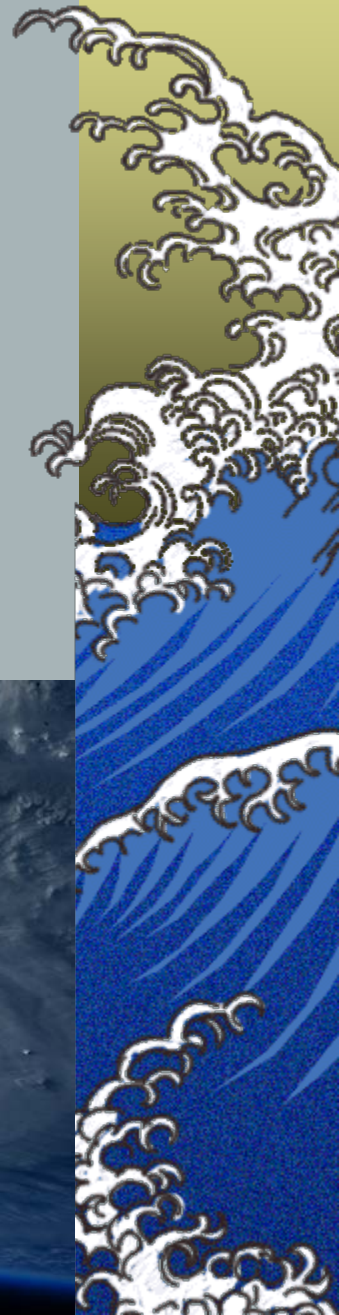
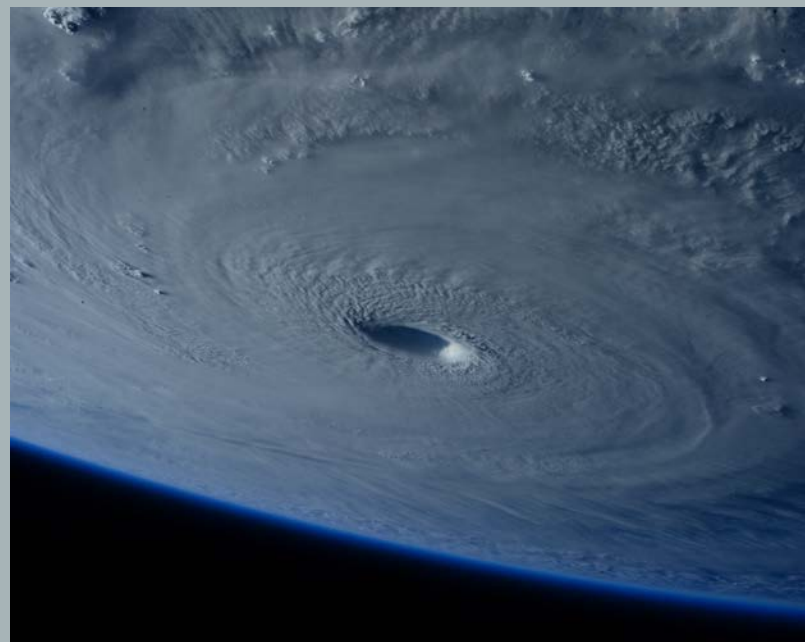
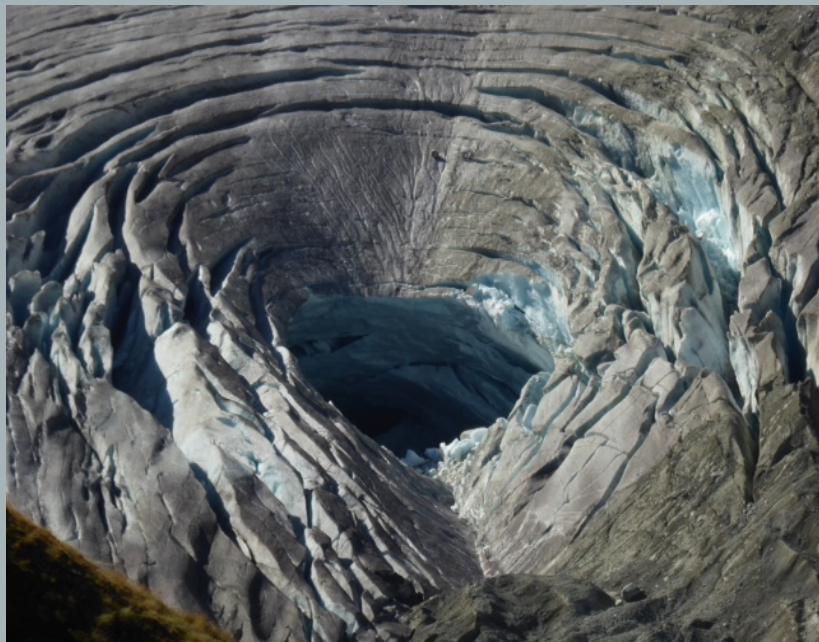
▲ Fitzpatrick, A. W. P., Falcon, B., He, S., Murzin, A. G., Murshudov, G., Garringer, H. J., . . . Scheres, S. H. W. (2017). Cryo-EM structures of tau filaments from Alzheimer's disease. *Nature*, 547(7662), 185-190. doi:10.1038/nature23002.



The Power of Knowledge



From Scarcity to Excess



Science without conscience
is but the ruin of the soul!

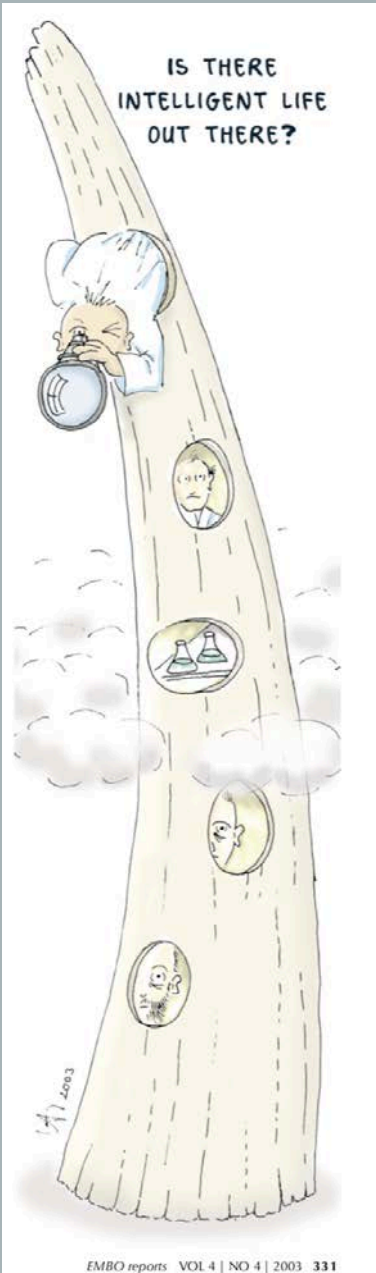
François Rabelais 1532



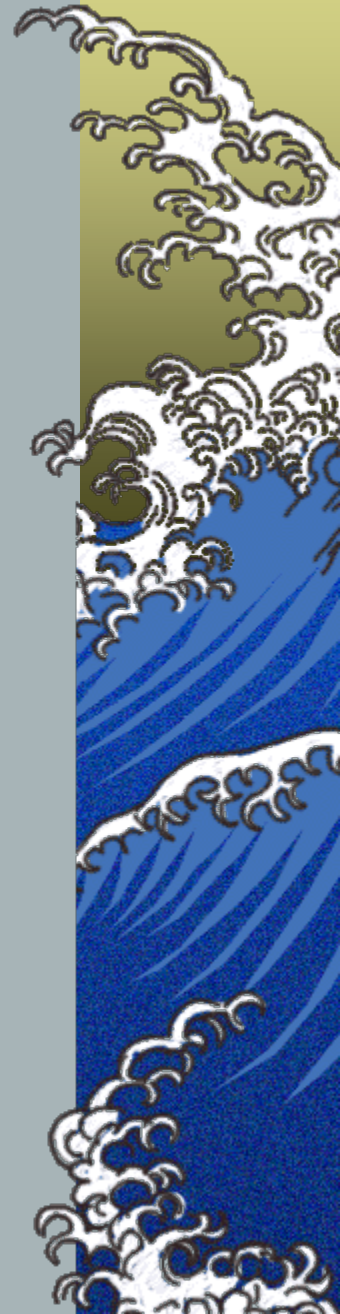
Coming out of the Ivory tower

A curriculum: Biology and Society

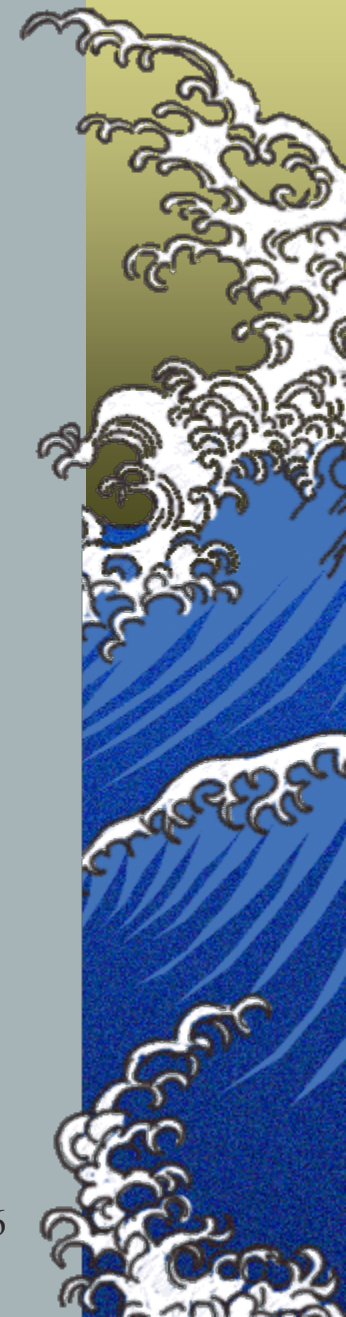
To ensure that our students turn out to be
as good citizens
as they are good biologists



How can we be as good in
using knowledge
for the well-being of all
as we are in producing it?



Imagine . . .



Imagine . . .



You may say I'm a dreamer
But I'm not the only one
I hope some day you'll join us
And the world will live as one

John Lennon



Thank-you

