Structural biology of mitochondria

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MAX-PLANCK-GESELLSCHAFT

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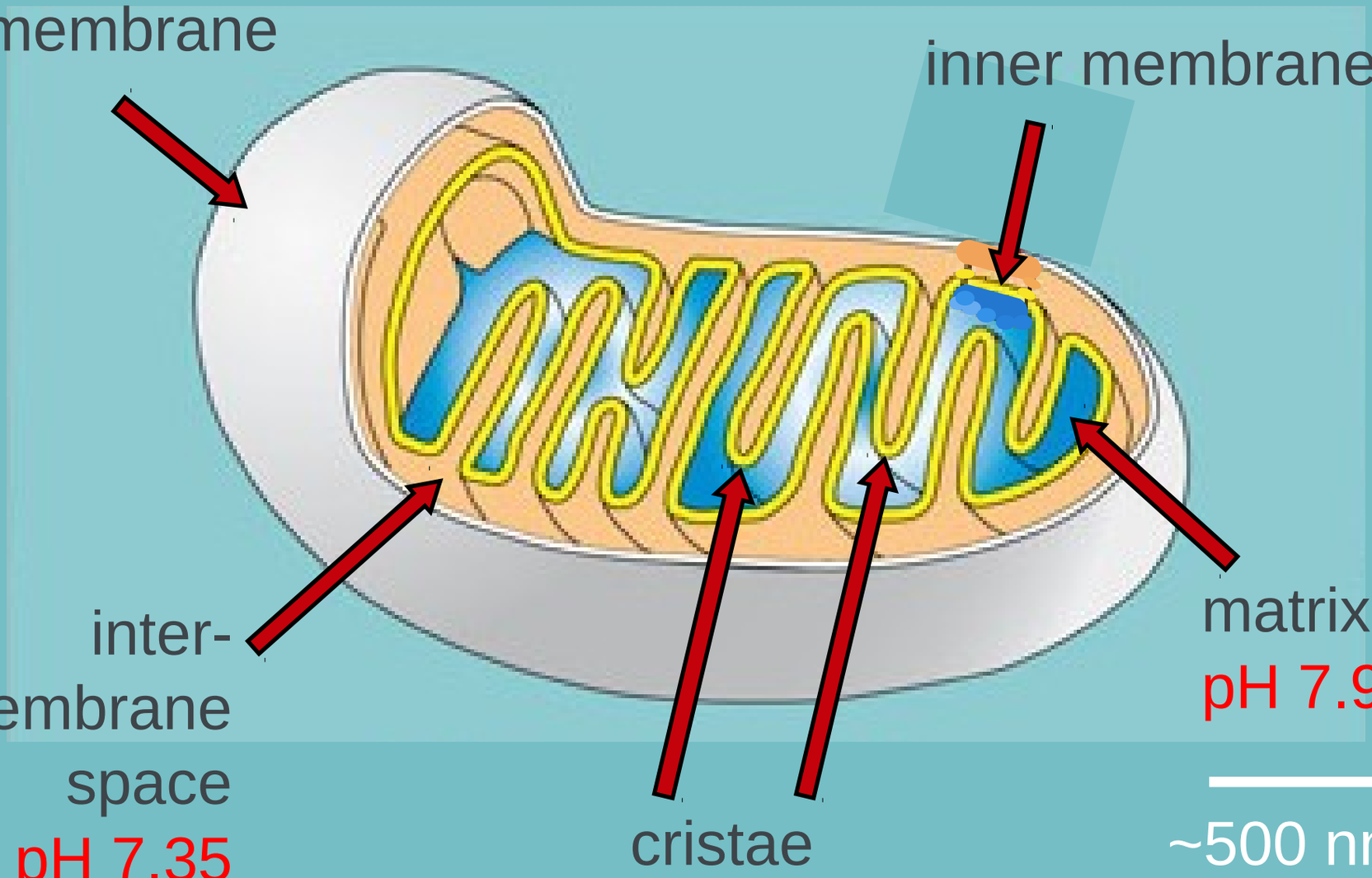
The mitochondrion

- Powerhouse of the eukaryotic cell
- Produces almost all ATP to drive cellular reactions
- Semi-autonomous cell organelle (division, fusion, own genetic system)
- Imports > 99% of proteins from cytoplasm
- Outer membrane is permeable to small molecules
- Inner membrane is site of respiration and ATP synthesis
- Major role in ageing and apoptosis

Schematic drawing of mitochondrion



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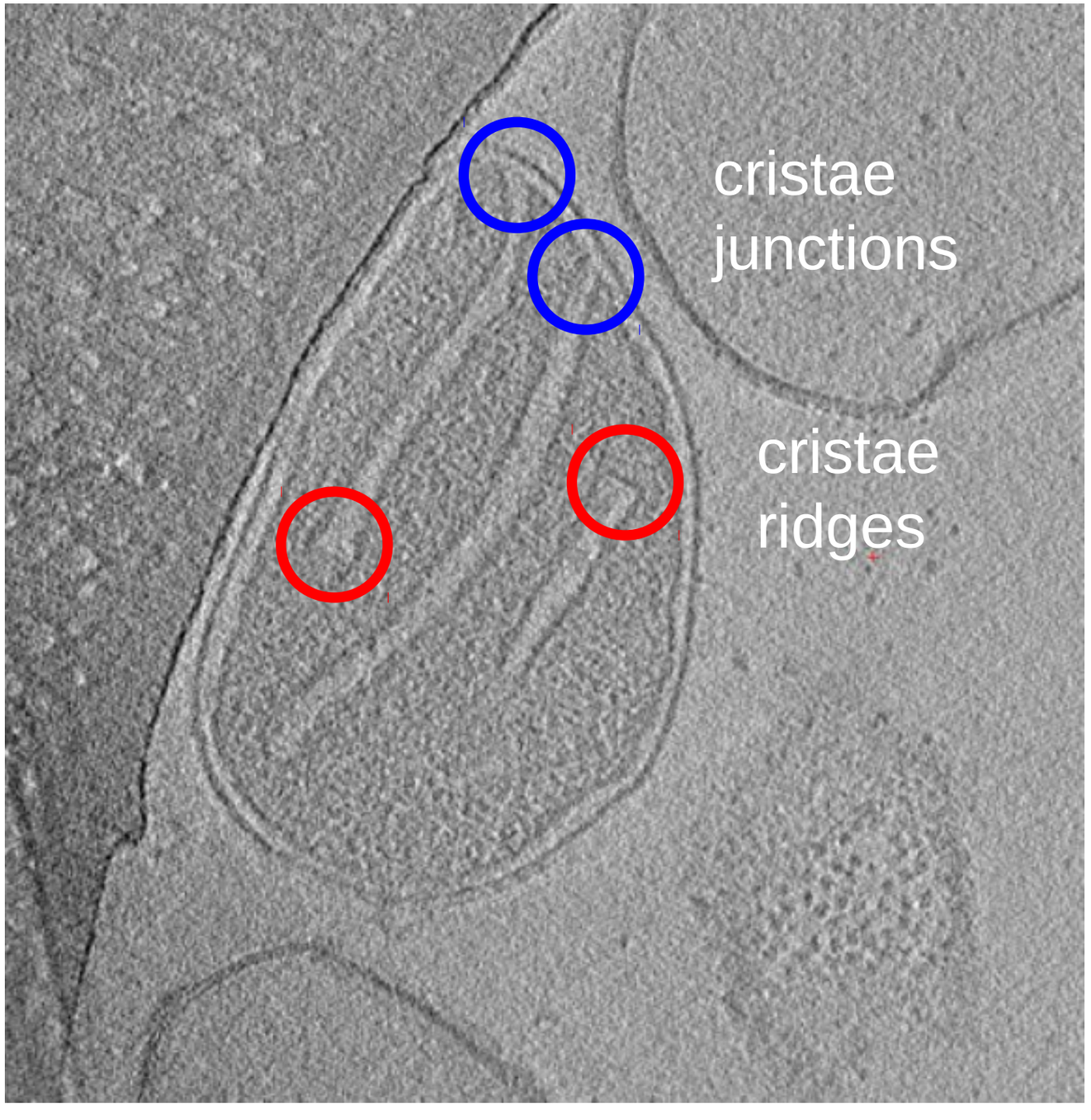
Mitochondria in a human endothelial cell

QuickTime™ and a
decompressor
are needed to see this picture.

~10 µm

Jürgen Bereiter-Hahn, Frankfurt University

Podospora anserina has smaller mitochondria with fewer cristae



Bertram Daum

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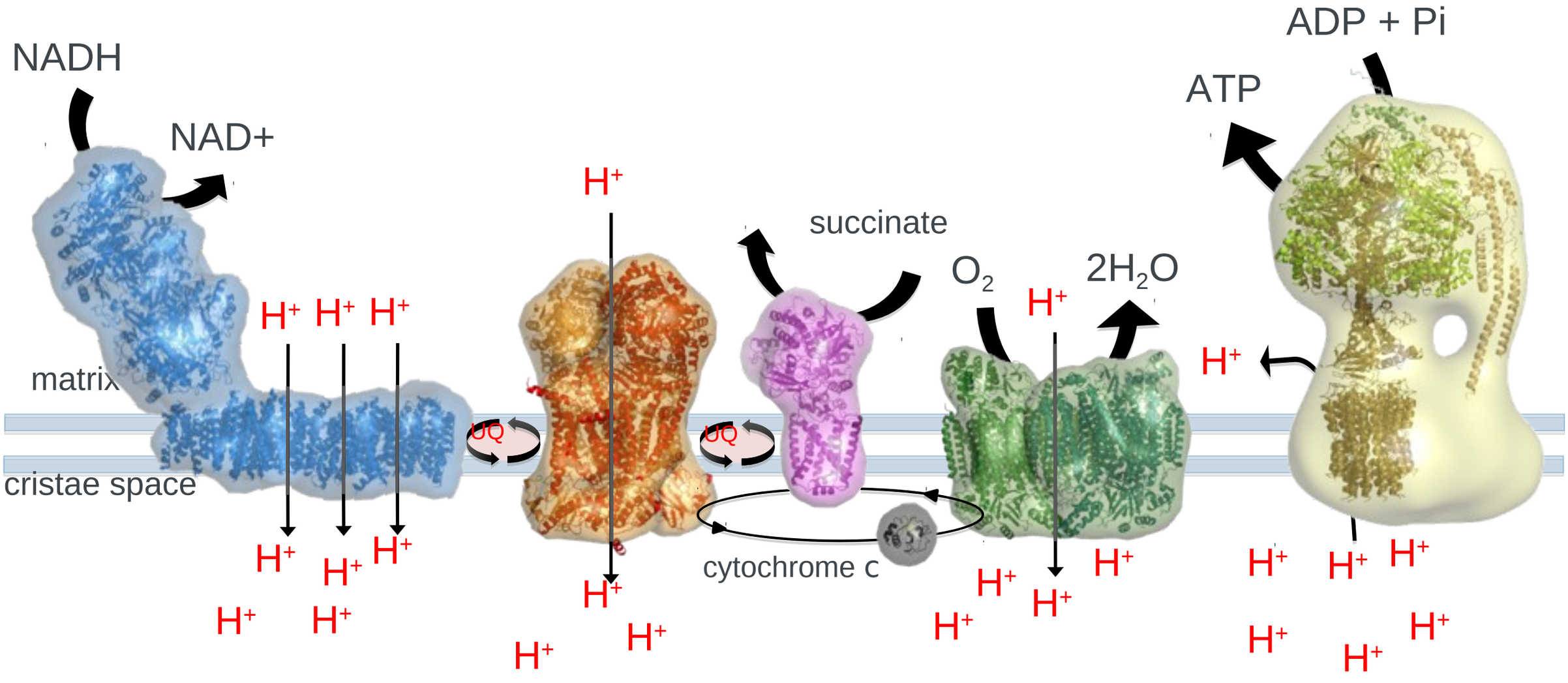
Arrangement of the mitochondrial ATP synthase

The mitochondrial respiratory chain



Complex I
NADH dehydrogenase

Complex III
cytochrome c reductase

Complex II
succinate dehydrogenase

Complex IV
cytochrome c oxidase

Complex V
ATP synthase

drawn by Karen Davies

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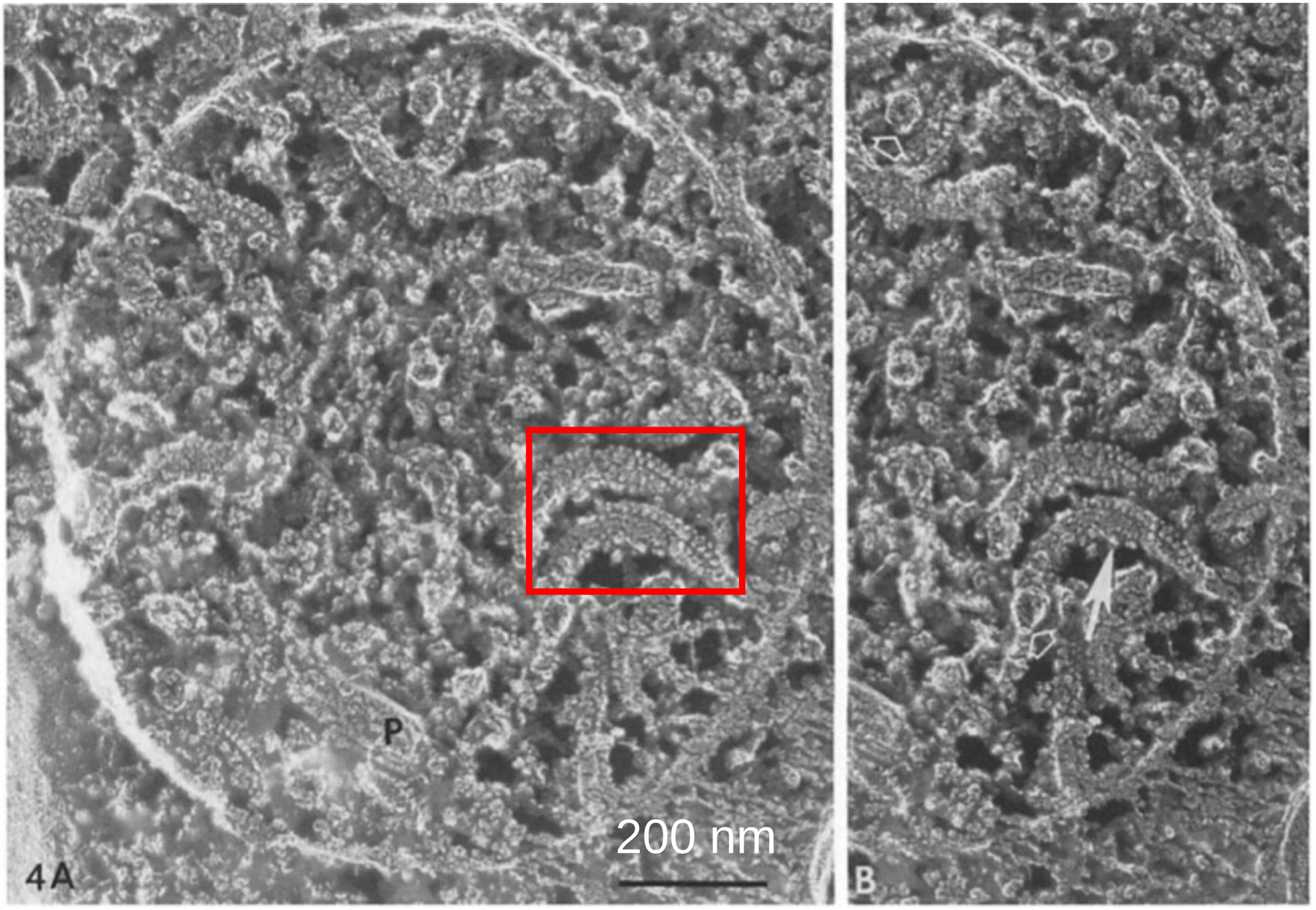
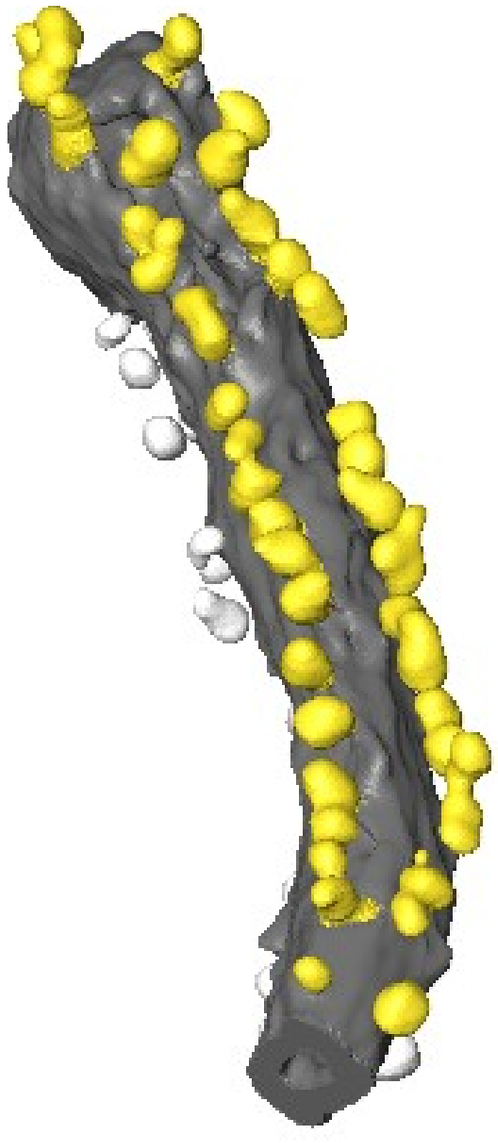
Deep-etched Paramecium mitochondrion

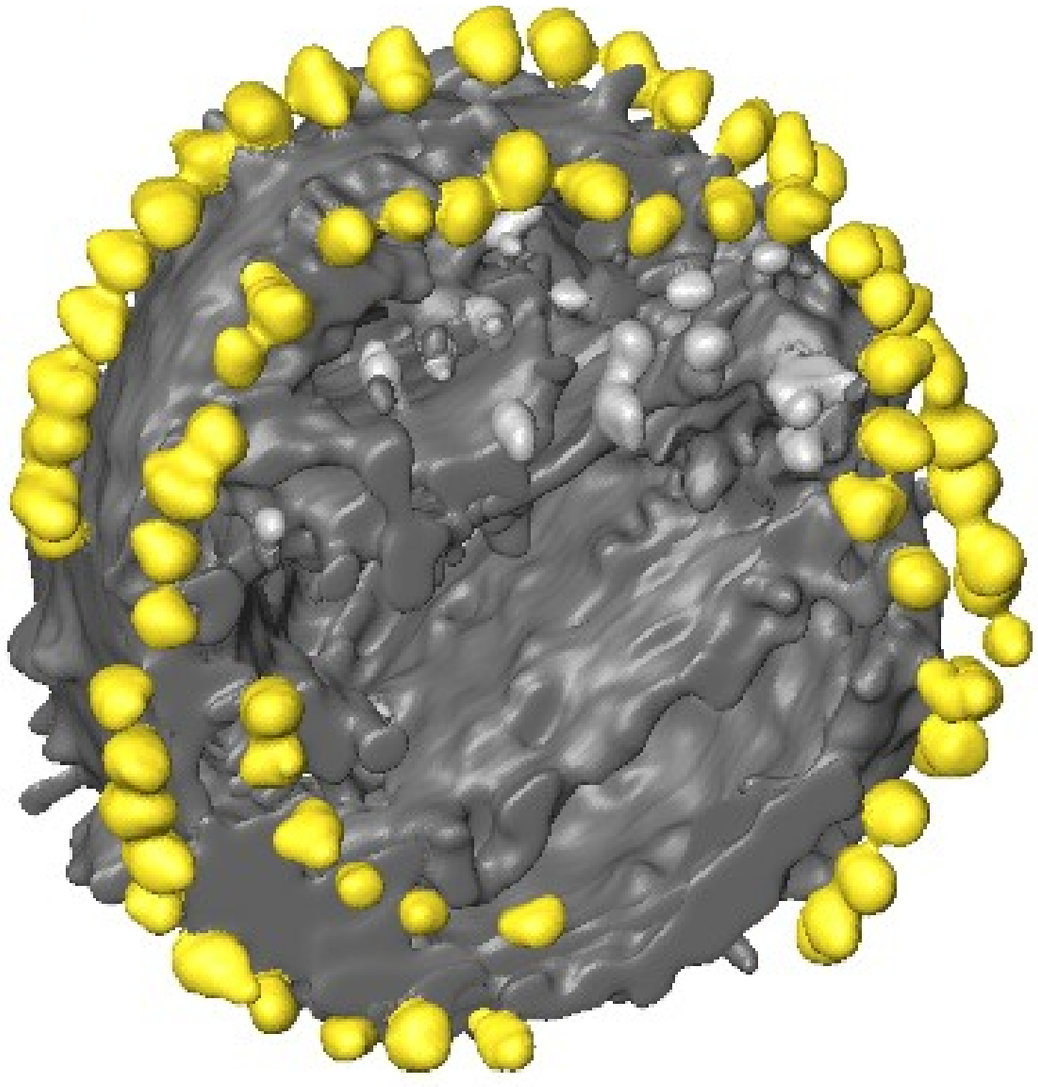


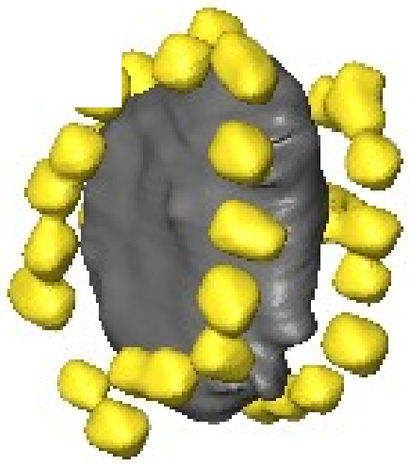
R.D.Allen et al, J.Cell Biol. 1989

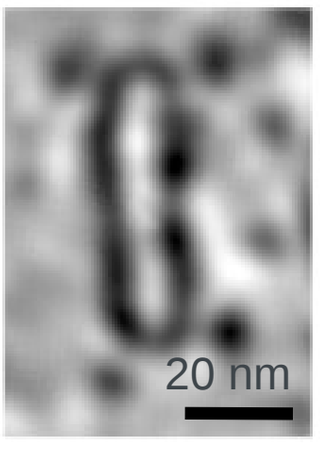
Dimer ribbons in mammalian mitochondria



rat liver:
tubular cristae







bovine heart:
lamellar cristae

Strauss et al, EMBO J 2008

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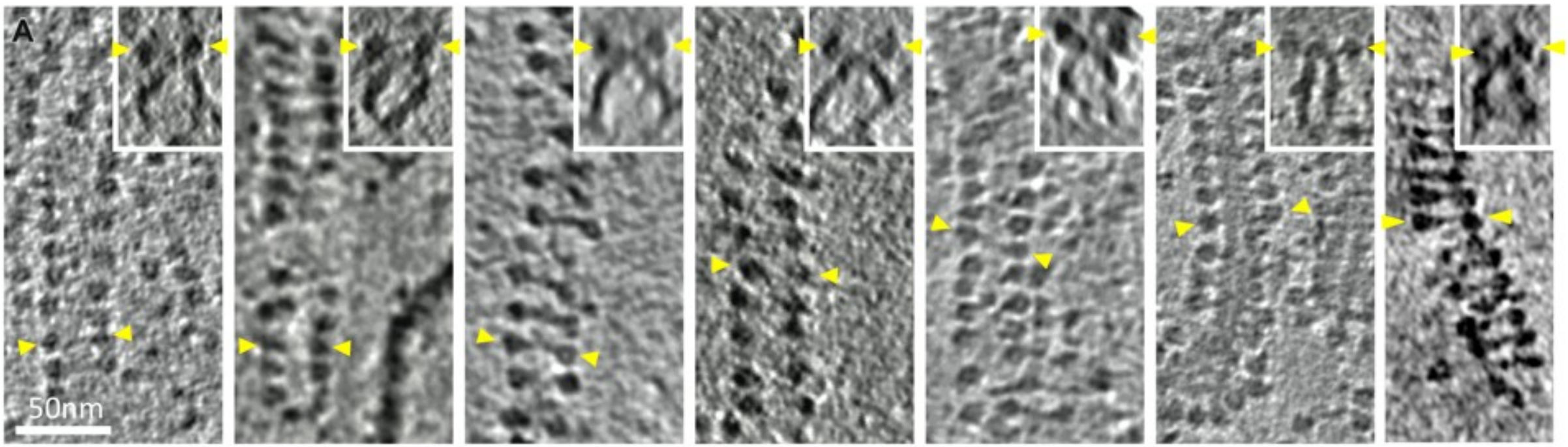
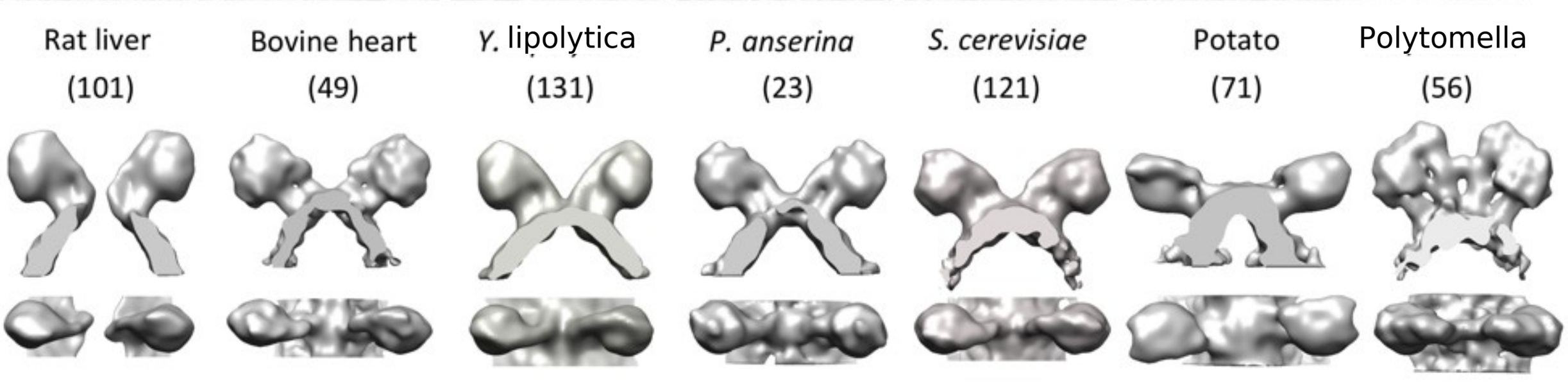
Dimer rows are ubiquitous





subtomogram averages

Karen Davies

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Cryo-ET of Podospora mitochondrion

QuickTime™ and a
decompressor
are needed to see this picture.

ATP synthase dimers

ribosomes

inner membrane

Davies et al, PNAS 2011

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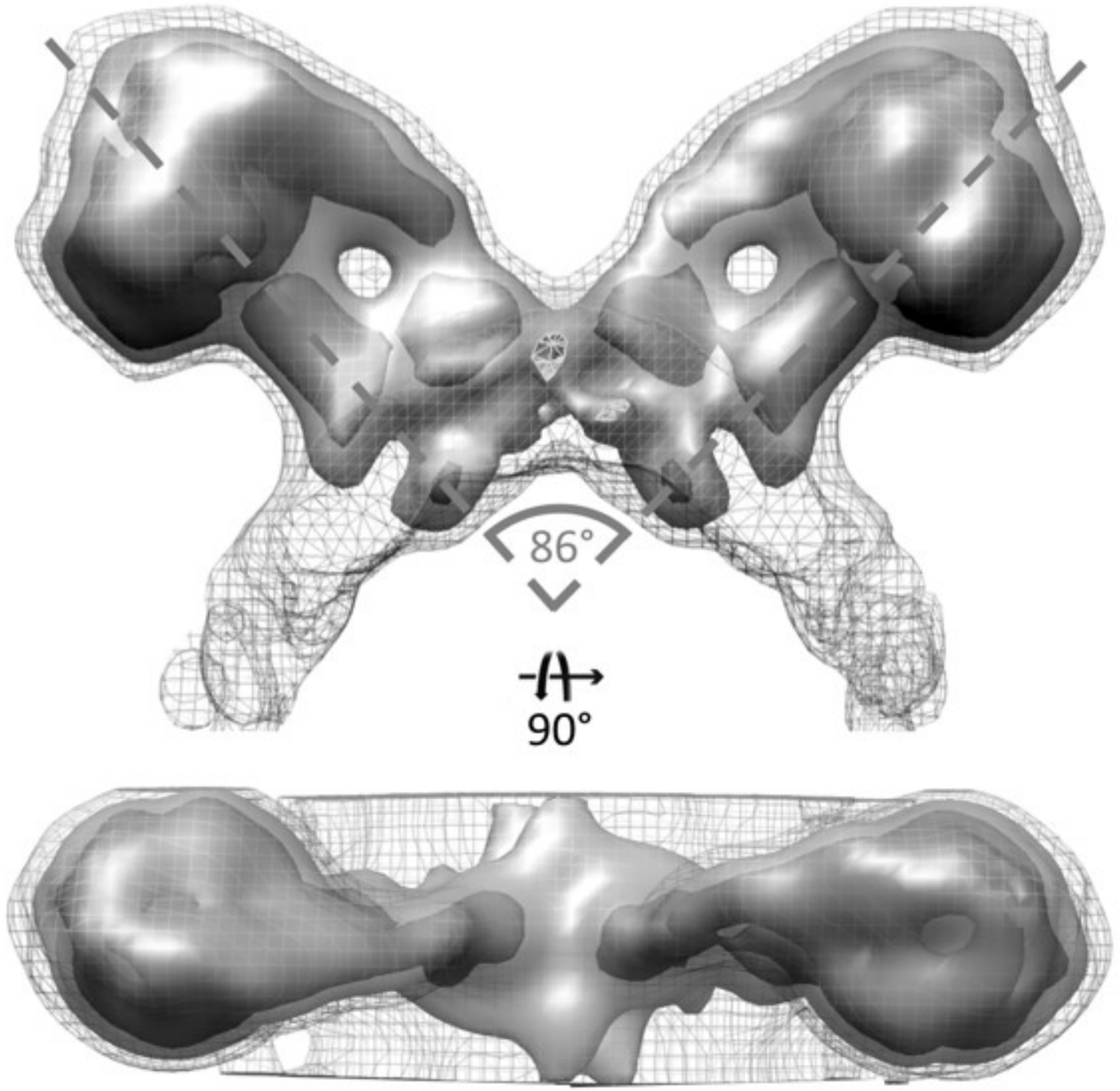
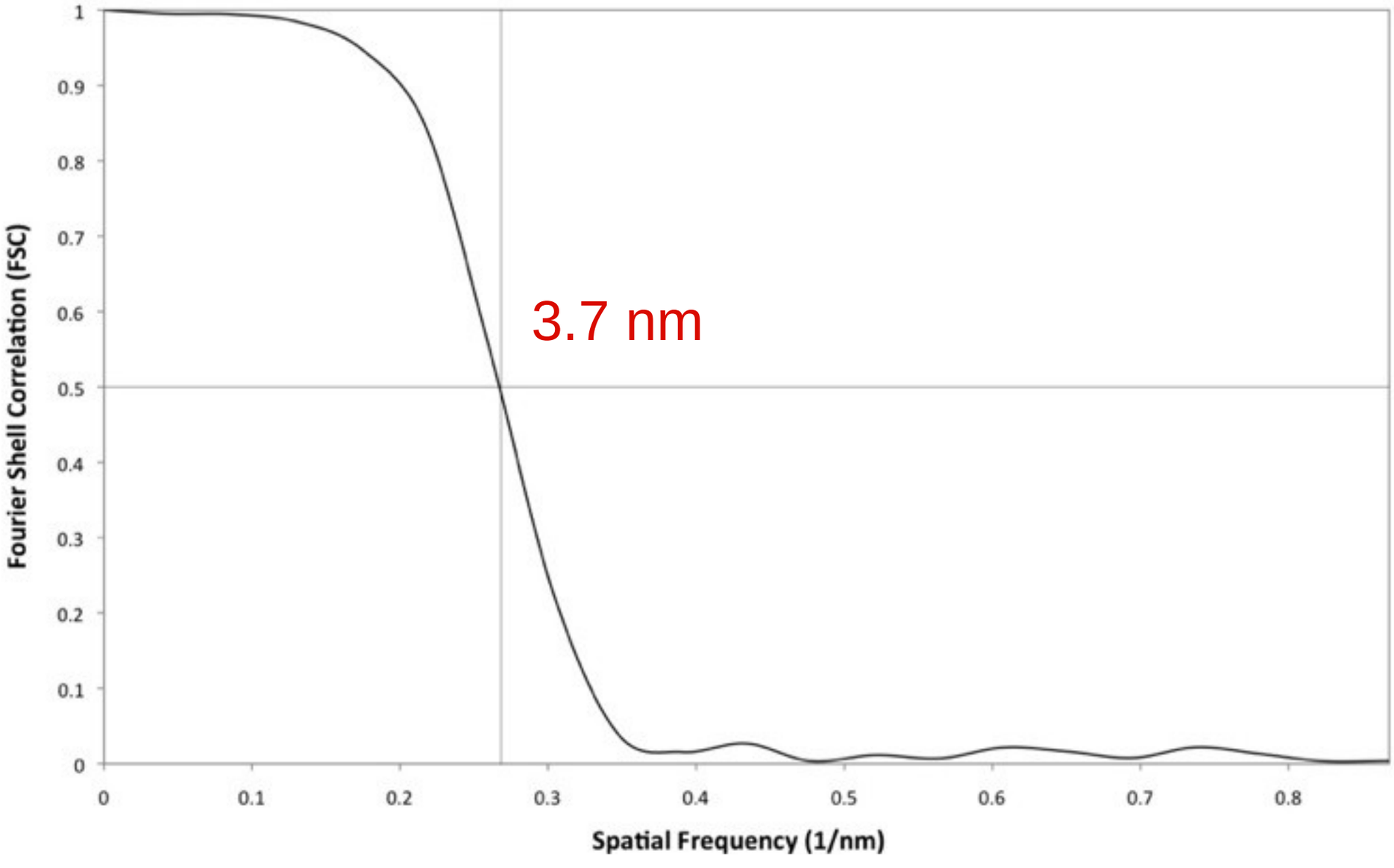
Sub-tomogram average of yeast dimer



Davies et al, PNAS 2012

Resolution estimate

average of 121 sub-tomograms



Davies et al, PNAS 2012

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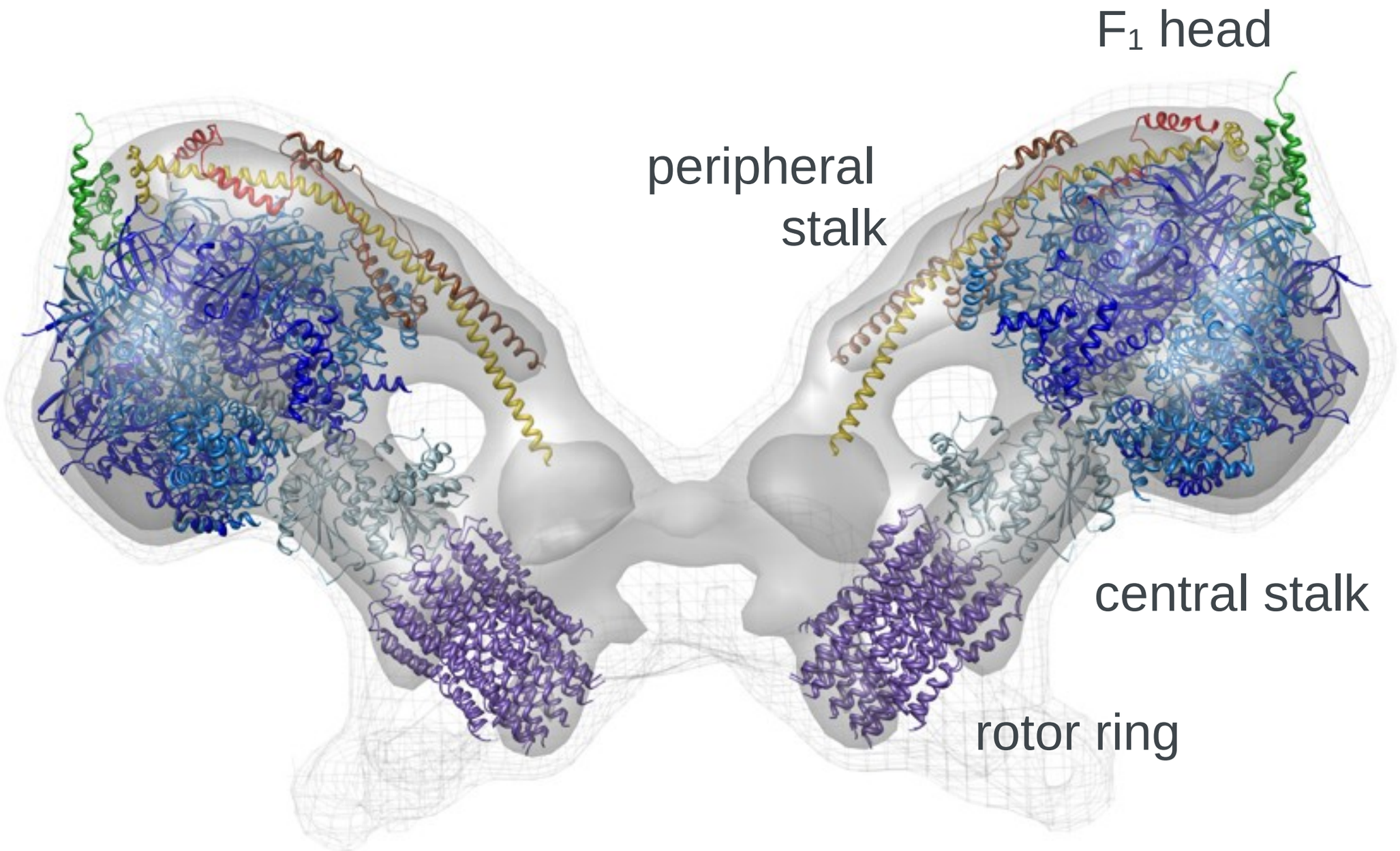
Sub-tomogram average of ATP synthase dimer



Davies et al, PNAS 2012

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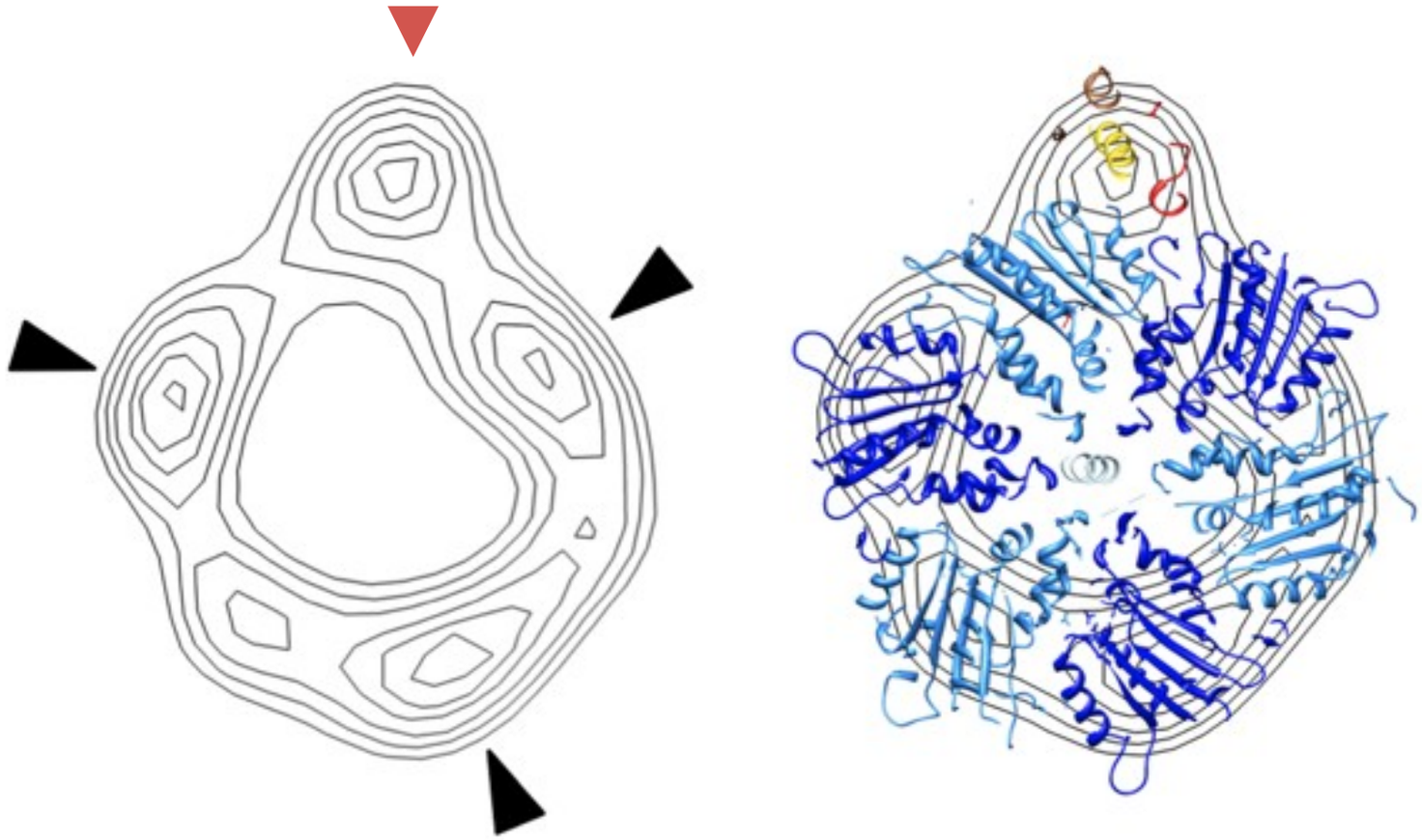
Sub-tomogram average of ATP synthase dimer

F_1 head

peripheral stalk

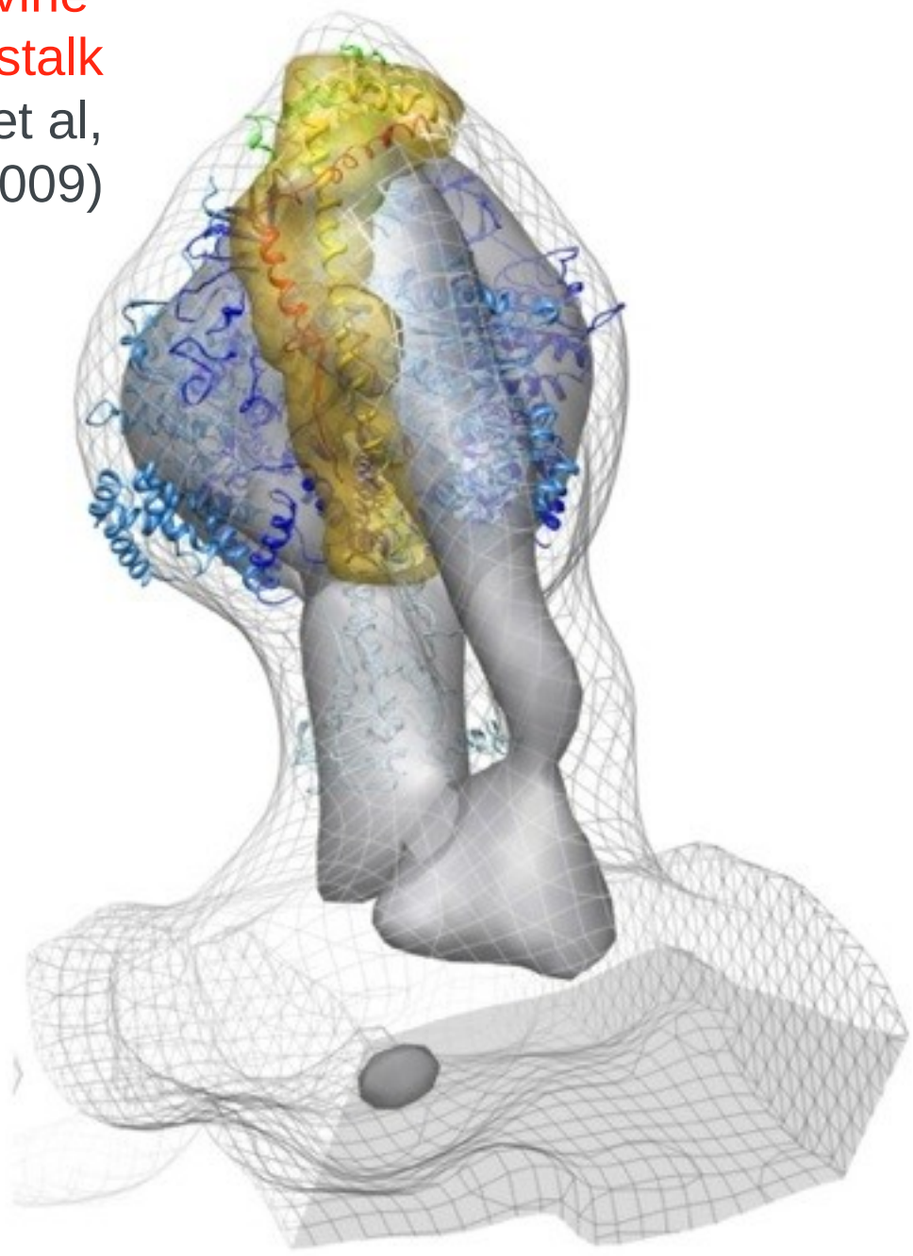


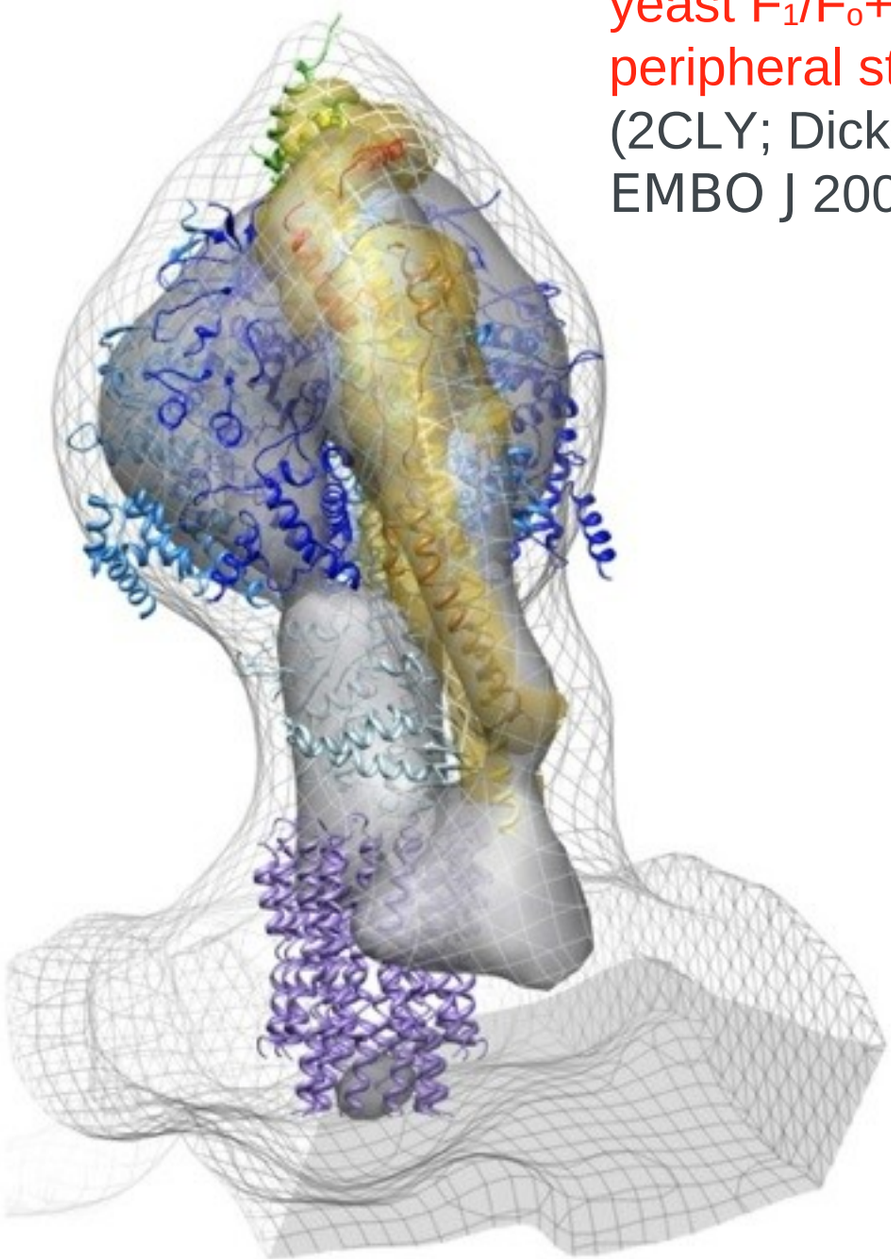
beta subunits

Davies et al, PNAS 2012

Fit of peripheral stalk

bovine F_1/peripheral stalk (2WSS; Rees et al, PNAS 2009)

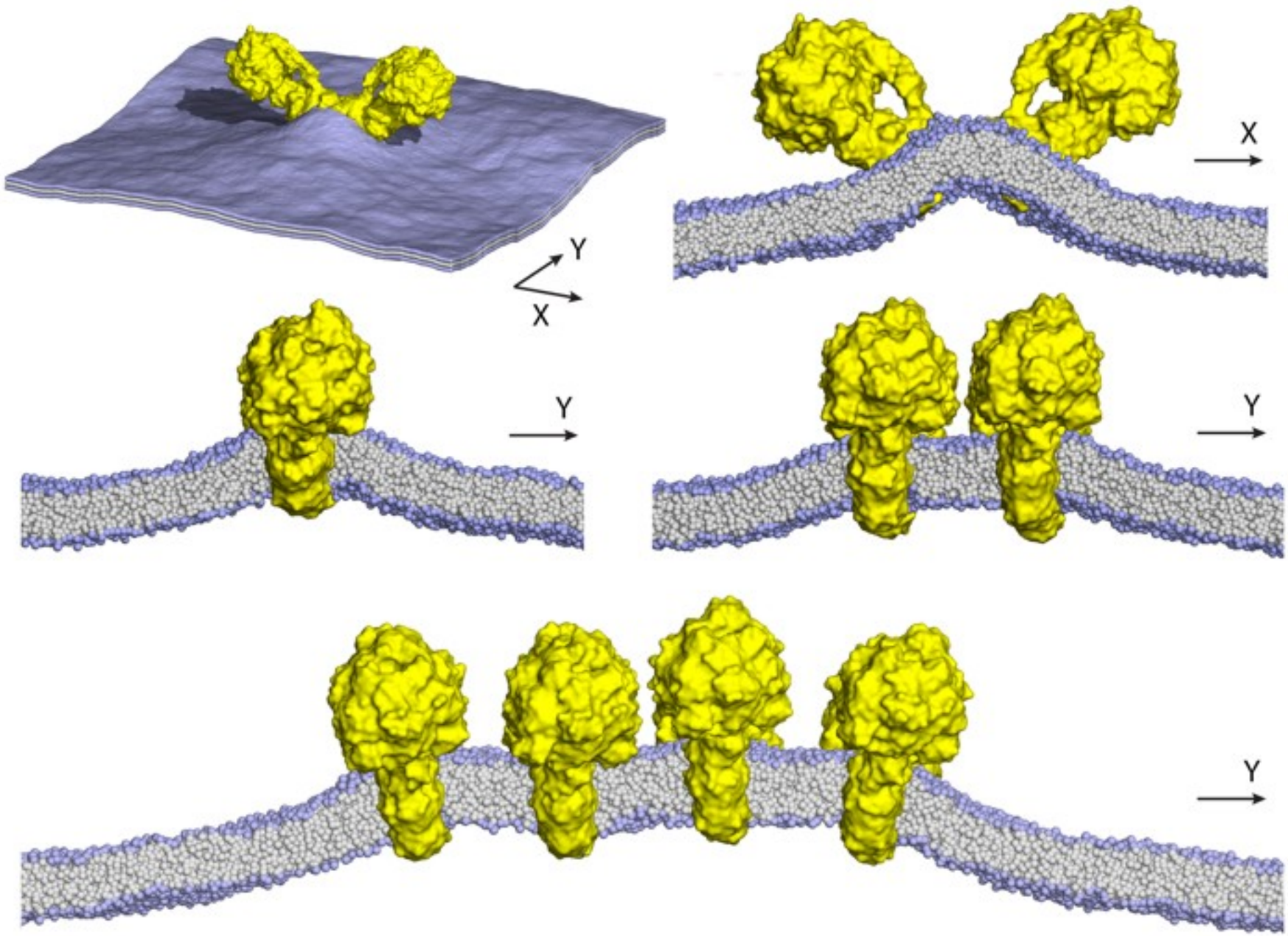




yeast F_1/F_o+bovine peripheral stalk (2CLY; Dickson et al, EMBO J 2006)

Davies et al, PNAS 2012

ATP synthase dimers self-organize into rows



coarse-grained MD simulation by
José Faraldo-Gomez, Claudio Anselmi, MPI of Biophysics

Davies et al, PNAS 2012

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Free energy of dimer association

Energy of elastic membrane deformation is > 6 kT per dimer

For comparison:
Free energy of protein-protein interaction (glycophorin A dimer) ~15 kT

José Faraldo-Gomez, Claudio Anselmi, MPI of Biophysics

Davies et al, PNAS 2012

ATP synthase monomers

stroma ~ pH 8

thylakoid lumen
~ pH 5

H^+ H^+ H^+ H^+

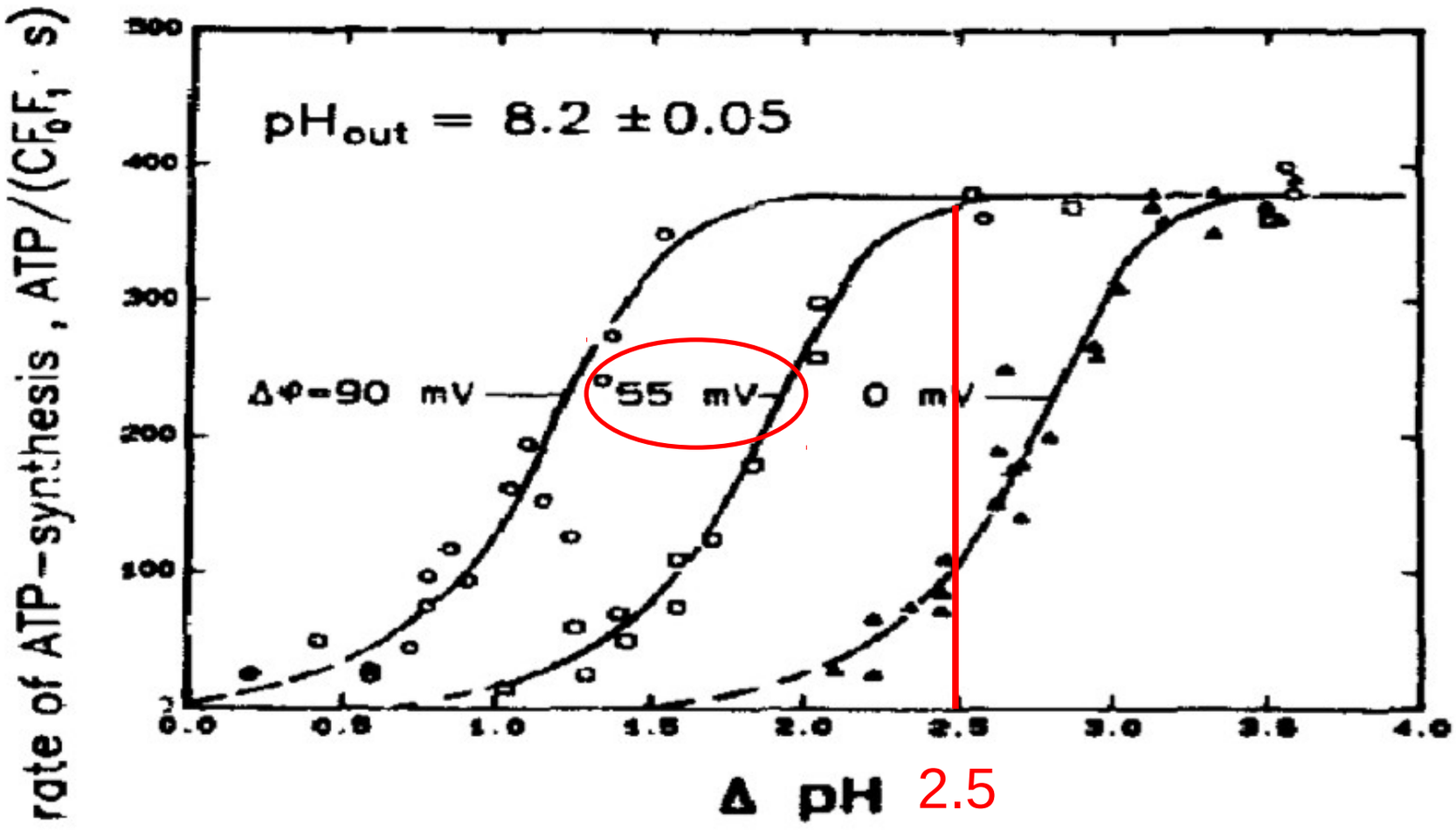
thylakoid membrane

inner membrane

outer membrane

Chloropla

ATP synthesis in chloroplasts



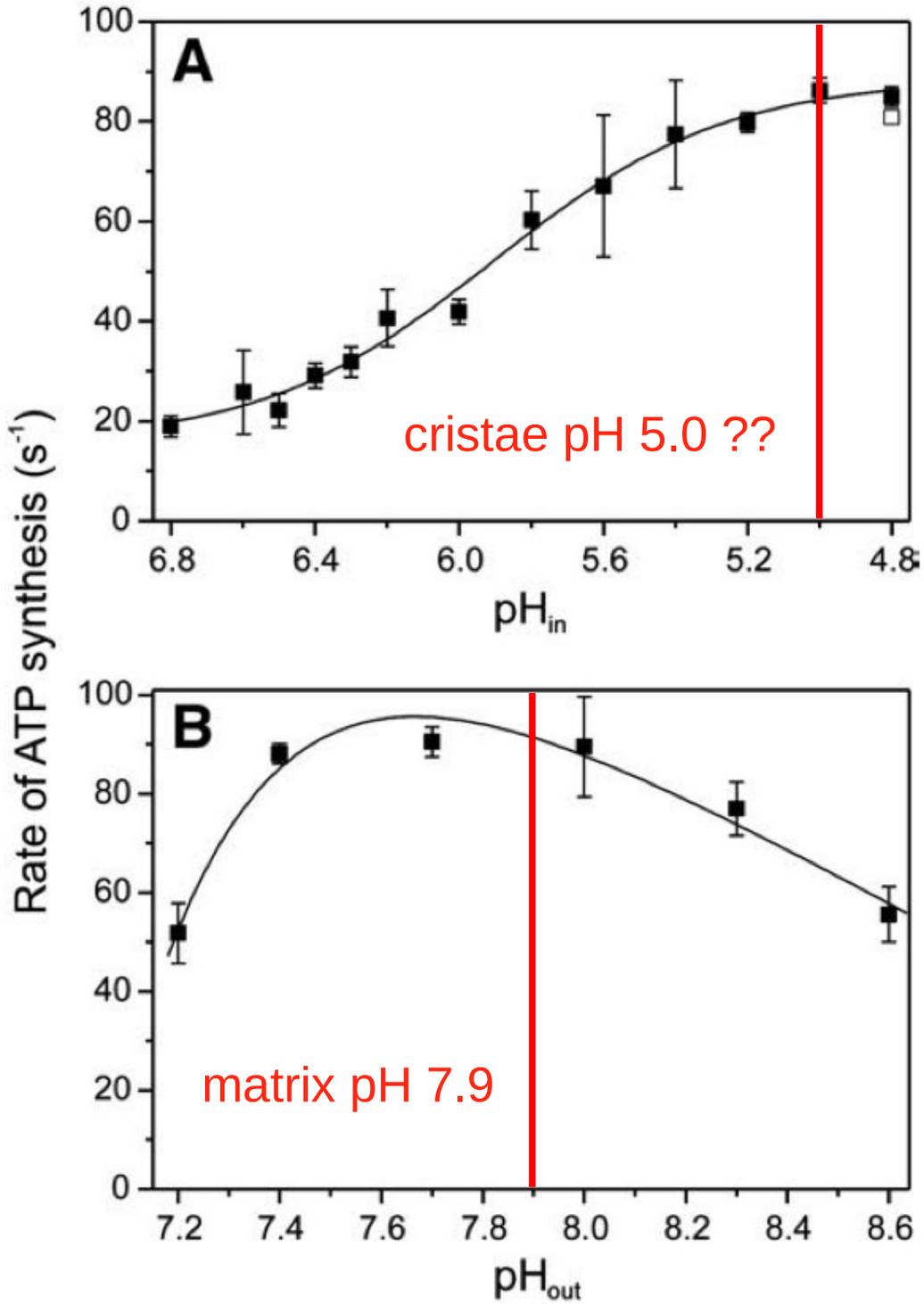
maximal rate
~400 ATP per synthase per second

at a delta pH of 2.5 and a membrane potential of 55 mV

Fig. 2. The rate of ATP synthesis as function of ΔpH at different superimposed diffusion potentials. Data was taken from Fig. 1 and additional sets of experiments.

Junesch and Gräber, FEBS Lett 1991

ATP synthesis in mitochondria



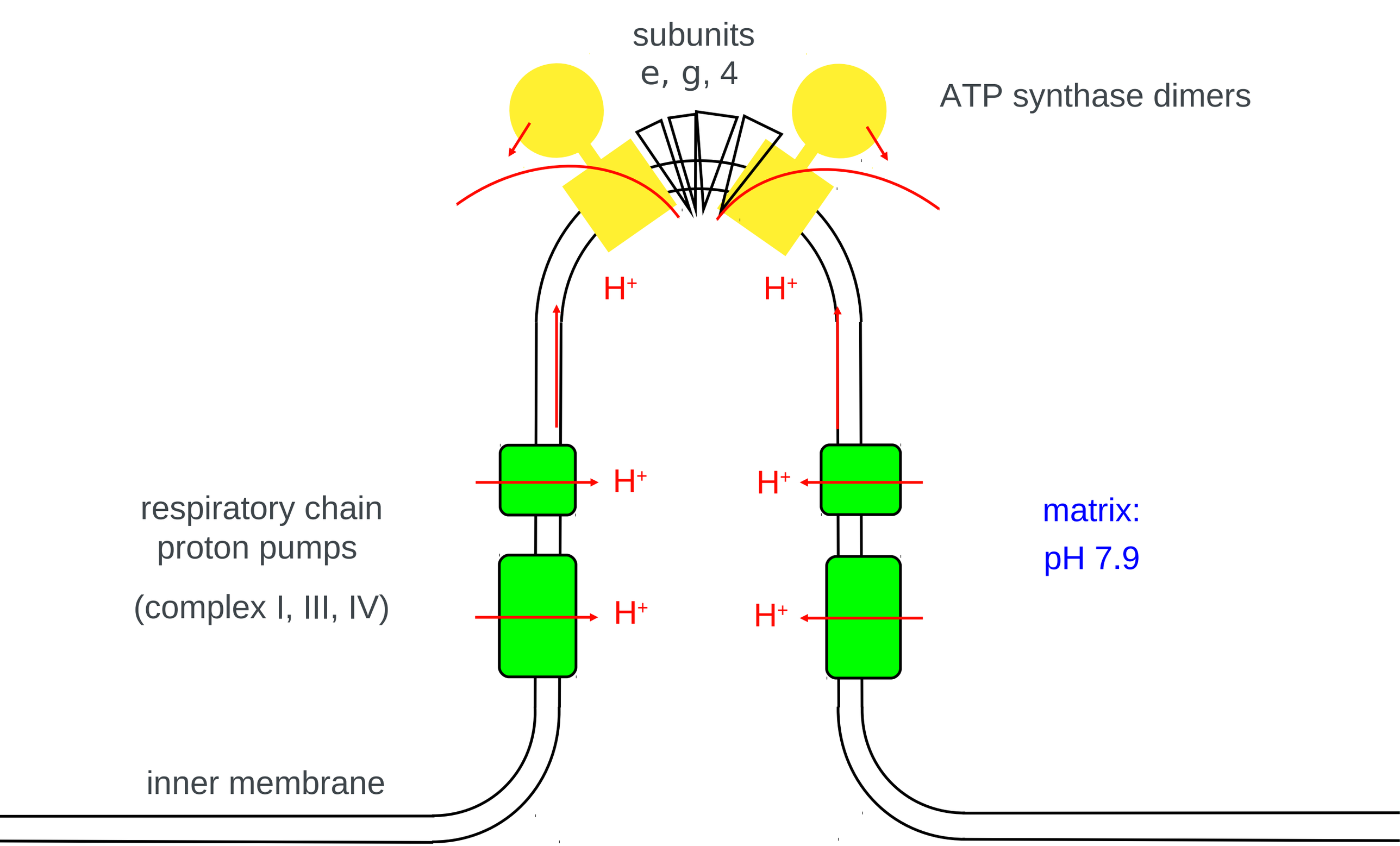
maximal rate
~80 ATP per synthase per second

at a delta pH of 2.9 and a membrane potential of 133 mV

Förster, Turina, Drepper, Hähnel, Fischer, Gräber, Petersen, BBA 2010

subunits
e, g, 4

ATP synthase dimers



respiratory chain
proton pumps

(complex I, III, IV)

matrix:

pH 7.9

inner membrane

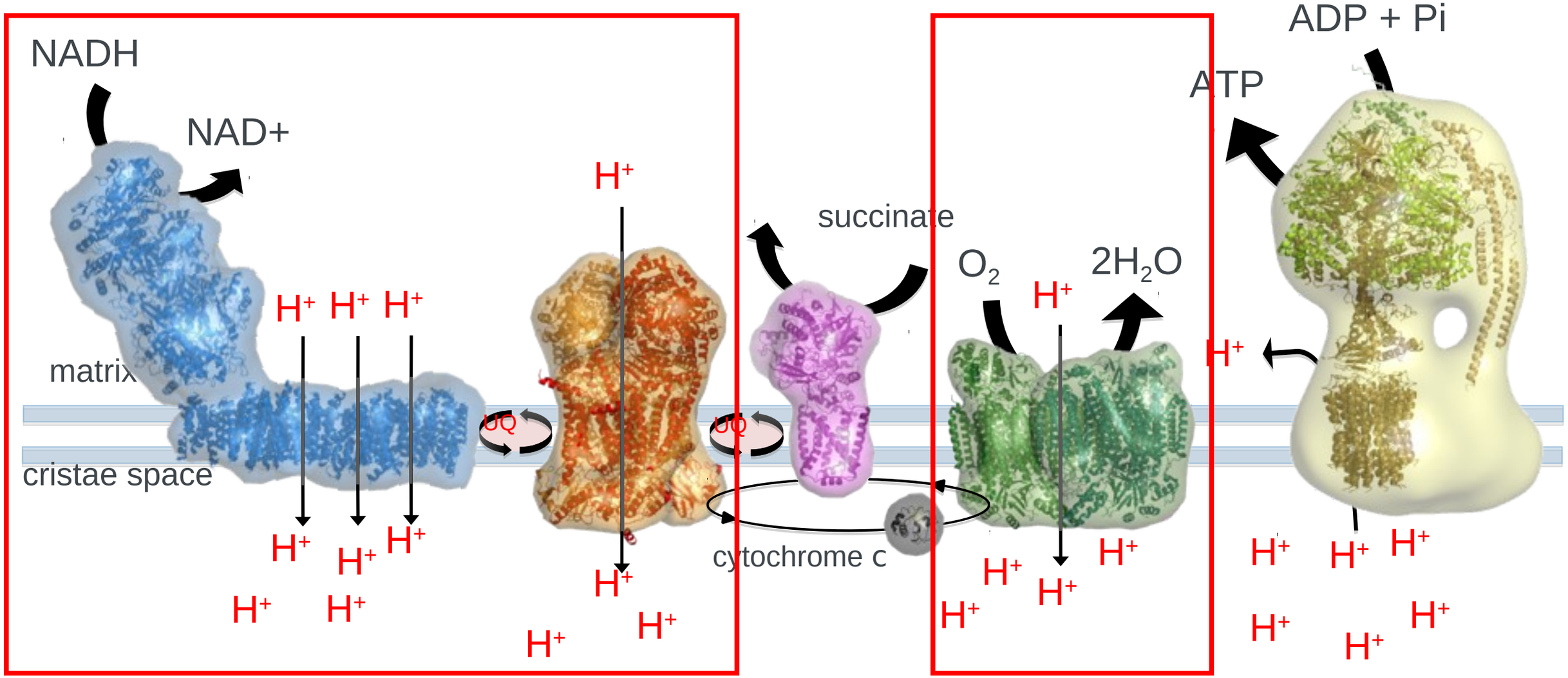
pH intermembrane space
= pH cytoplasm: 7.35

outer membrane

Mitochond

Respiratory chain supercomplex

The mitochondrial respiratory chain



Complex I
NADH dehydrogenase

Complex III
cytochrome c reductase

Complex II
succinate dehydrogenase

Complex IV
cytochrome c oxidase

Complex V
ATP synthase

drawn by Karen Davies

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Podospora cristae vesicle

QuickTime™ and a
decompressor
are needed to see this picture.

ATP synthase
dimer row 1

ATP synthase
dimer row 2

respiratory chain
complexes

crista membrane

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Davies et al, PNAS 2011

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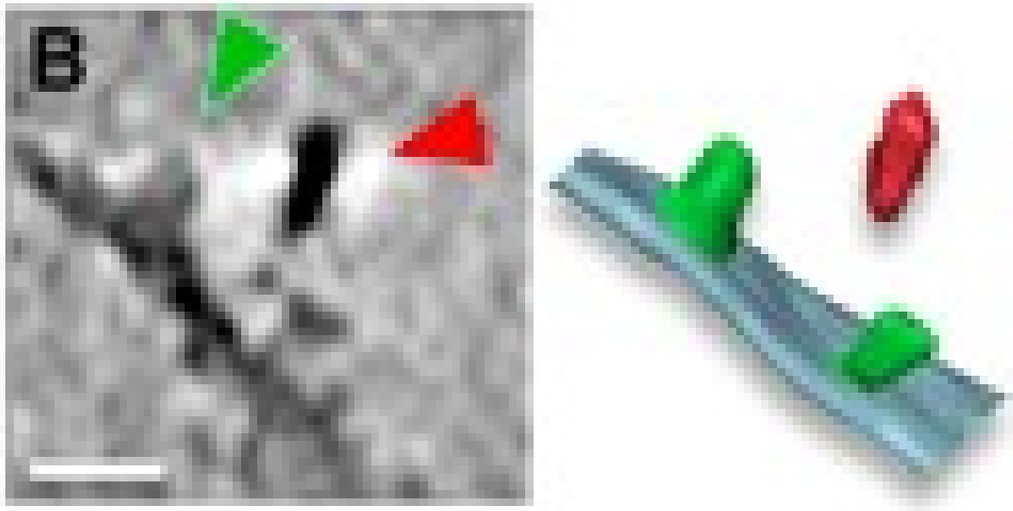
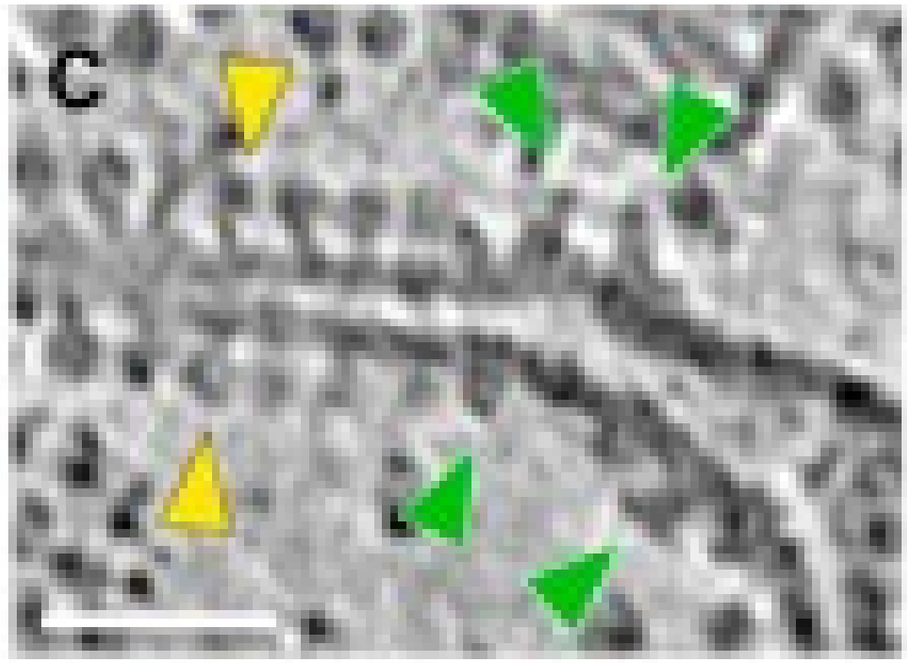
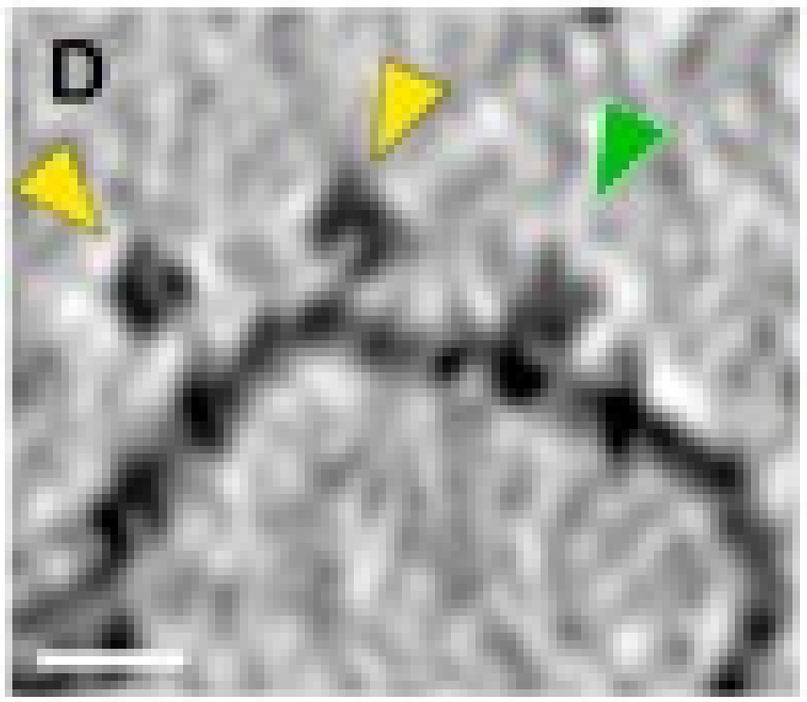
Supercomplex in cristae membranes



quantum-dot labelled complex I

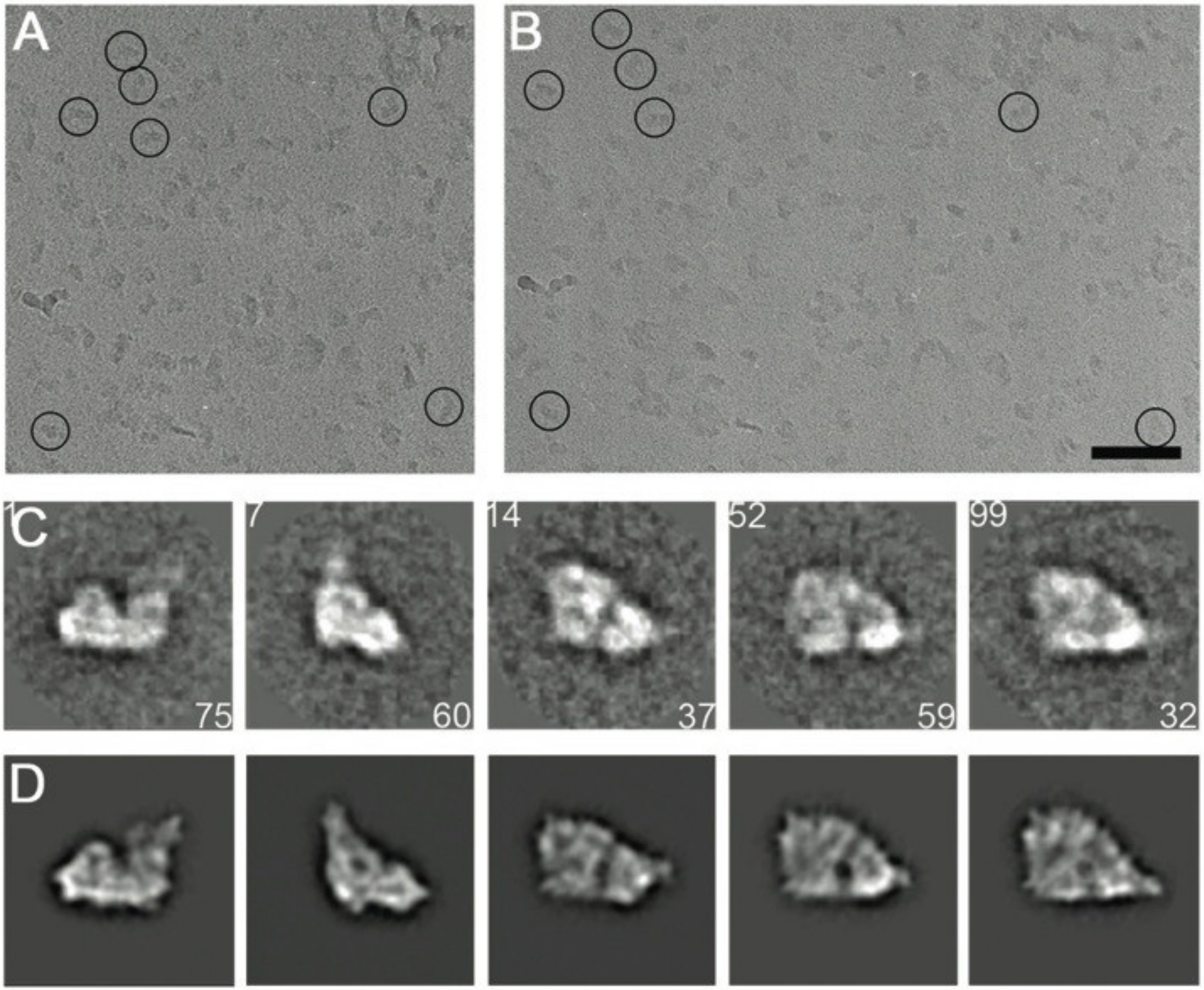




supercomplex
next to dimer row

Davies et al, PNAS 2011

Respiratory chain supercomplex $I_1III_2IV_1$



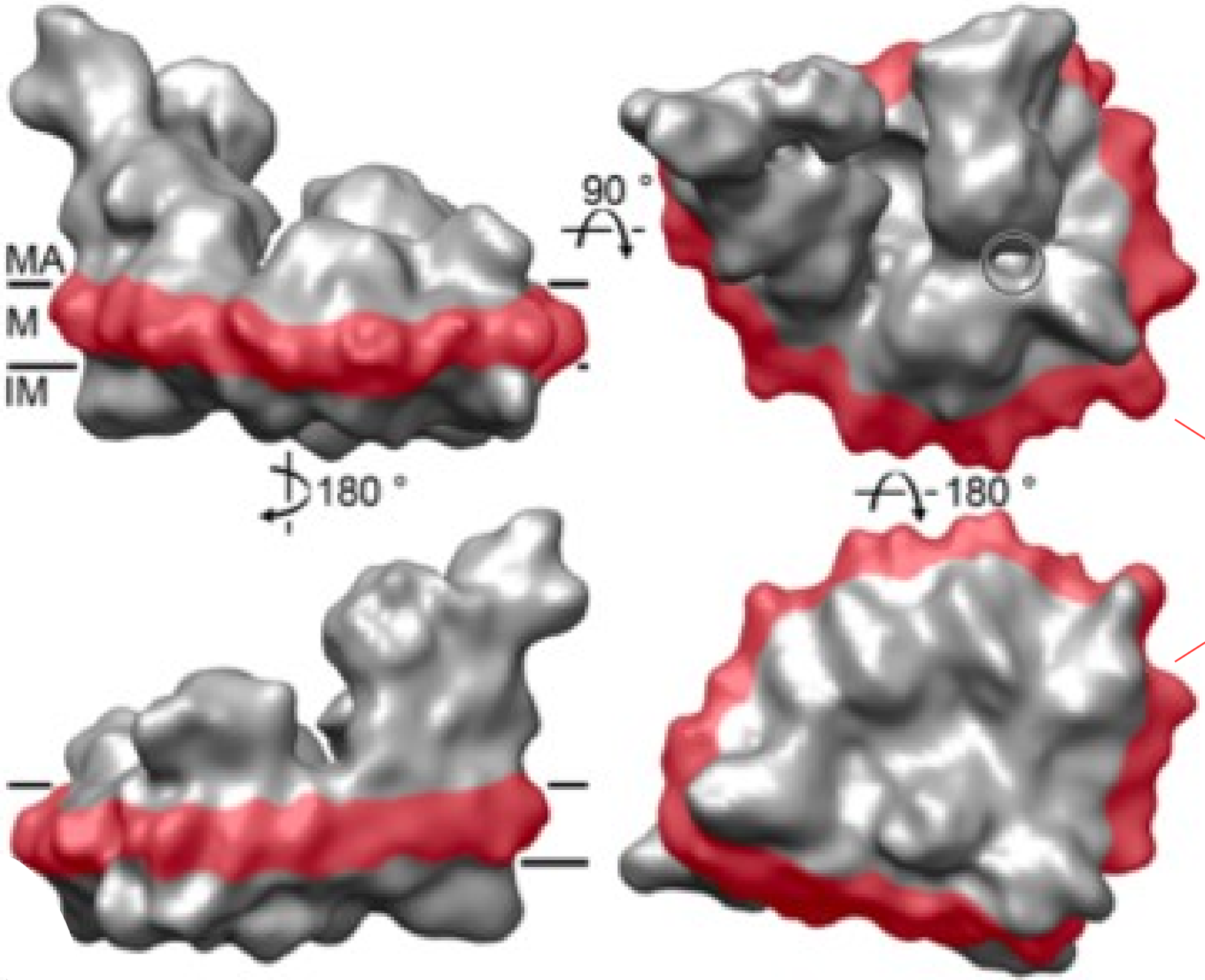
random
conical tilt
on thin C film

class
averages

reprojections
of final volume

Althoff et al, EMBO J 2011

3D cryo-EM map



Althoff et al, EMBO J 2011

Respiratory chain supercomplex $I_1III_2IV_1$

complex I (NADH UQ oxidoreductase)

Hunte, Zickermann et al, 2010

complex III_2 (cytochrome c reductase)

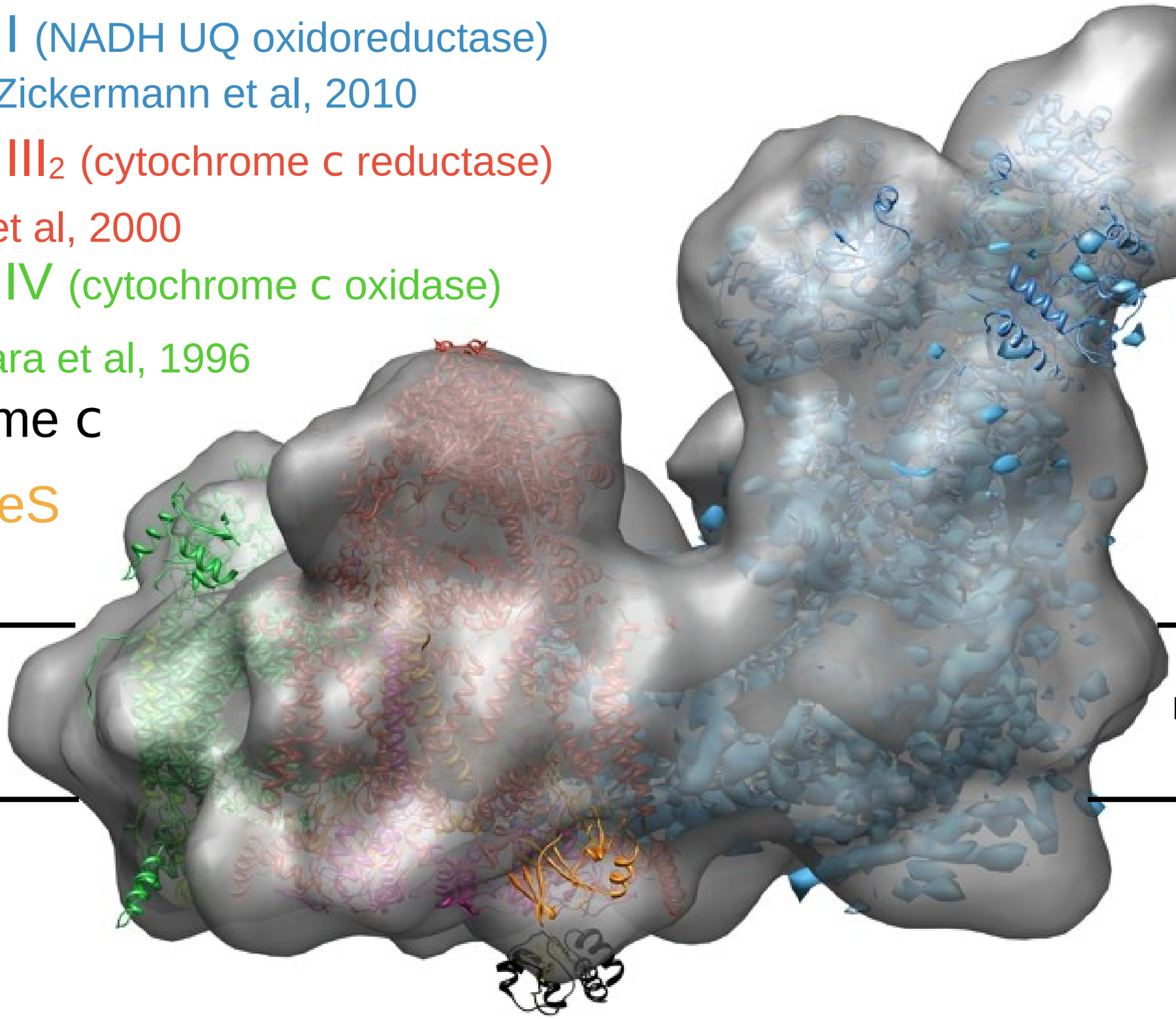
Hunte et al, 2000

complex IV (cytochrome c oxidase)

Tsukihara et al, 1996

cytochrome c

Rieske FeS



Althoff et al, EMBO J 2011

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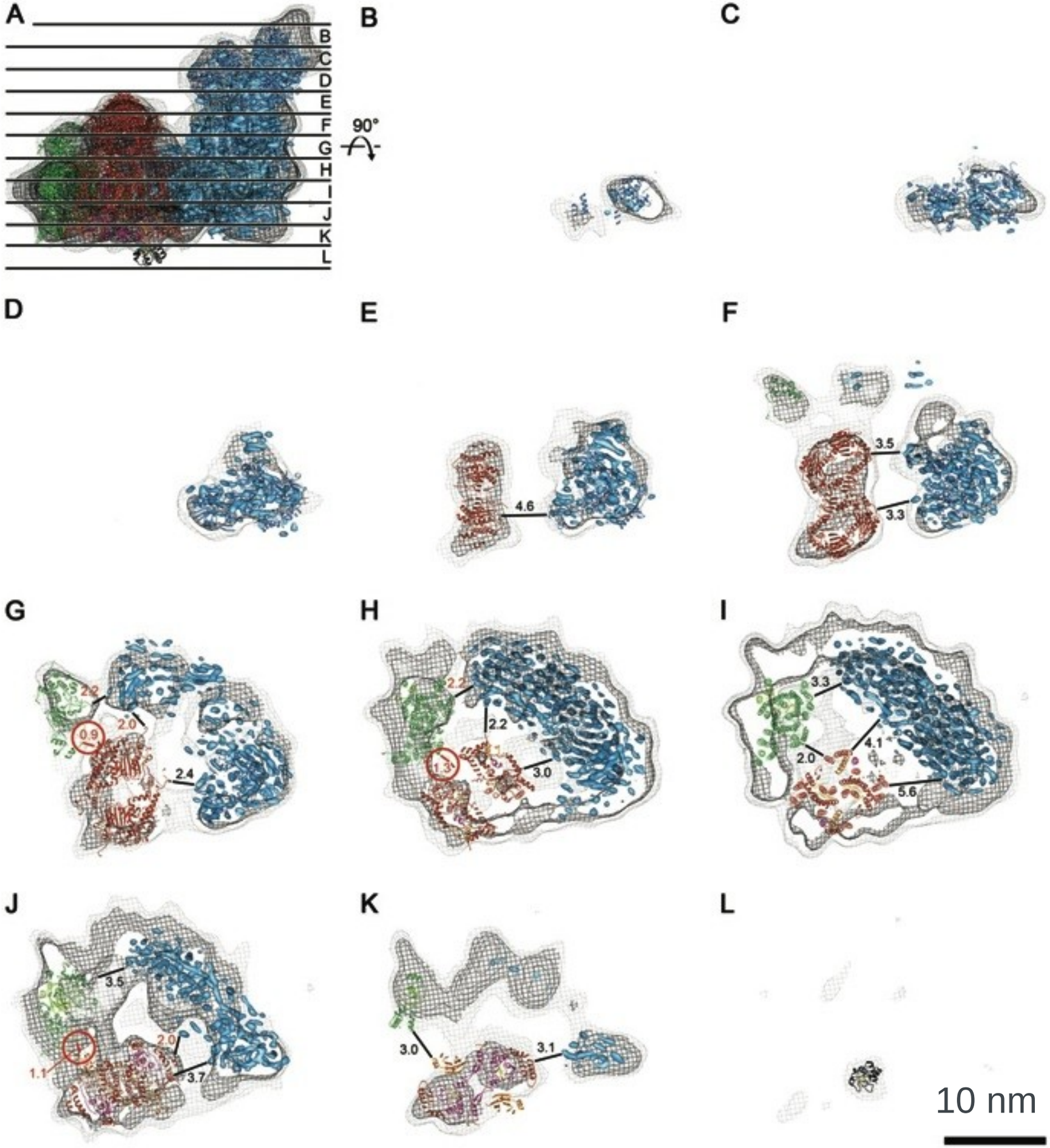

A
B
C
D
E
F
G
H
I
J
K
L
90°
4.6
3.5
3.3
2.2
2.0
0.9
2.4
2.2
2.2
1.3
3.0
3.3
4.1
2.0
5.6
3.5
2.0
1.1
3.7
3.0
3.1
10 nm

Electron transfer pathways

complex I
to complex III:
UQ

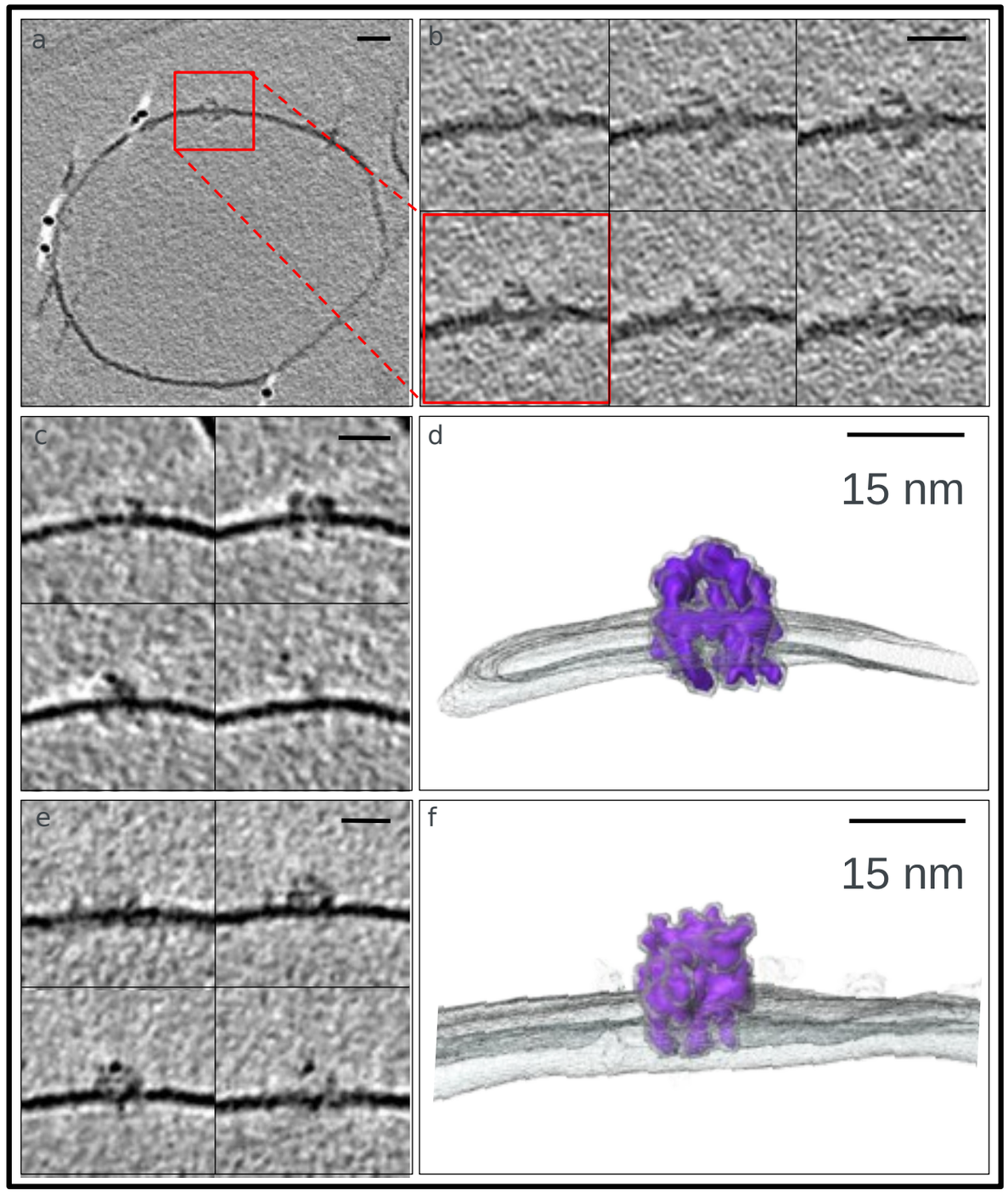
complex III
to complex IV:
cyt c

Althoff et al, EMBO J 2011

Sites of oxygen radical production

Protein import

Cryo-ET of chloroplast protein translocase



Bertram Daum with Enrico Schleiff, Frankfurt;
Sommer et al, PNAS 2011

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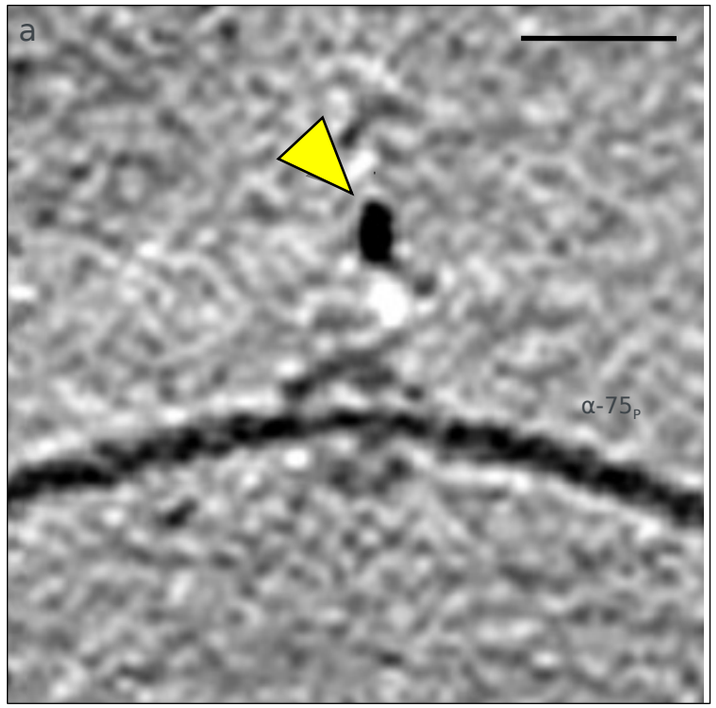
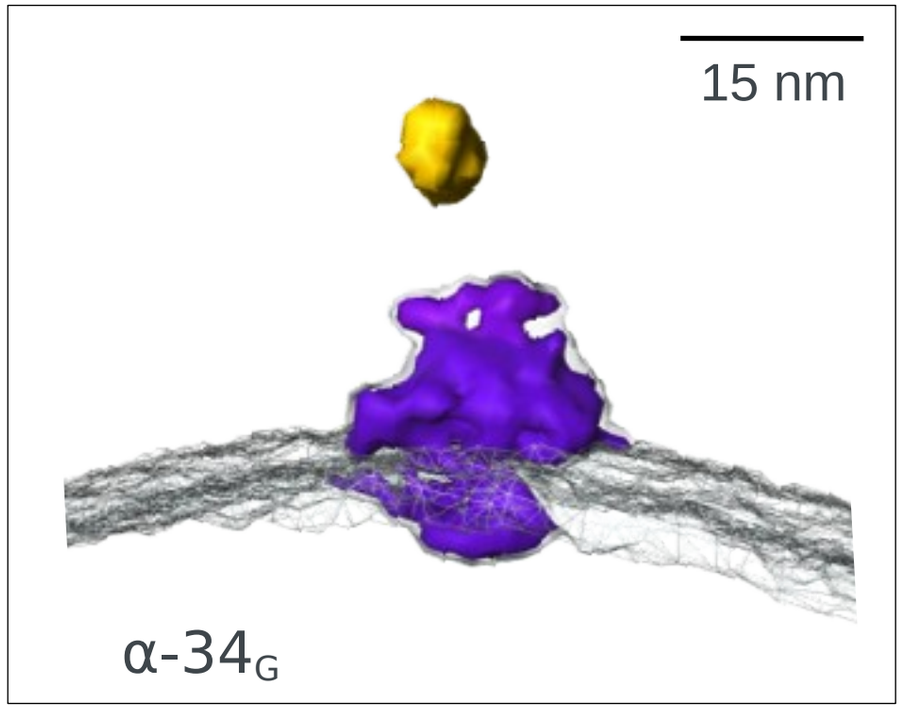
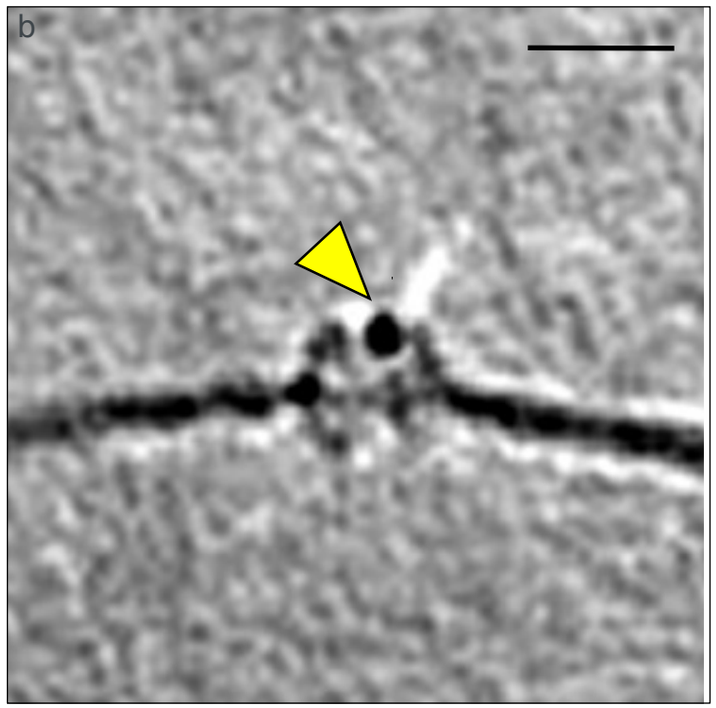
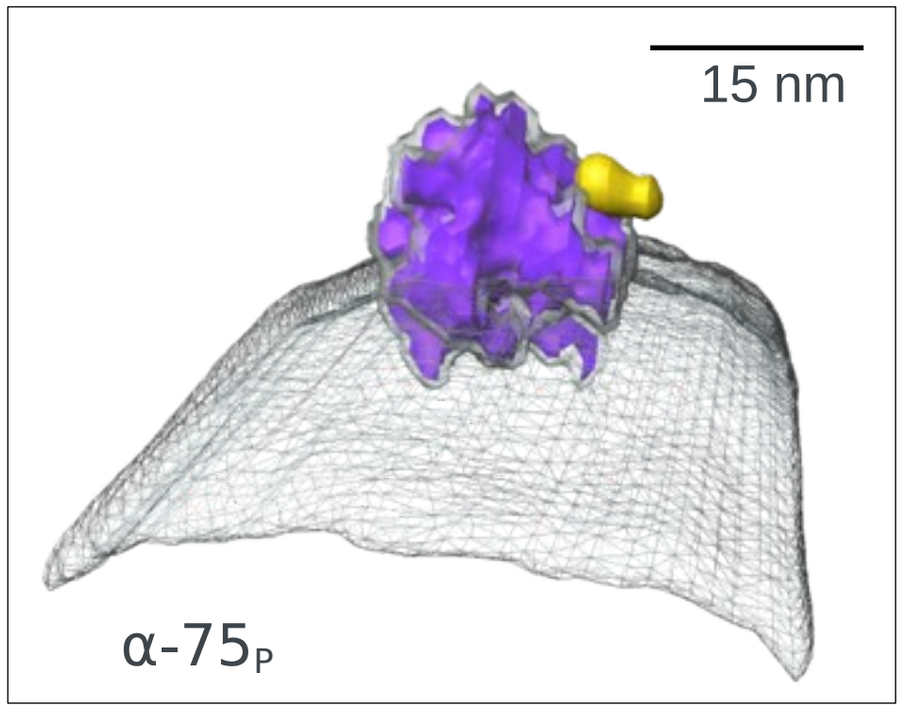
Quantum dot labelling of TOC subunits





cytoplasmic location of TOC receptor GTPase





cytoplasmic location of TOC75 POTRA domain

Bertram Daum with Enrico Schleiff, Frankfurt;
Sommer et al, PNAS 2011

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Ageing

Podospora anserina:
filamentous fungus with a fixed lifespan

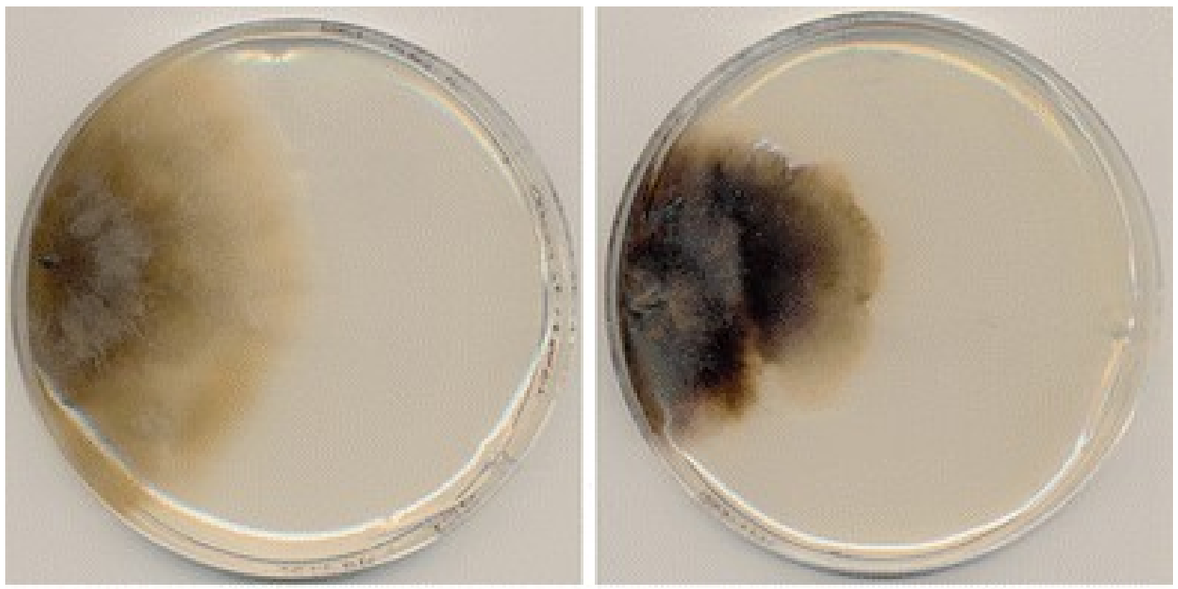
filamentous, multicellular fungus

fixed lifespan of ~20 days

long-lived and immortal mutants

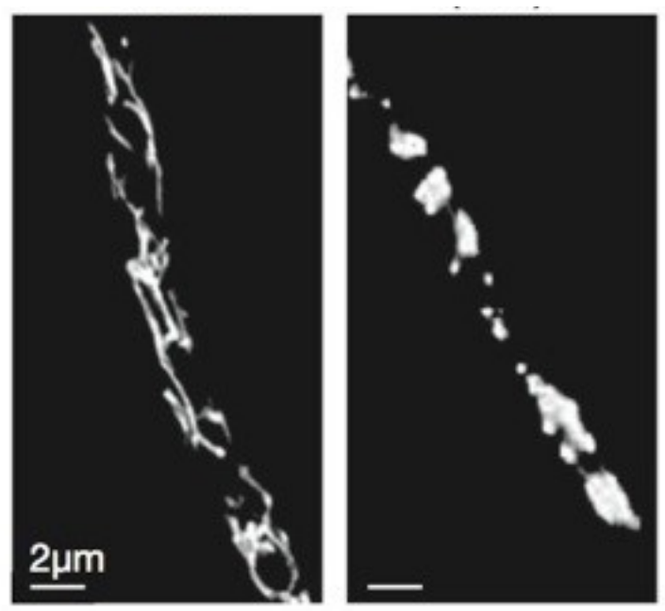
hyphae

culture



9 days 18 days (senescent)

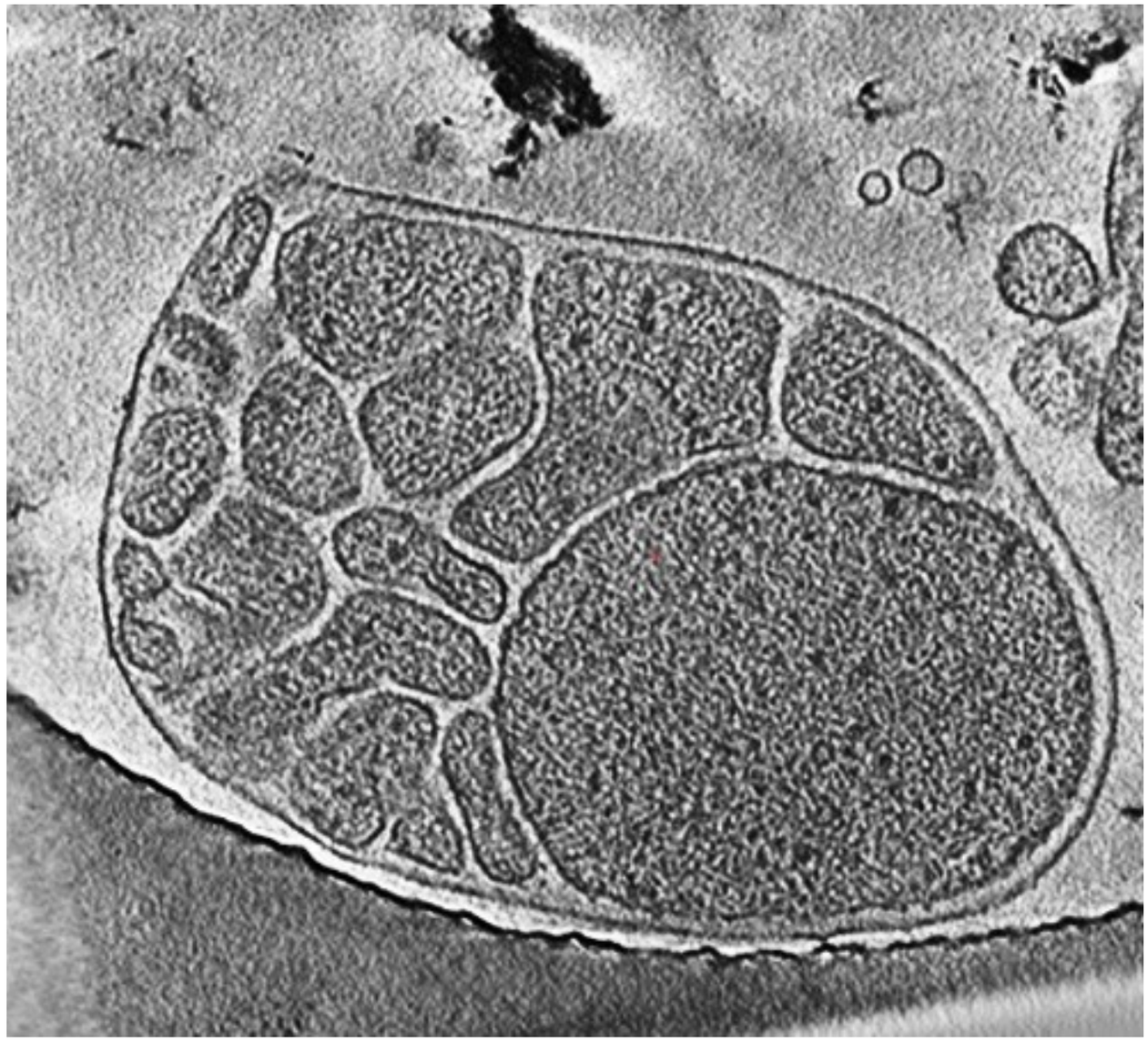
mitochondria



6 days (juvenile) 18 days (senescent)

from Scheckhuber et al, 2006

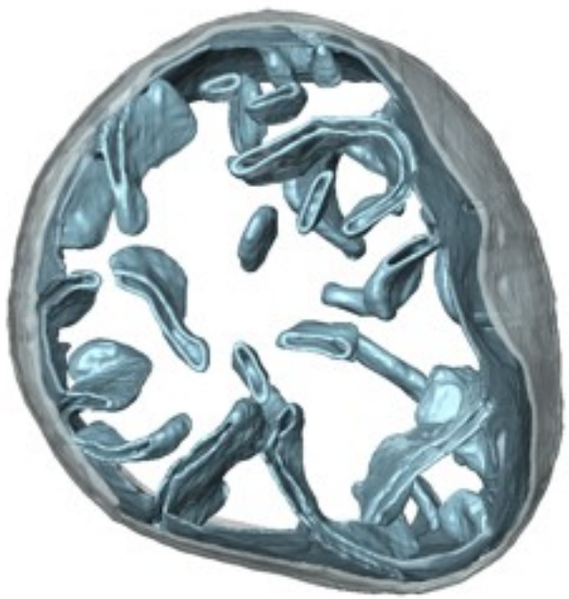
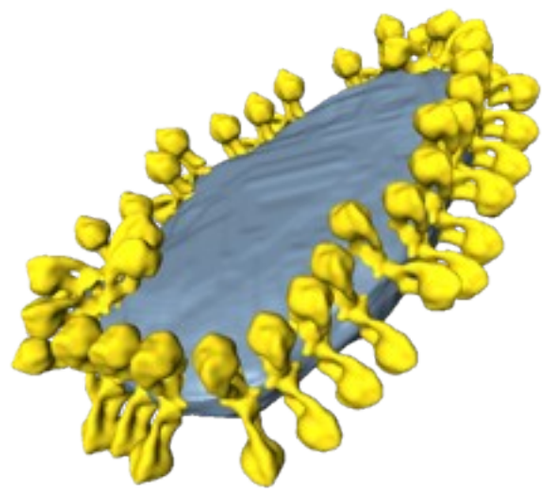
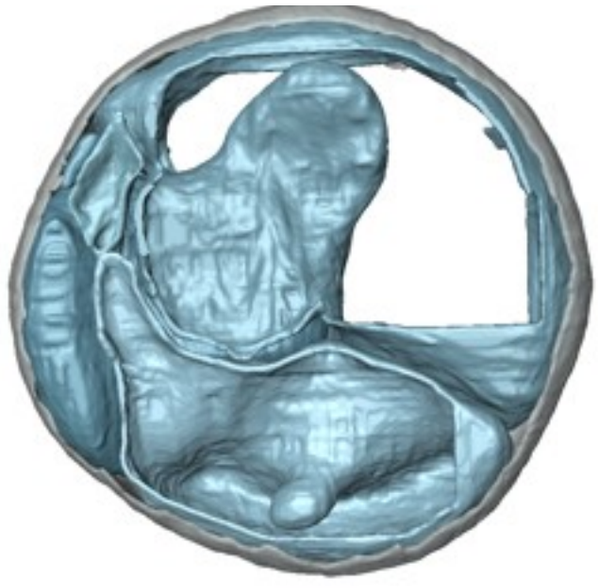
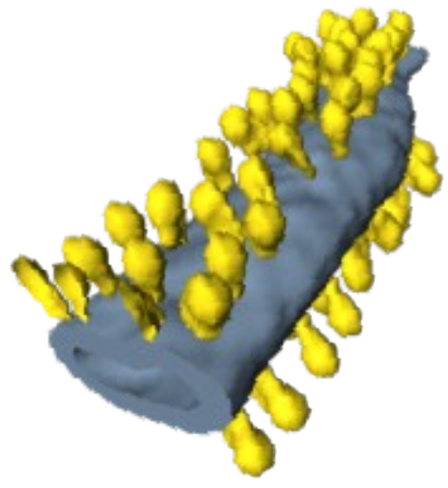
Age-dependent change of mitochondria



young (6 days) P. anserina old (18 days)

Bertram Daum with Heinz Osiewacz, Frankfurt

Dimer-specific subunit knockouts

	cristae morphology	ATP synthase arrangement	
wild type yeast			dimer rows along edges
subunit g knockout			randomly distributed monomers

Davies et al, PNAS 2012

Single-particle team

Electron tomography team

Goodbye JEOL 3000 SFF

1996-2012

After many years of faithful service our JEOL is going to retire on **the 26th of November.**

To honor the memory of the JEOL we invite you and your partner to a party on this evening in the MPI bistro beginning at 6 PM.

Dress: fancy dress, anything related to electron microscopy (including structures solved by this technique)

Events will include **a slide show** on the history of the JEOL and its users, a **quiz**, a **photo shoot** in the JEOL room, and election of **the best fancy dress.**

Please let us know if you are coming at deryck.mills@biophys.mpg.de

Hope to see you there,

Deryck & Janet

Open V13?
close V12?
close V8?
make a coffee ?
fill with LN2?
have breakfast?
turn up HT?
water plants?
turn on dryer?
EM? (check notes)
go home?

How to fix it
if it gets broken
by Deryck -
First & last edition