
JVK
2004

SBCS-922 Membrane Proteins

Mitochondria and respiratory chains

John F. Allen

School of Biological and Chemical Sciences,
Queen Mary, University of London

Presentations
and
supplementary information

jfallen.org/lectures/

Queen Mary
University of London

Lectures in Membrane Proteins

- Lecture 1. Mitochondrial membranes and chemiosmotic coupling. (Acrobat - .pdf)
- Lecture 2. Redox carriers. (Acrobat - .pdf)
- Lecture 3. Complex I. Structure and Function. Part 1 (Acrobat - .pdf)

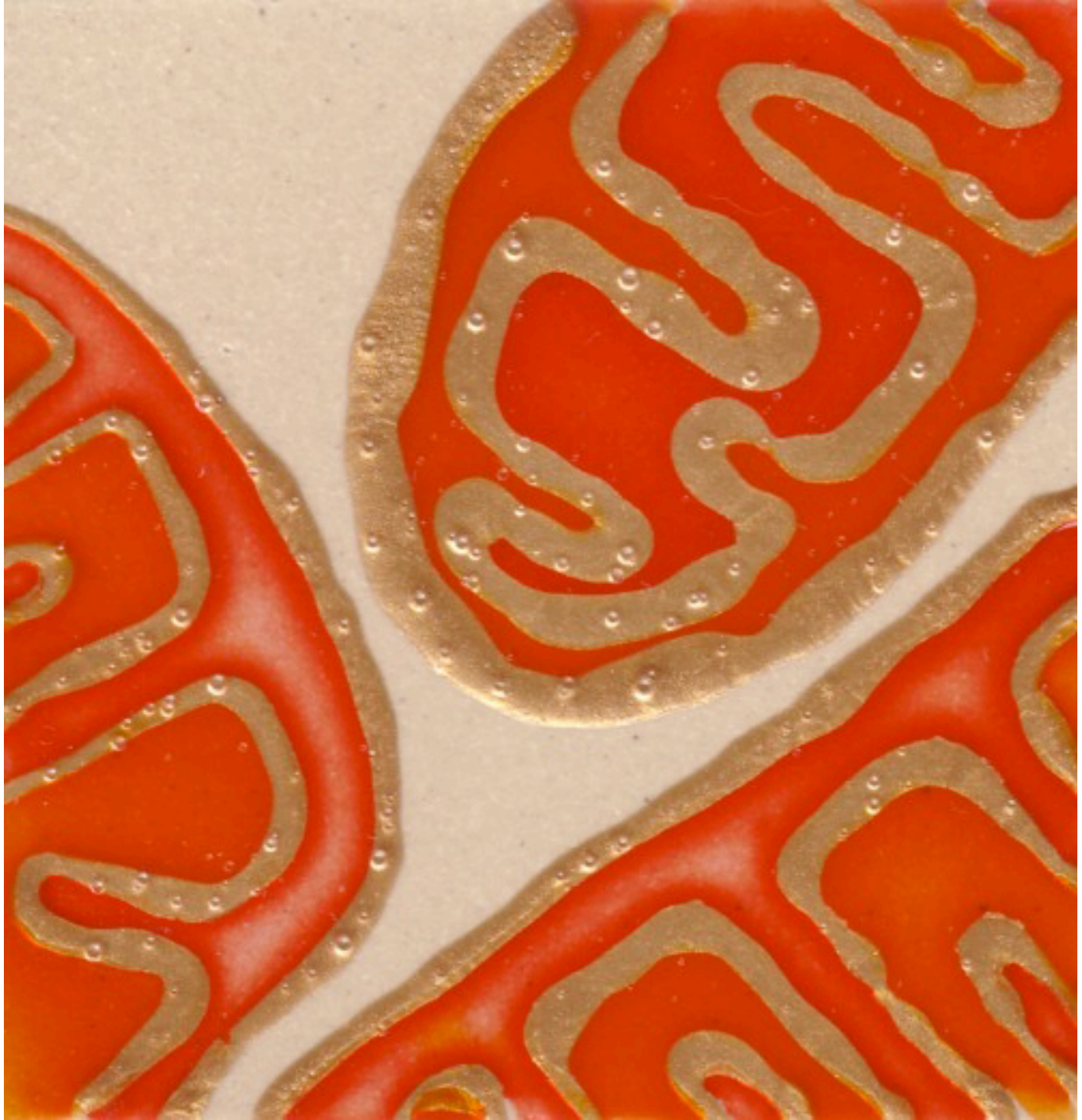
- Lecture 1. Mitochondrial membranes and chemiosmotic coupling. (Powerpoint - .ppt)
- Lecture 2. Redox carriers. (Powerpoint - .ppt)
- Lecture 3. Complex I. Structure and Function. Part 1 (Powerpoint - .ppt)

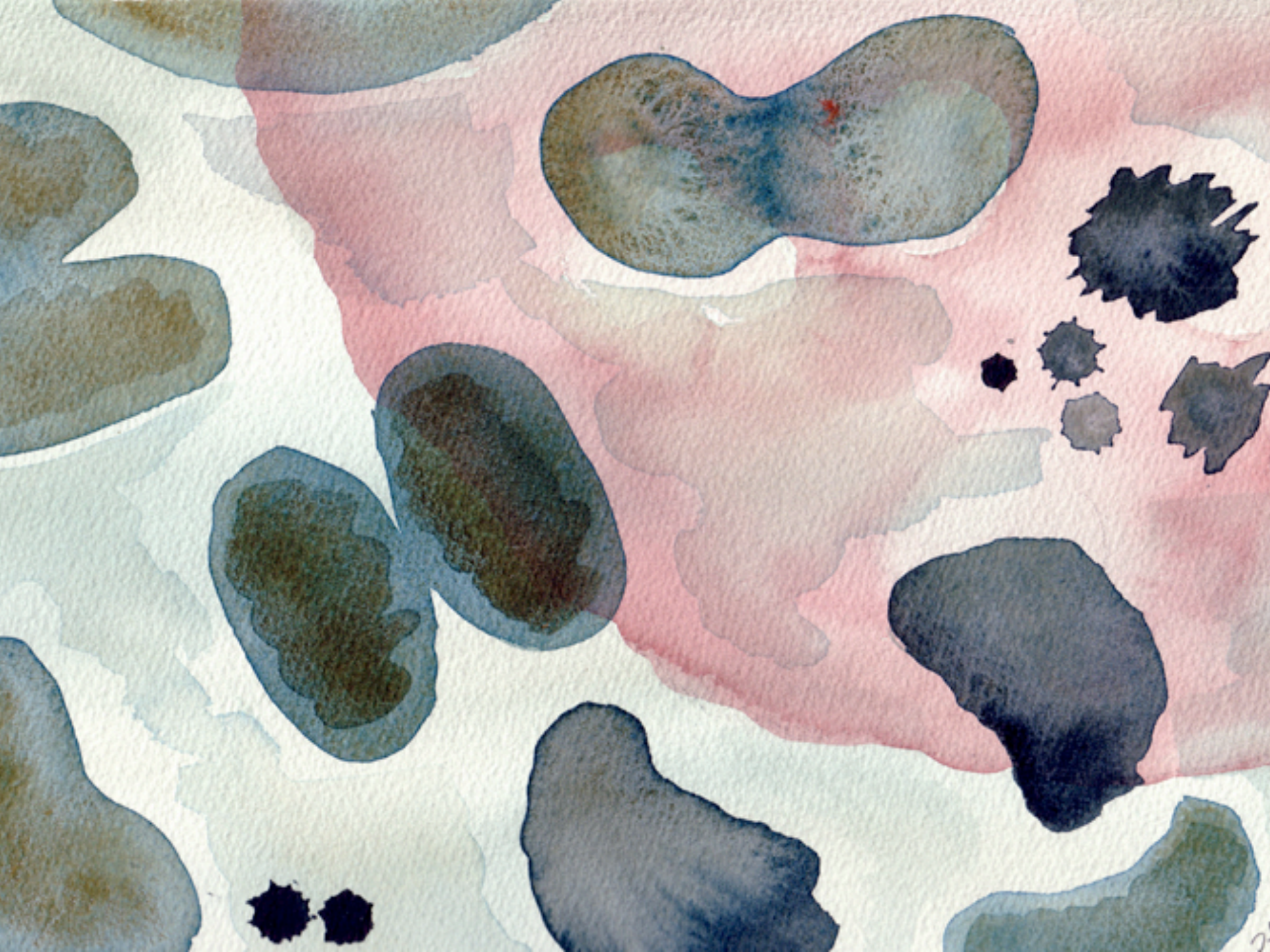
Membrane Proteins

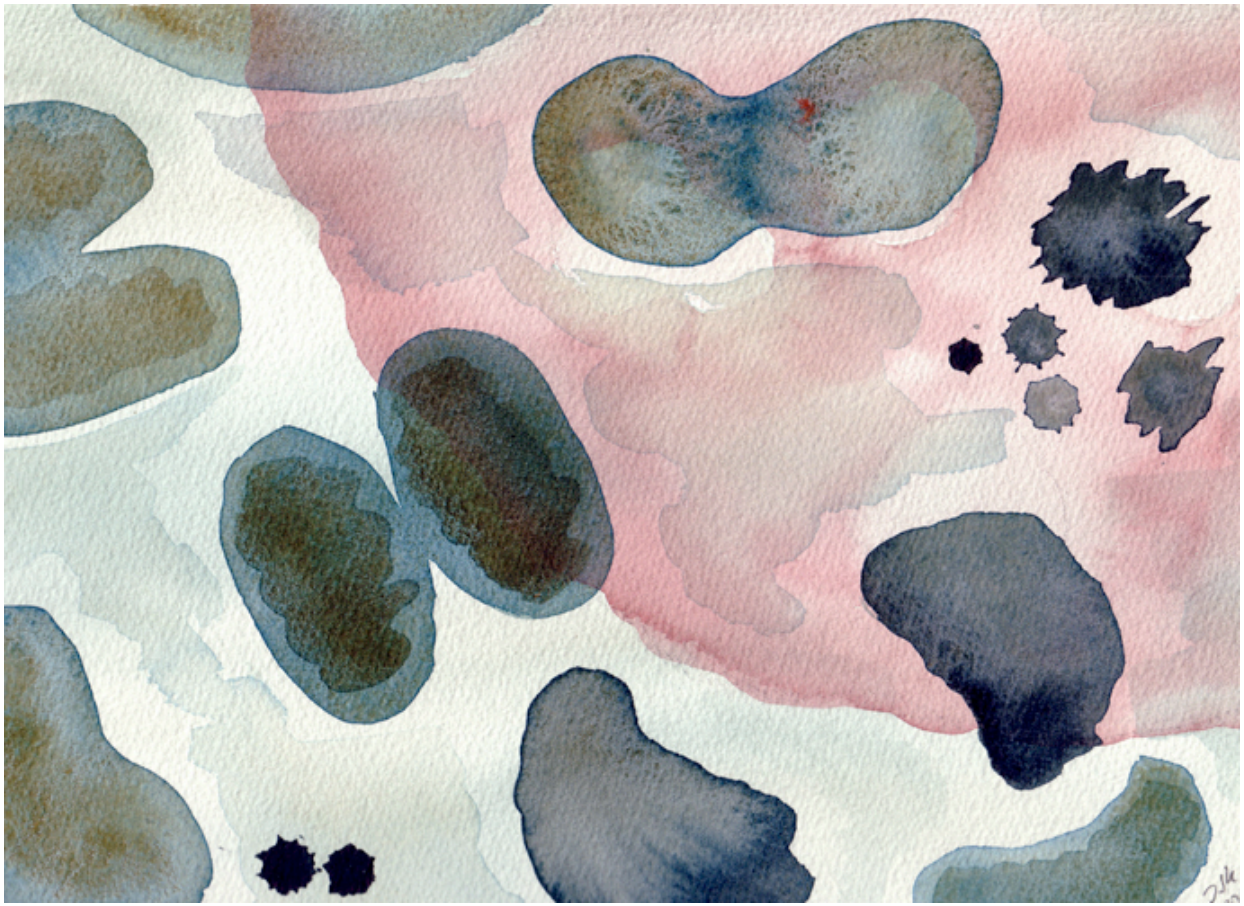
- Membrane Proteins course web page

References

- Nicholls DJ, Ferguson, SJ. Bioenergetics3. Academic Press/Elsevier Science 2002
- Molecular Biology of the Cell. Bruce Alberts, Alexander Johnson, Julian Lewis, Martin Raff, Keith Roberts, and Peter Walter. 5th edition. 2007. Garland Science. 4th Edition online at NCBI...





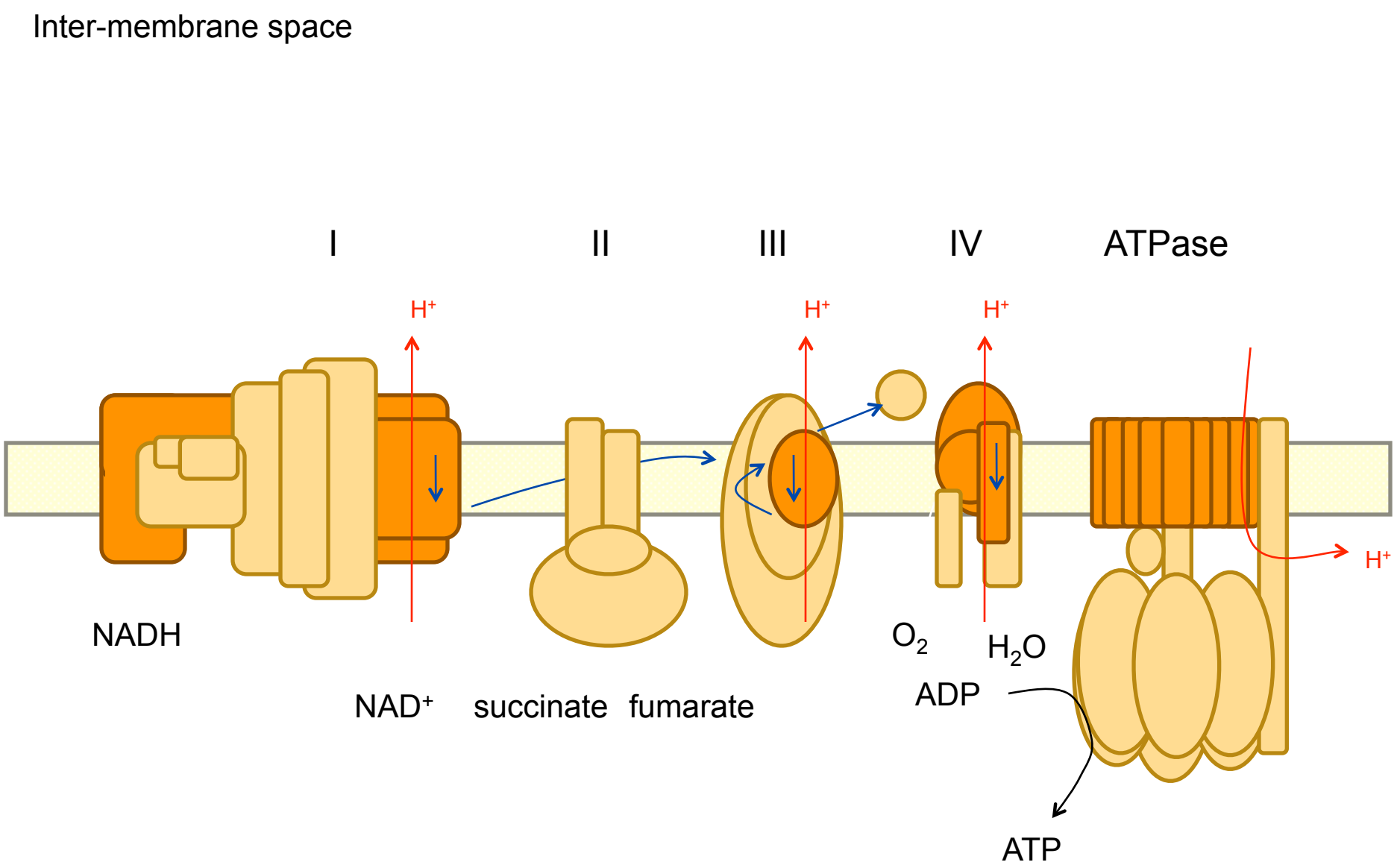


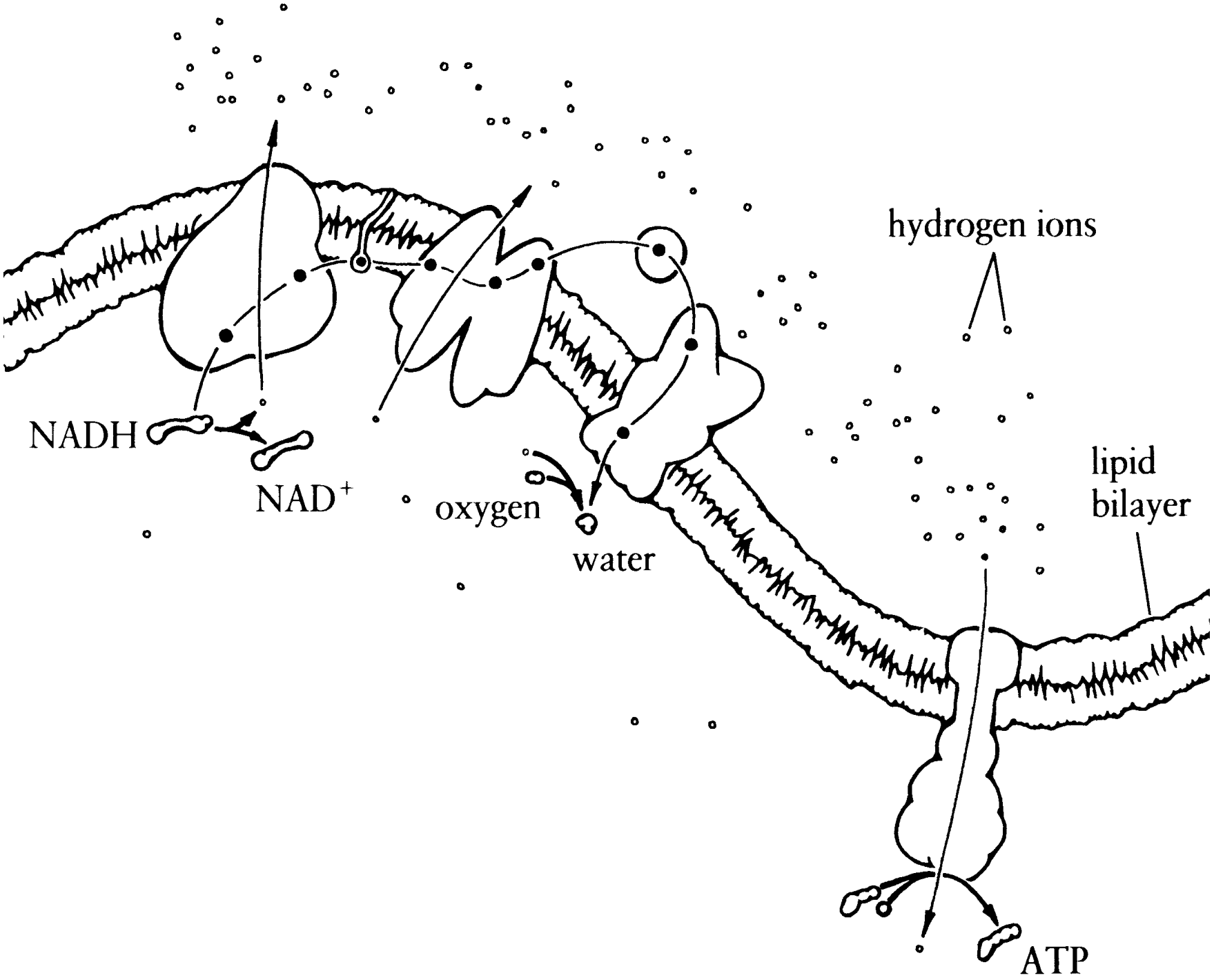
Ageing and death—mitochondria divide or die, depending on their interactions with the nucleus

Animals with a fast metabolic rate tend to age quickly and succumb to degenerative diseases such as cancer. Birds are an exception because they combine a fast metabolic rate with a long lifespan, and a low risk of disease. They achieve this by leaking fewer free radicals from their mitochondria. But why does free-radical leakage affect our vulnerability to degenerative diseases that on the face of it have little to do with mitochondria? A dynamic new picture is emerging, in which signalling between damaged mitochondria and the nucleus plays a pivotal role in the cell's fate, and our own.

ATP synthase. Structure and function

jfallen.org/lectures/


Inter-membrane space
I
II
III
IV
ATPase
H+
H+
H+
H+
NADH
NAD+
succinate
fumarate
O2
H2O
ADP
ATP
Mitochondrial matrix


hydrogen ions
NADH
NAD+
oxygen
water
lipid
bilayer
ATP

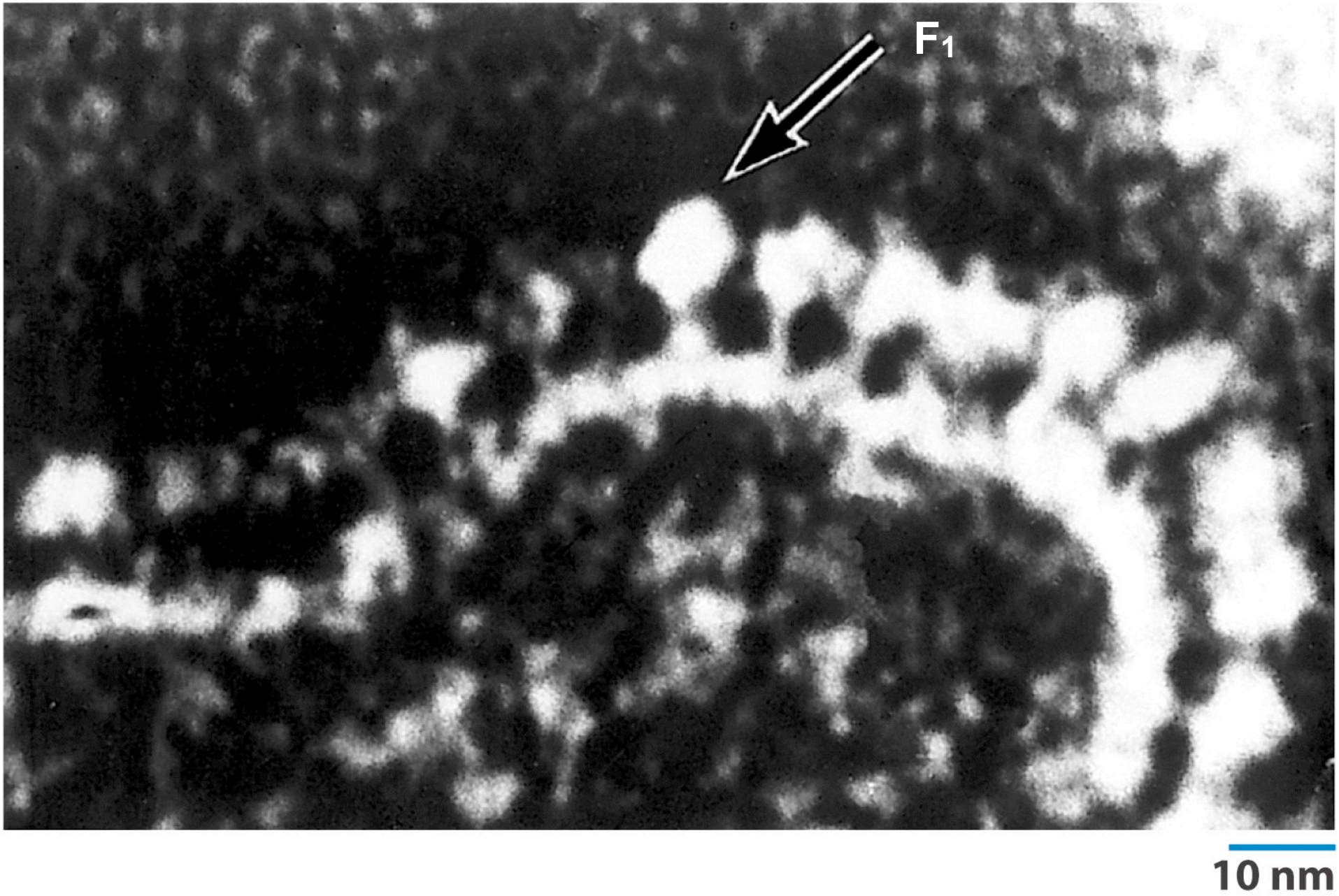


Figure 5-21 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

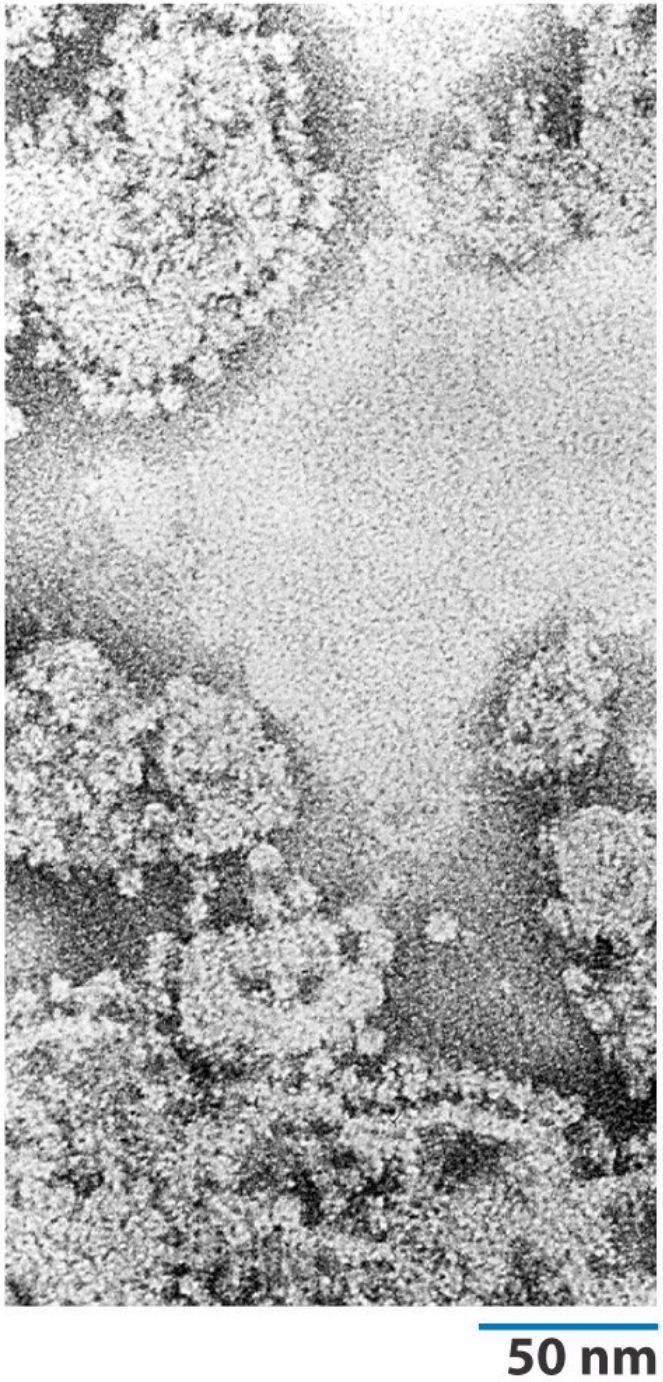
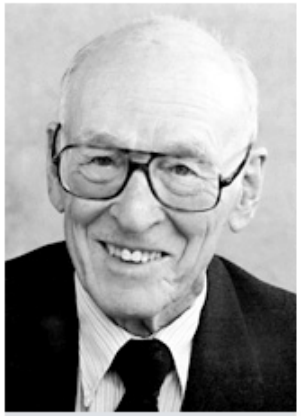


Figure 5-25a Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

The Nobel Prize in Chemistry 1997

"for their elucidation of the enzymatic mechanism underlying the synthesis of adenosine triphosphate (ATP)"

"for the first discovery of an ion-transporting enzyme, Na+, K+ - ATPase"



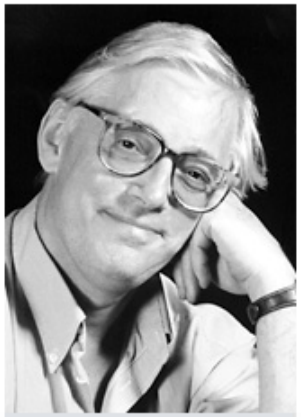
Paul D. Boyer

1/4 of the prize

USA

University of California
Los Angeles, CA, USA

b. 1918



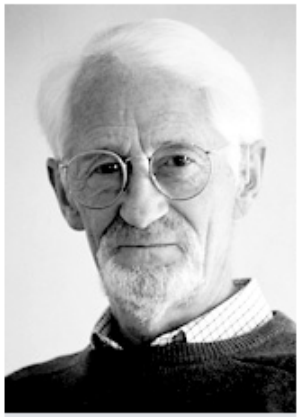
John E. Walker

1/4 of the prize

United Kingdom

MRC Laboratory of Molecular Biology
Cambridge, United Kingdom

b. 1941



Jens C. Skou

1/2 of the prize

Denmark

Aarhus University
Aarhus, Denmark

b. 1918

Printer Friendly
Comments & Questions
Tell a Friend

The 1997 Prize in:
Chemistry
Prev. year | Next year

The Nobel Prize in Chemistry 1997
Press Release
Presentation Speech
Illustrated Presentation

Paul D. Boyer
Autobiography
Nobel Lecture
Interview
Nobel Diploma
Photo Gallery
Other Resources

John E. Walker
Autobiography
Nobel Lecture
Nobel Diploma
Photo Gallery
Other Resources

Jens C. Skou
Autobiography
Nobel Lecture
Nobel Diploma
Photo Gallery
Banquet Speech
Other Resources

Quiz this year's Nobel Laureates
Sign up for *News from Nobelprize.org*
Oldest, youngest, most awarded
How do we hear? Play and learn.
Memories of *that* call

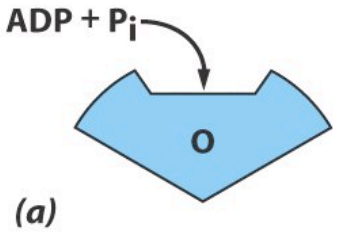


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

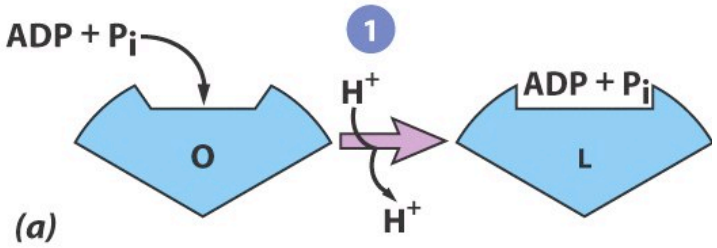


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

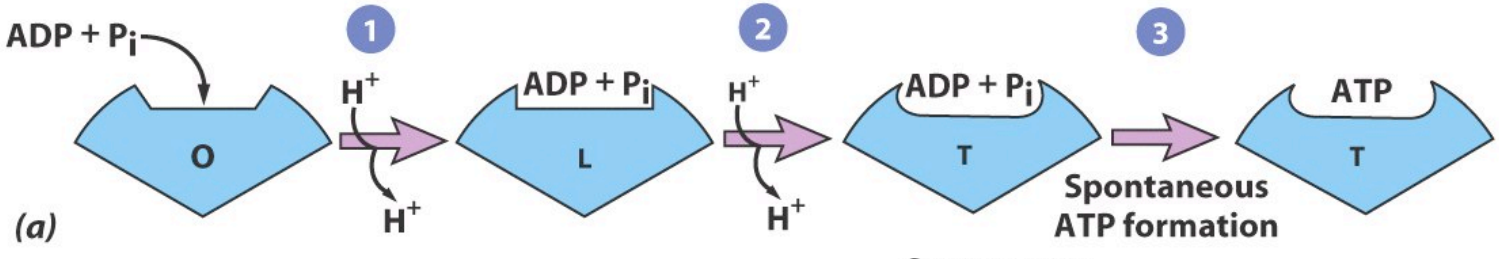


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

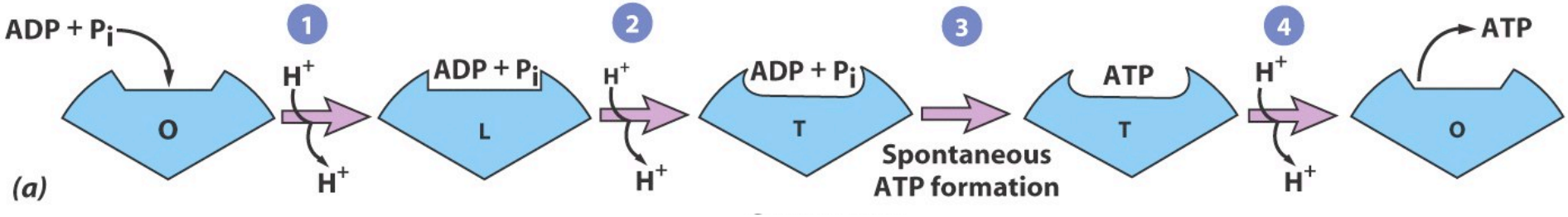


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

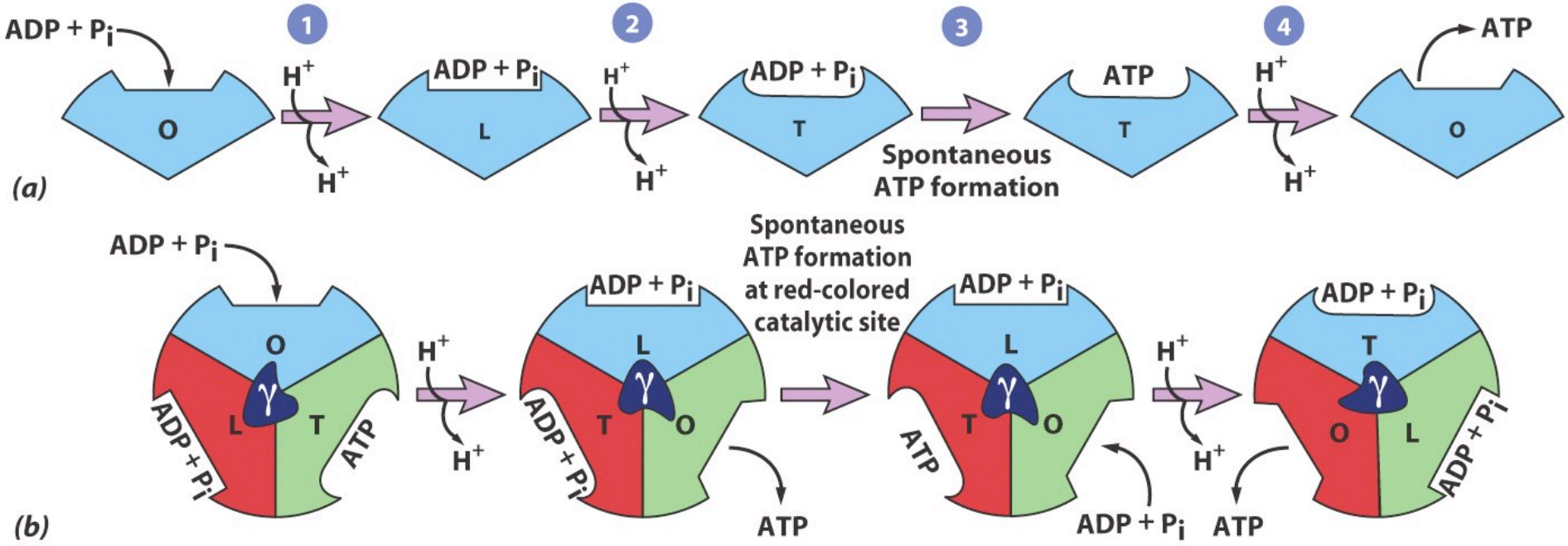


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

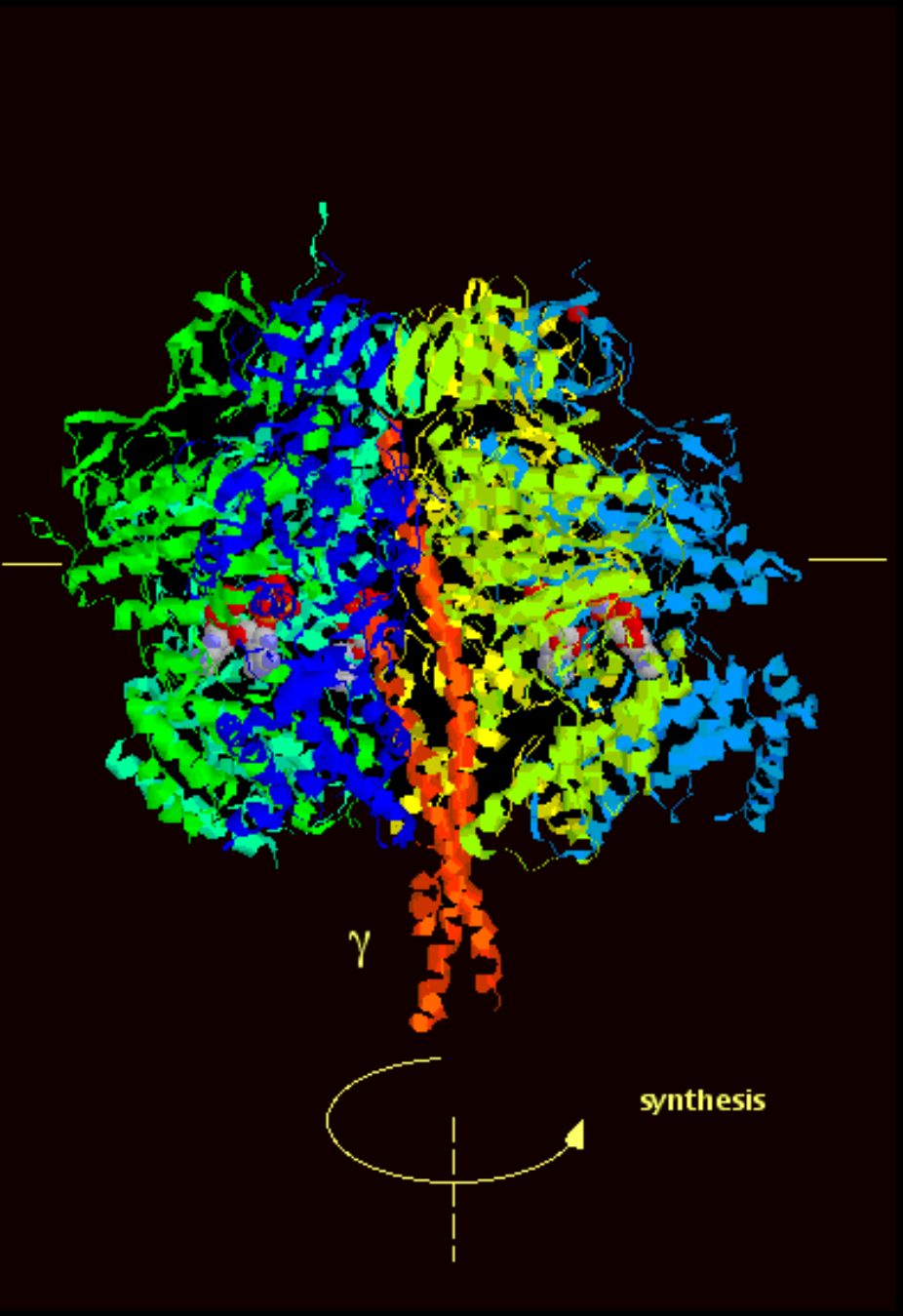


Figure from: ALLEN, J F (2002) Photosynthesis of ATP - Electrons, Proton Pumps, Rotors, and Poise. Cell 110, 273–276

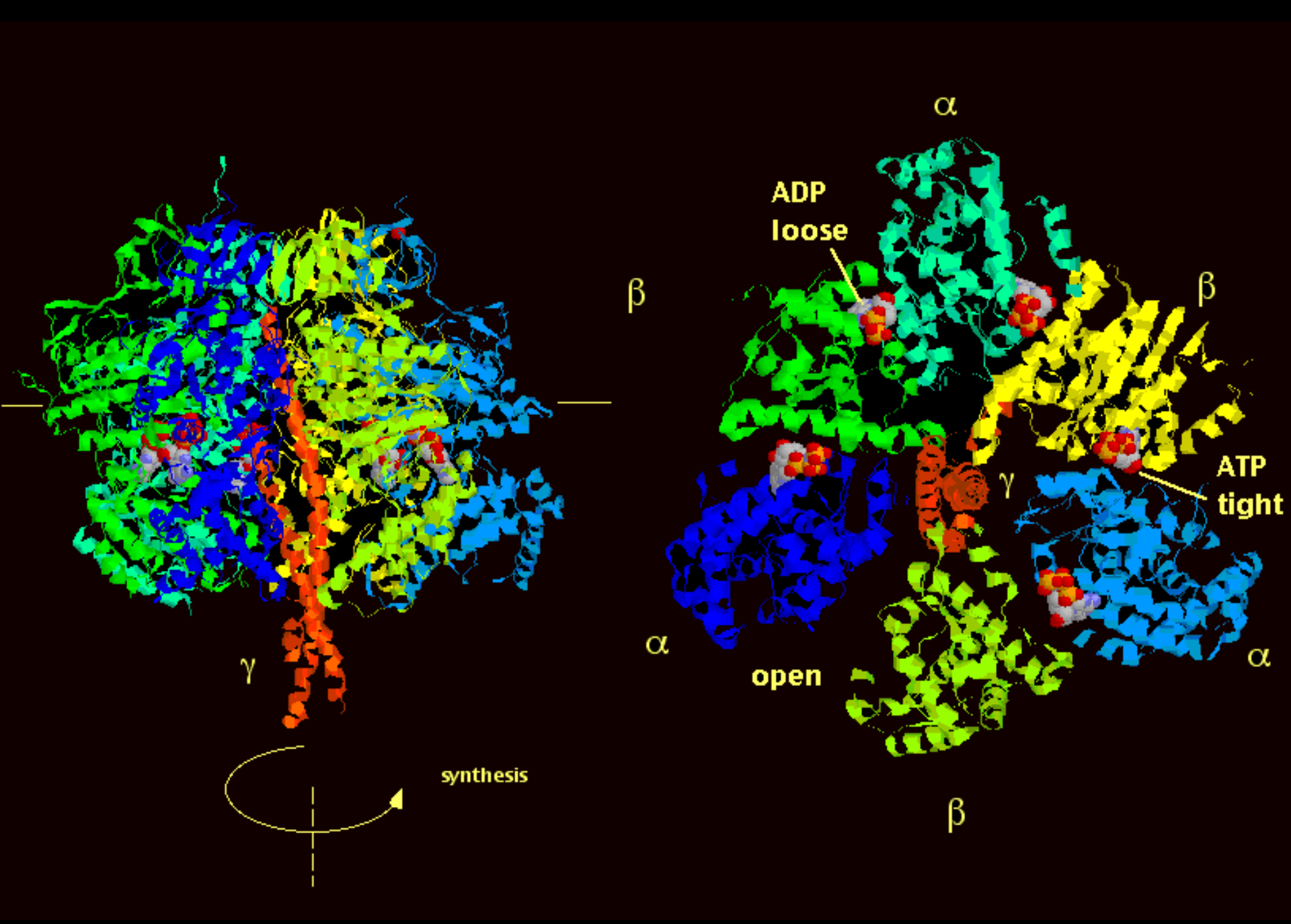


Figure from: ALLEN, J F (2002) Photosynthesis of ATP - Electrons, Proton Pumps, Rotors, and Poise. Cell 110, 273–276

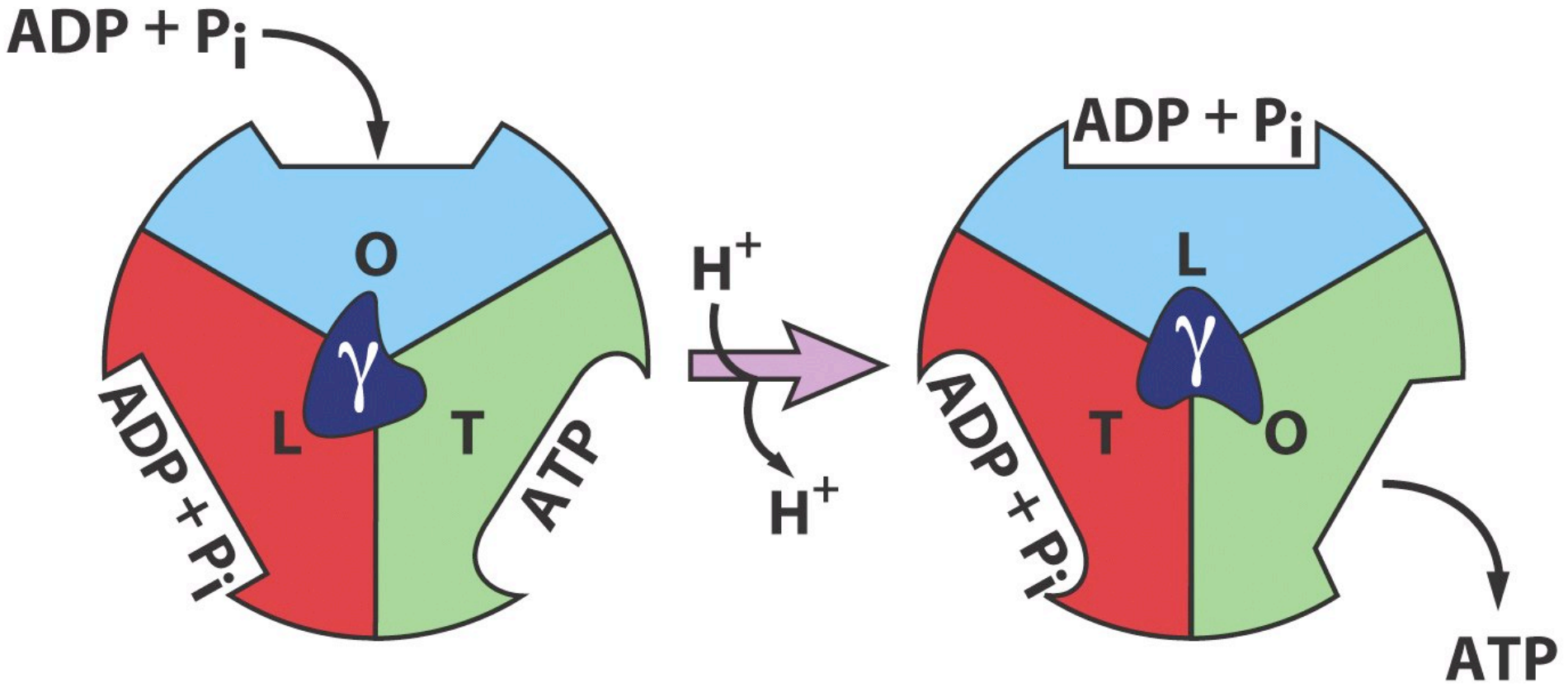


Figure 5-27b part 1 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

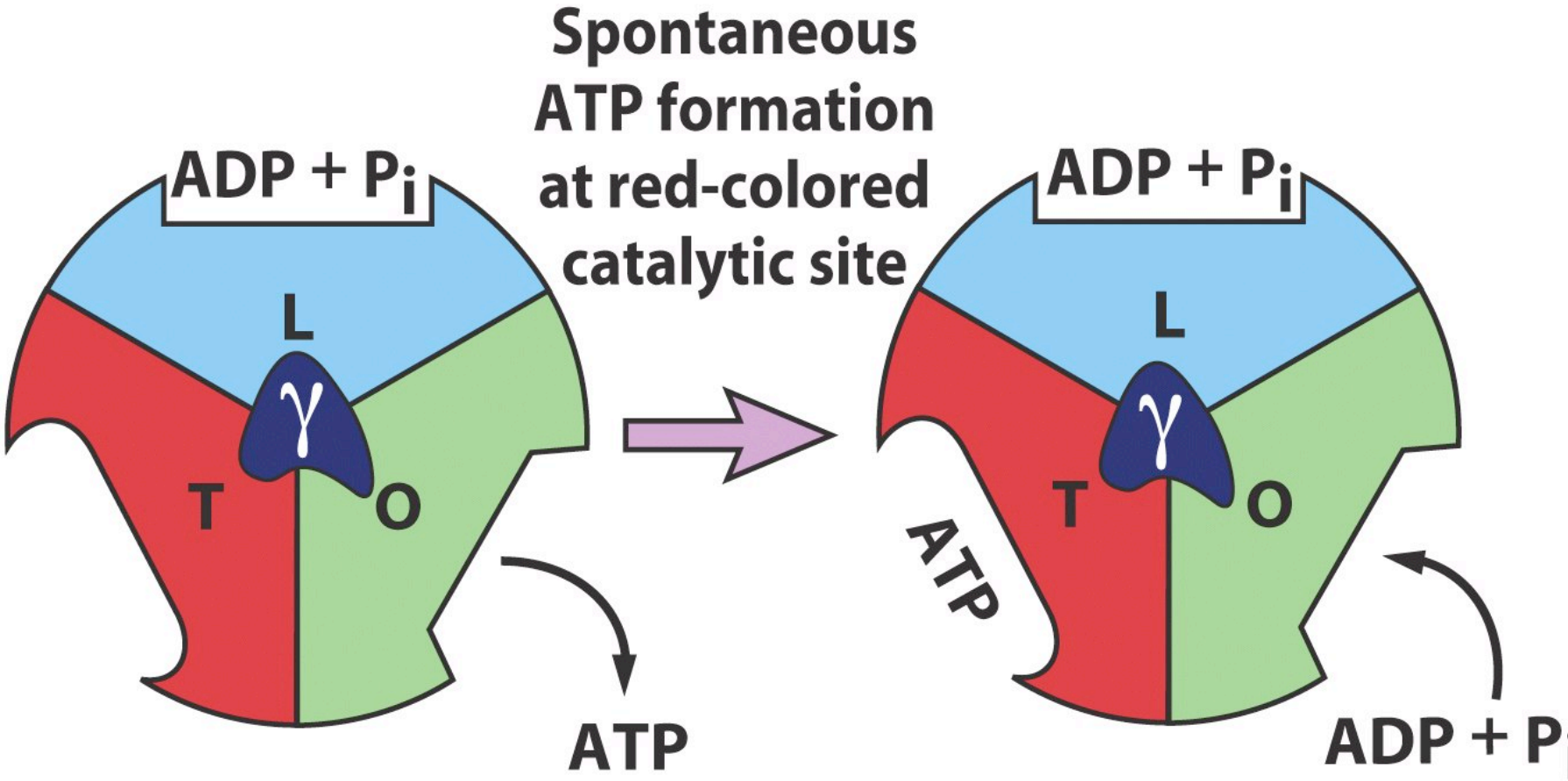


Figure 5-27b part 2 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

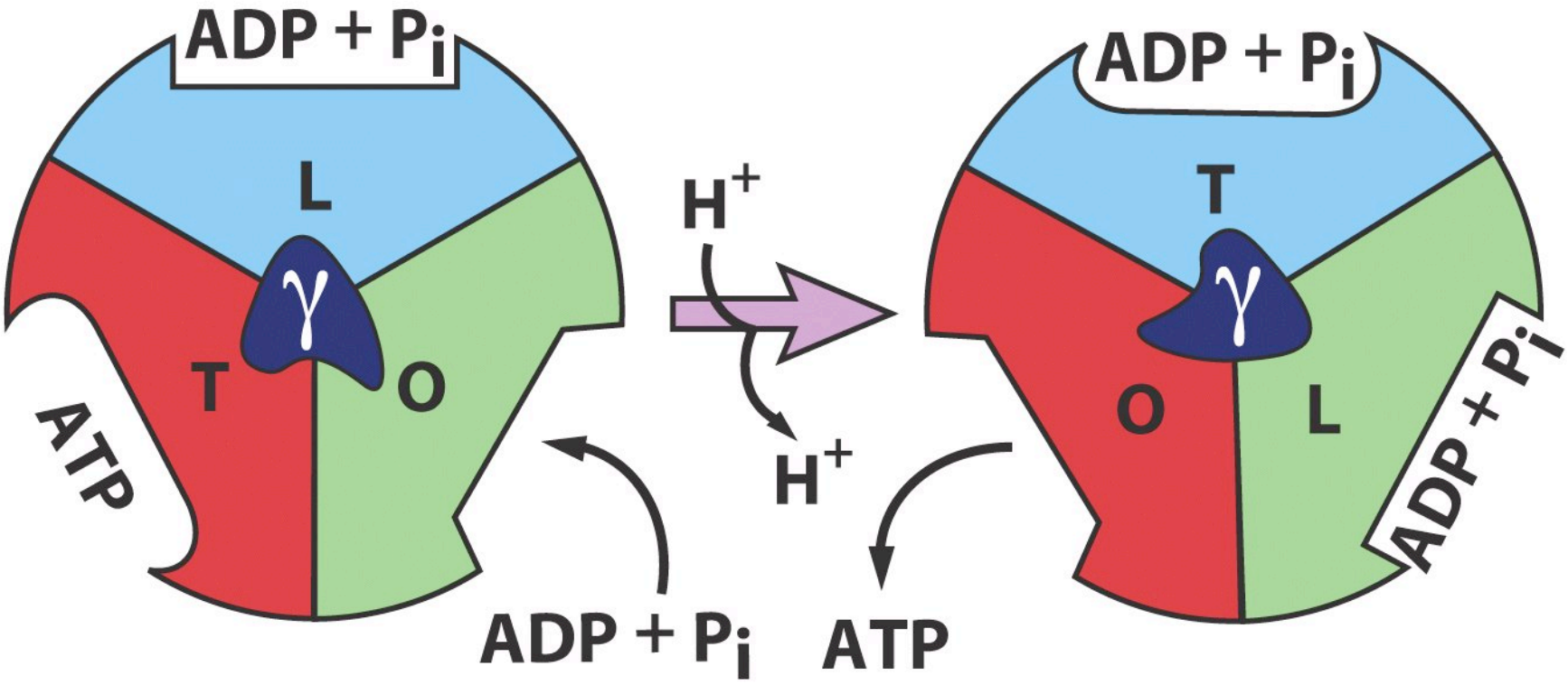


Figure 5-27b part 3 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

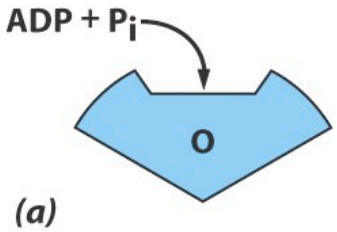


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

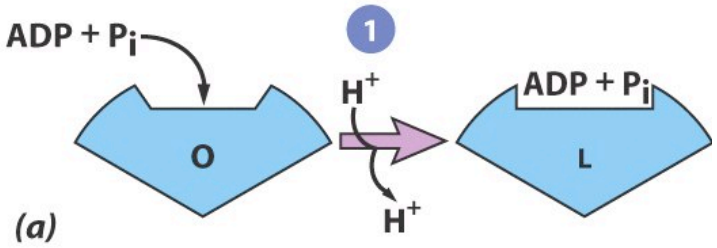


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

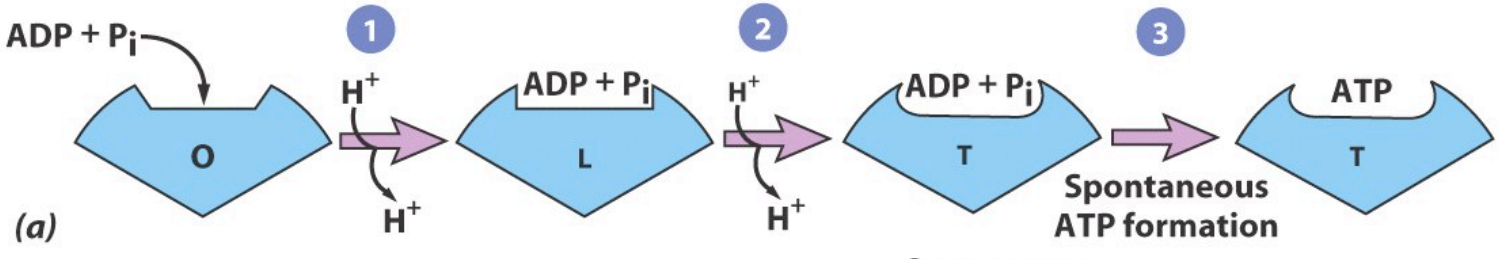


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

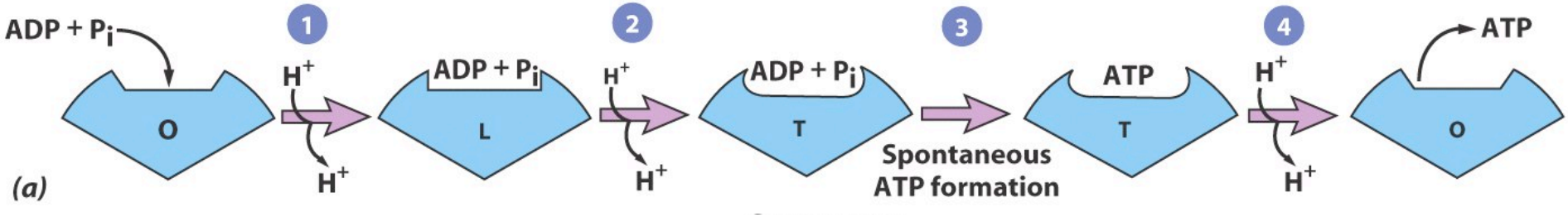


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

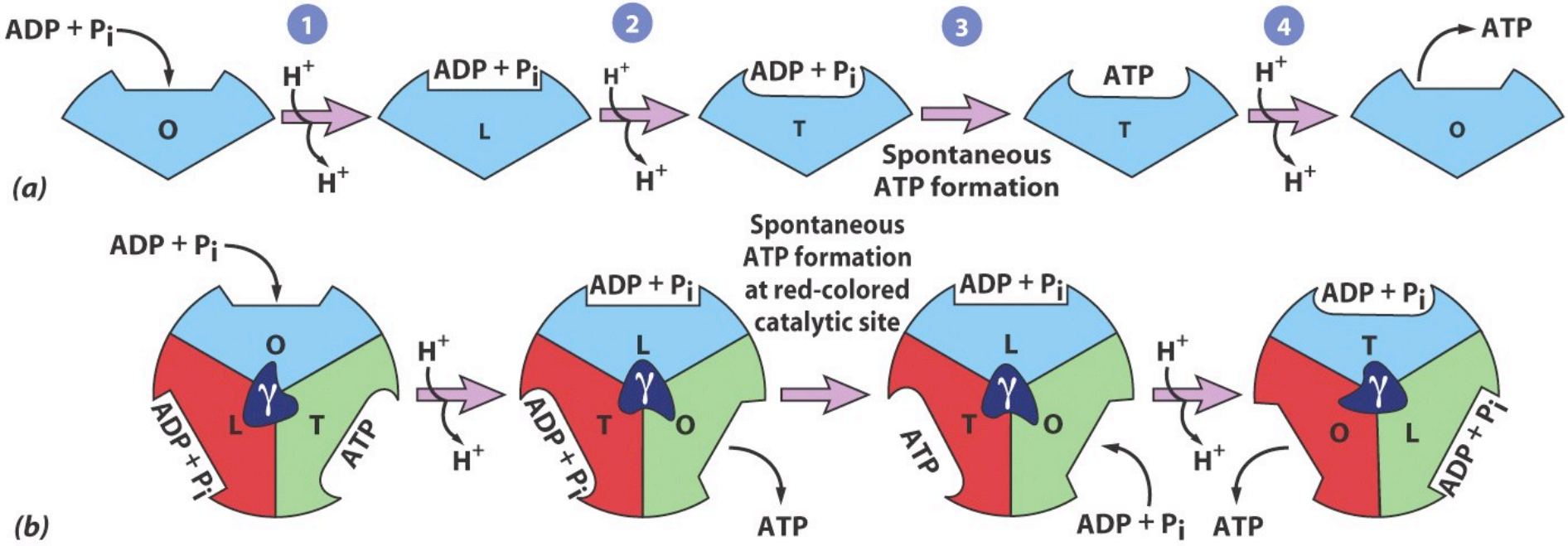


Figure 5-27 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

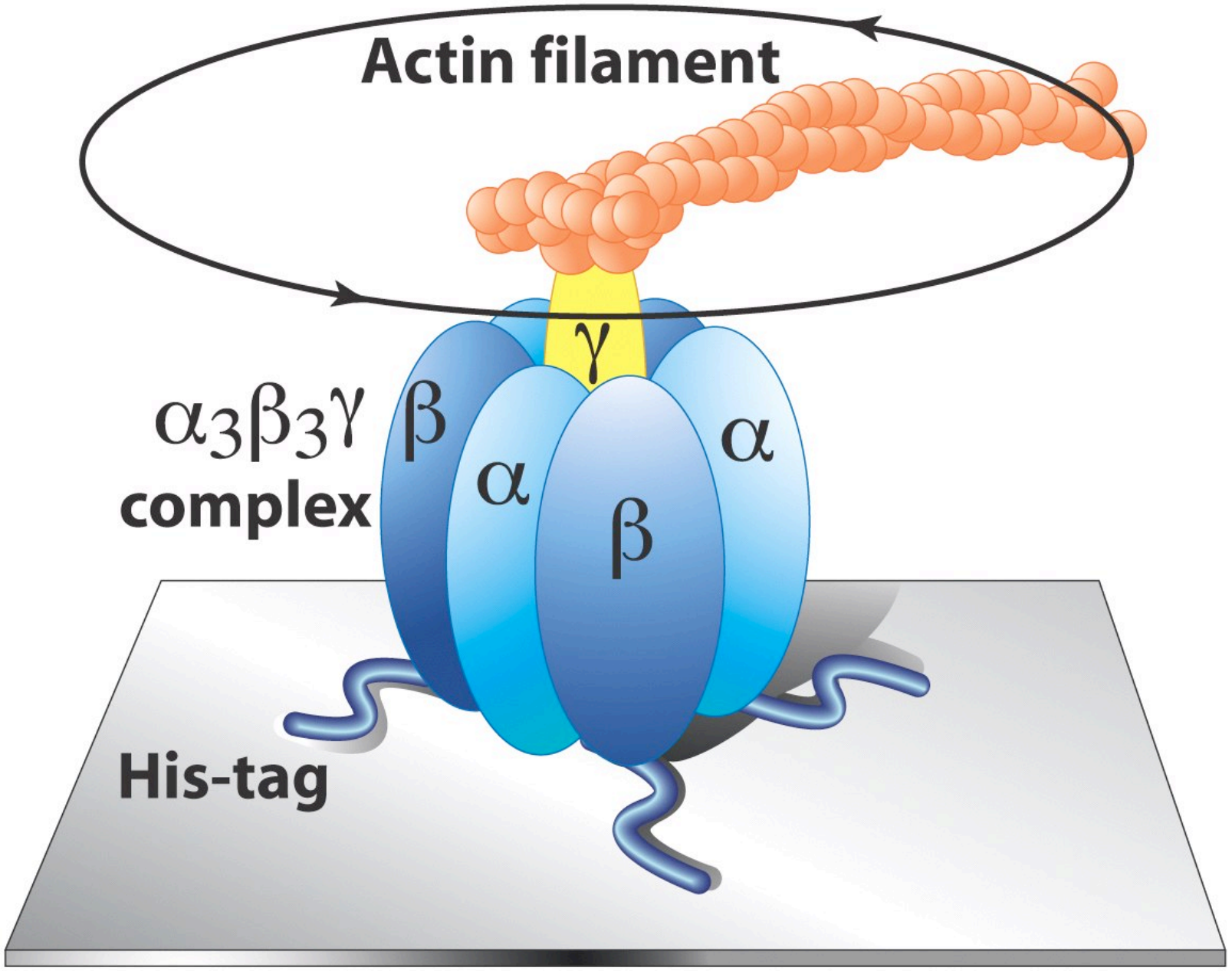
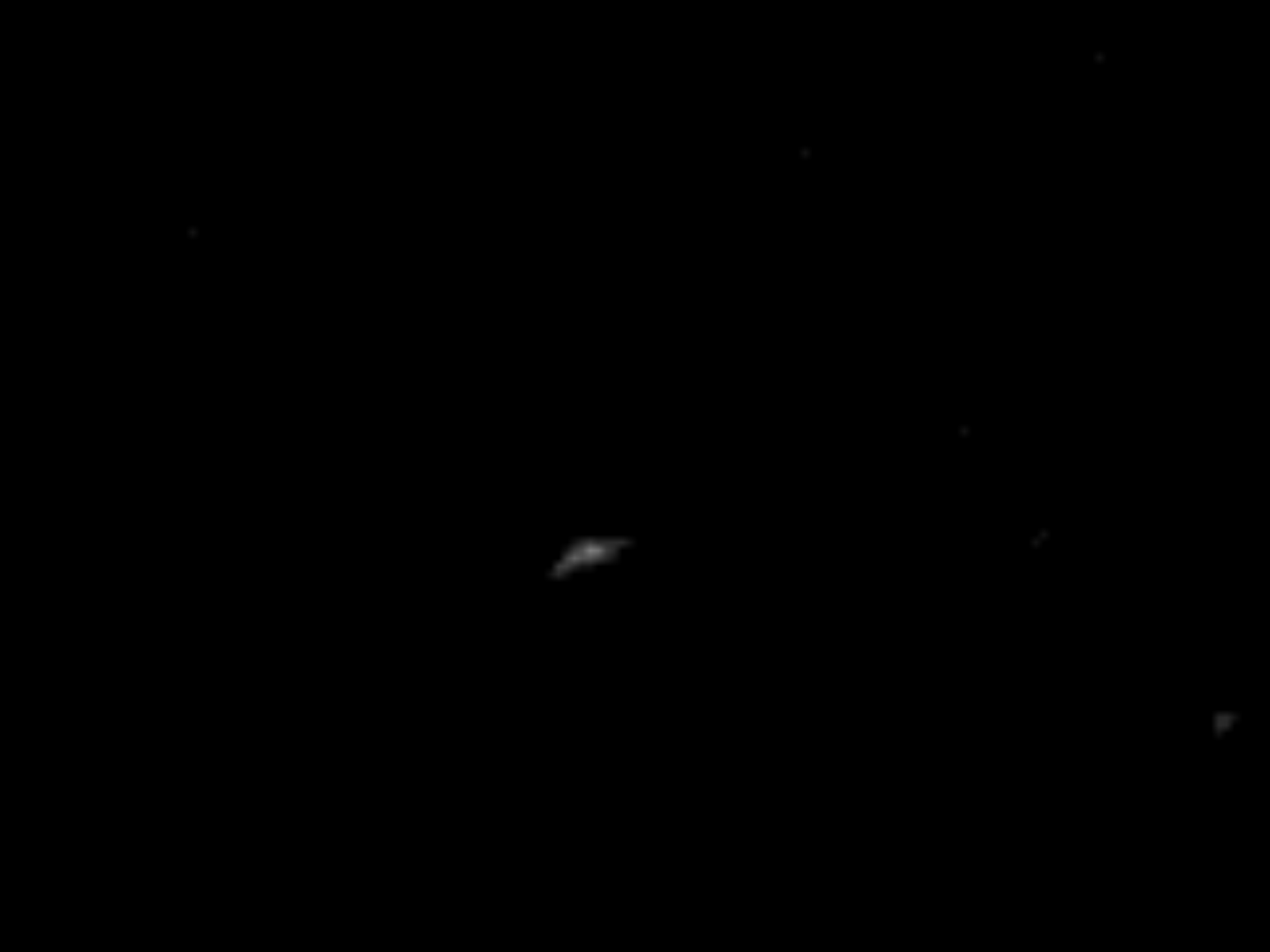
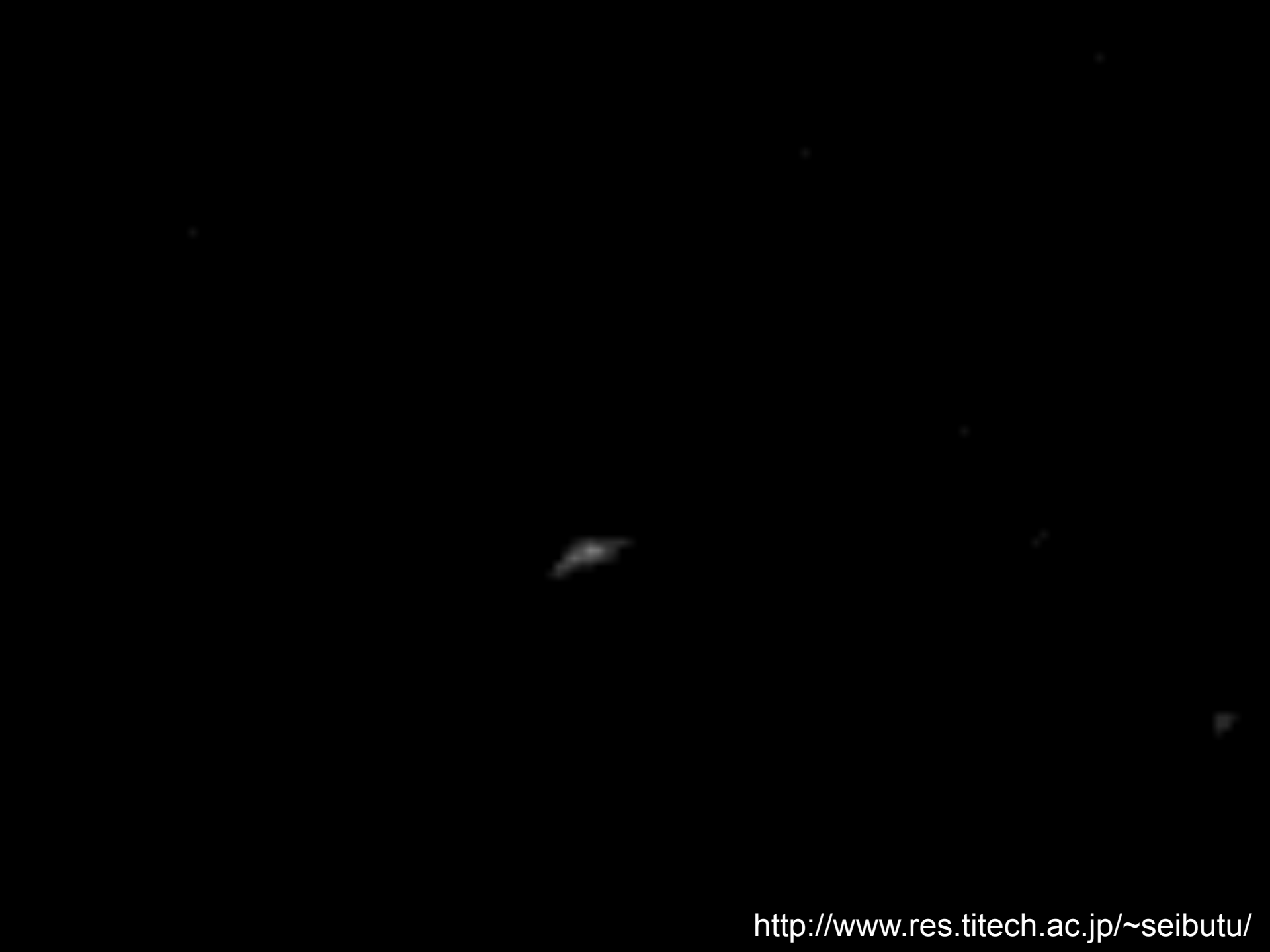


Figure 5-28 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)





http://www.res.titech.ac.jp/~seibutu/

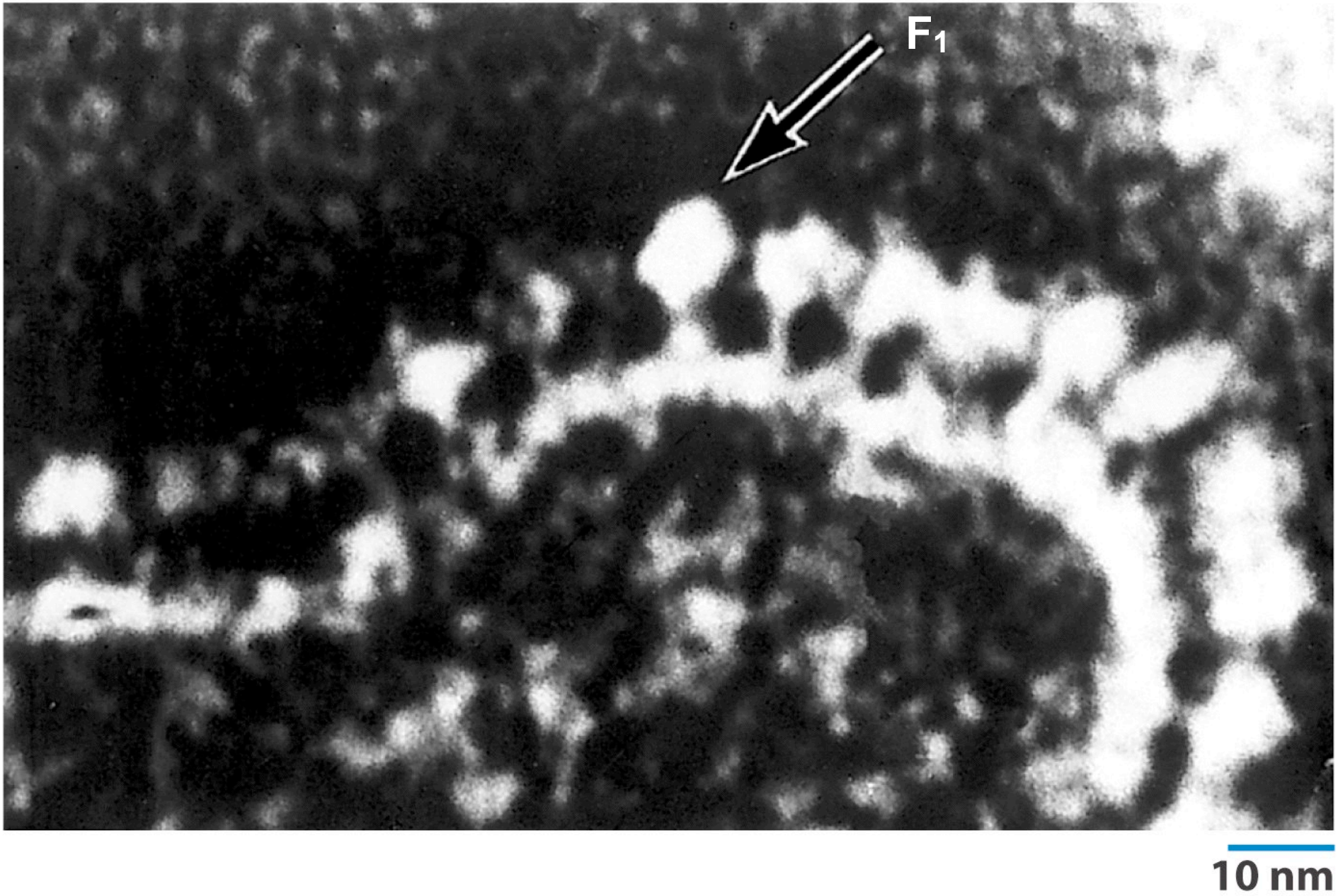


Figure 5-21 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

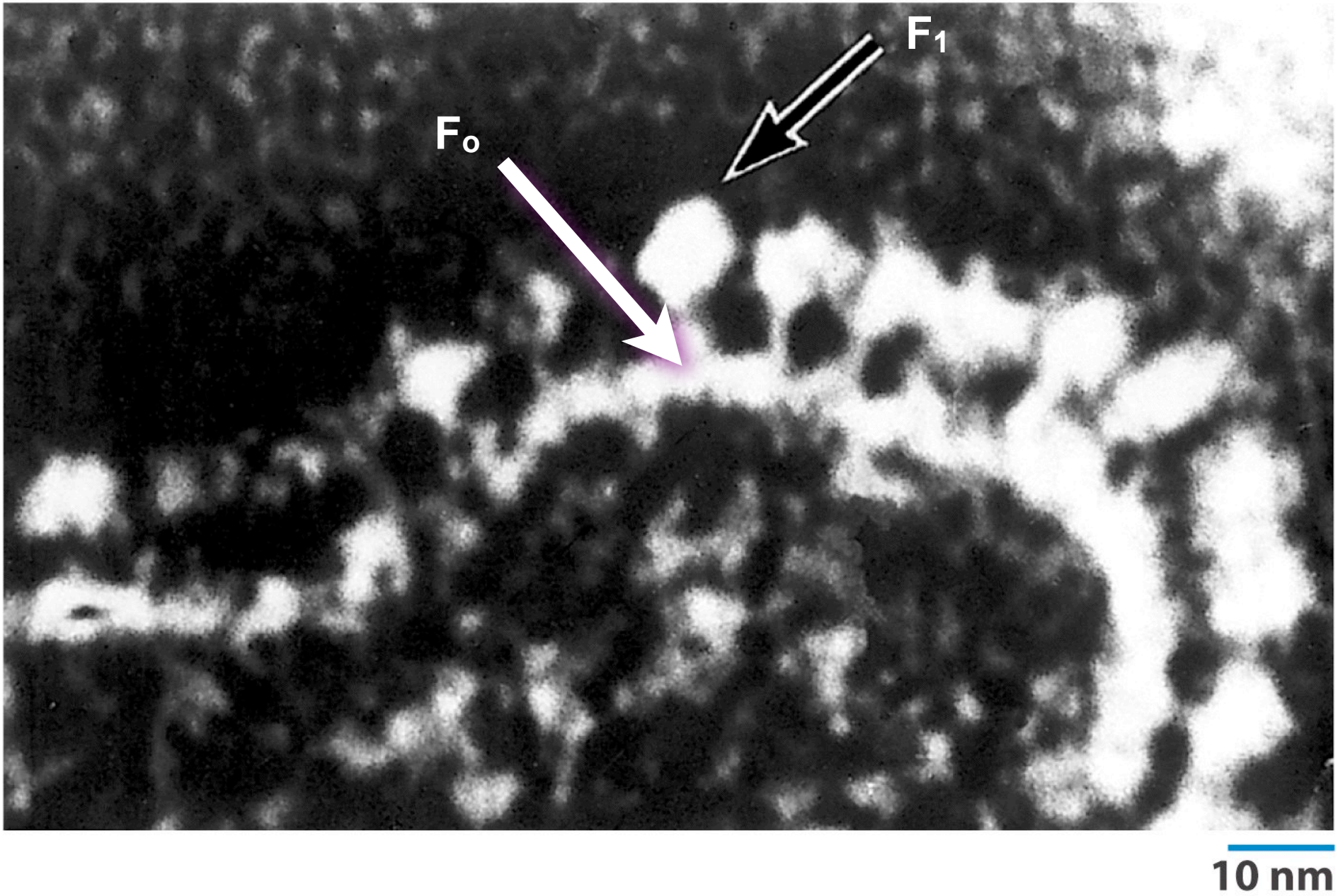
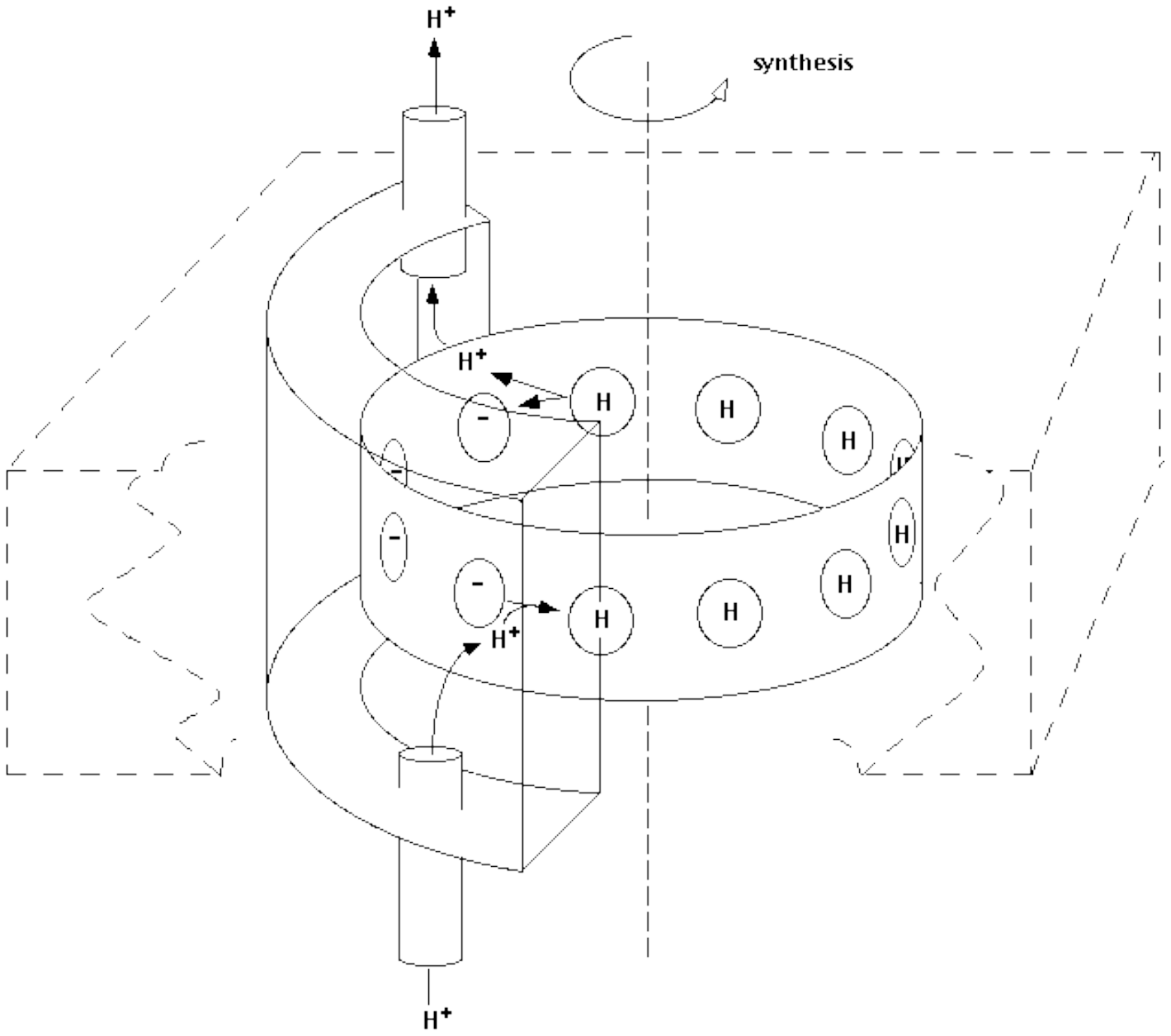
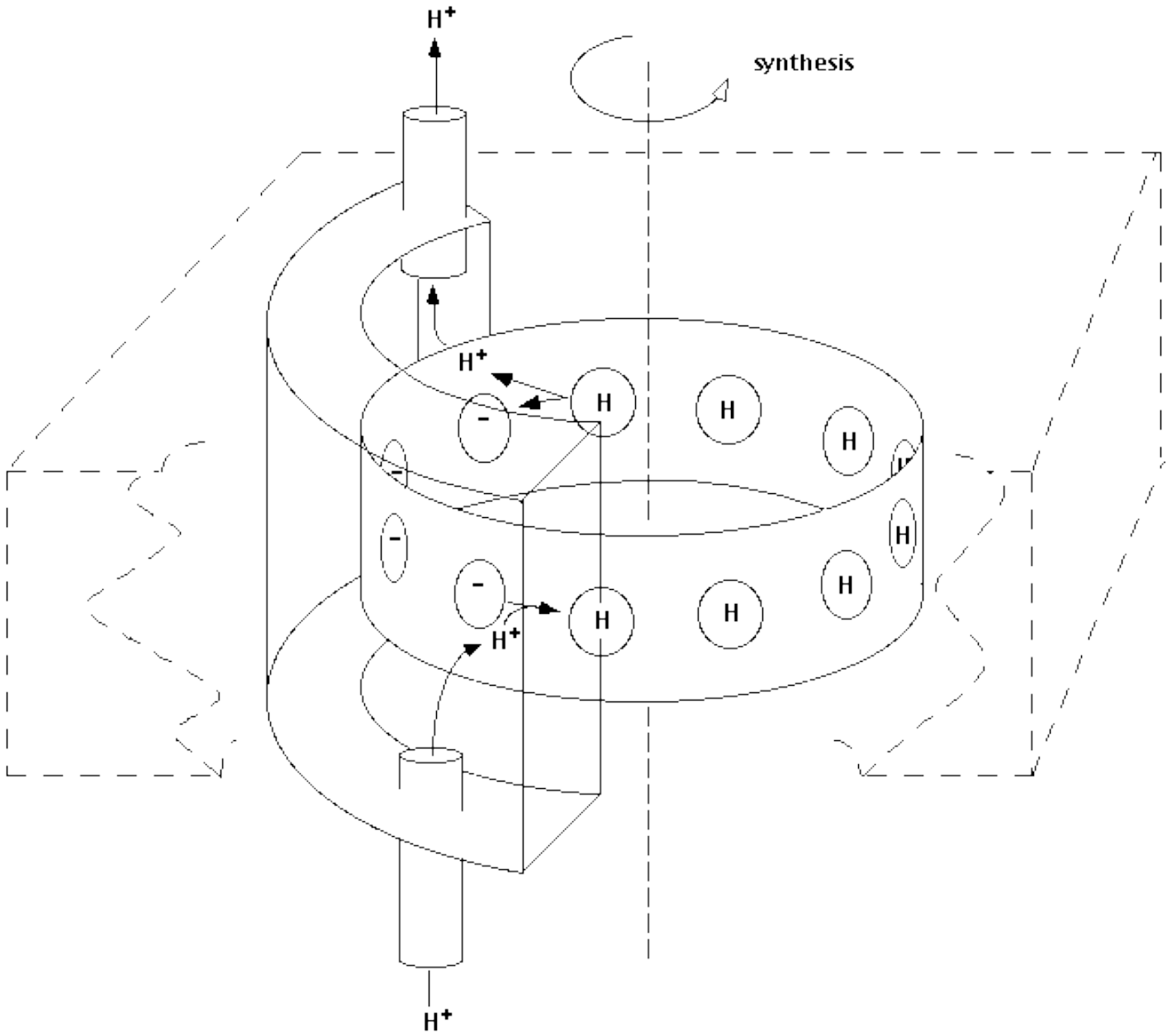


Figure 5-21 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

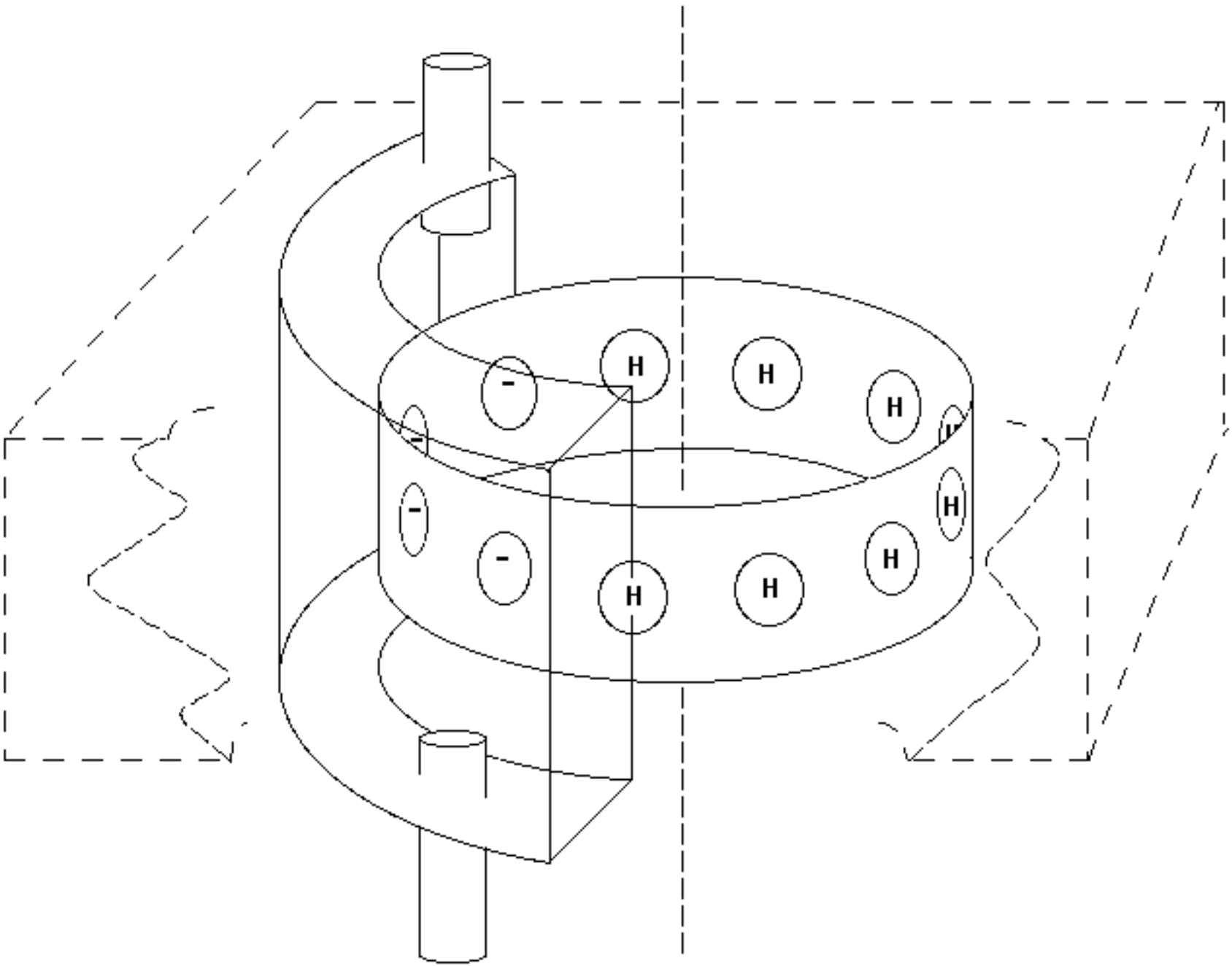


Rotation of the Fo-ATPase.Fo-ATPase as a proton-driven, rotary stepping motor, as proposed by Junge (1997).



Rotation of the Fo-ATPase.Fo-ATPase as a proton-driven, rotary stepping motor, as proposed by Junge (1997).

http://jfa.sbcs.qmul.ac.uk/~john/webstar/ltm/06/3ATP.html


H
H
H
H
H
H
H
H
-
-
-
-

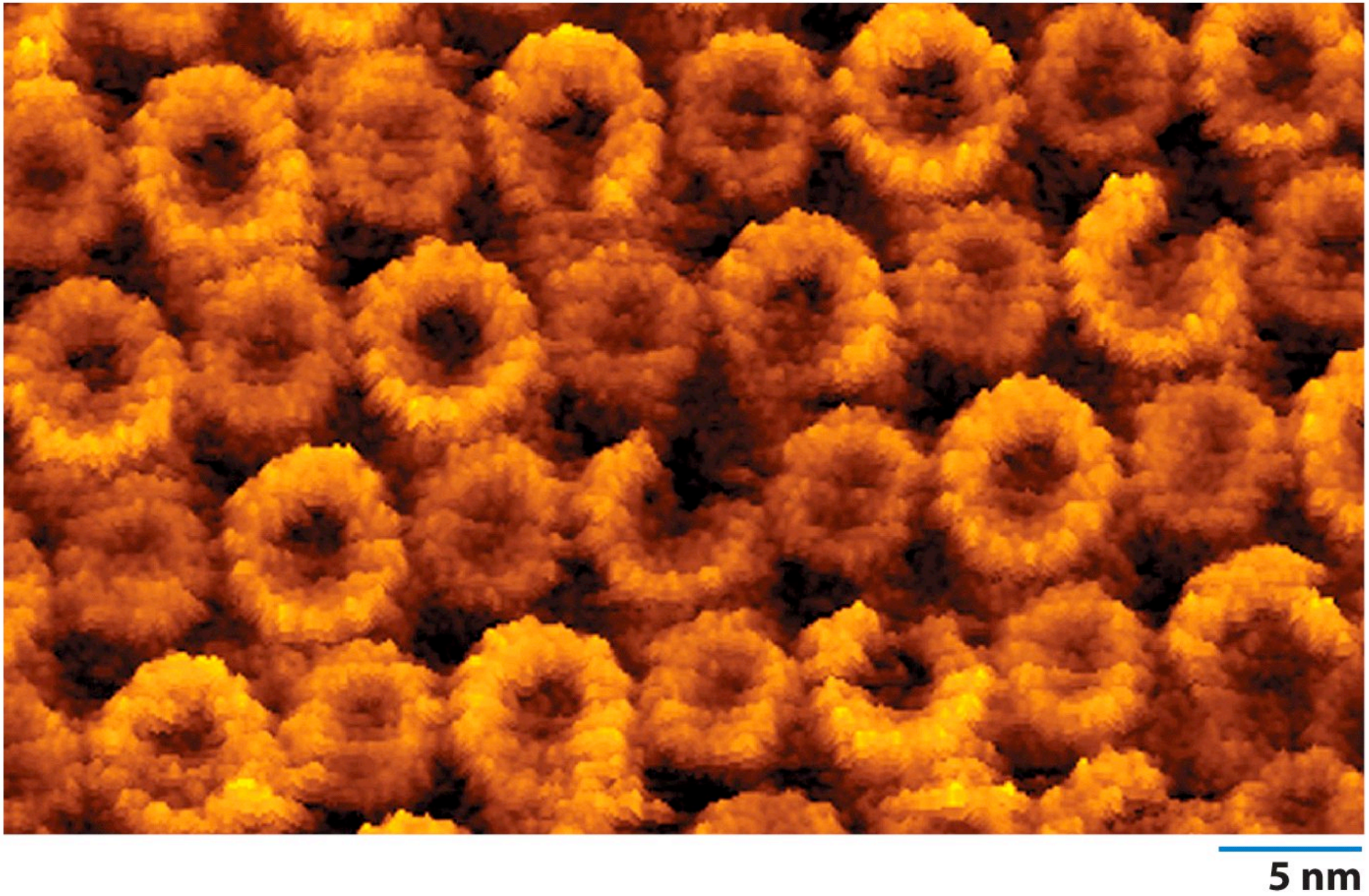


Figure 5-24a Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

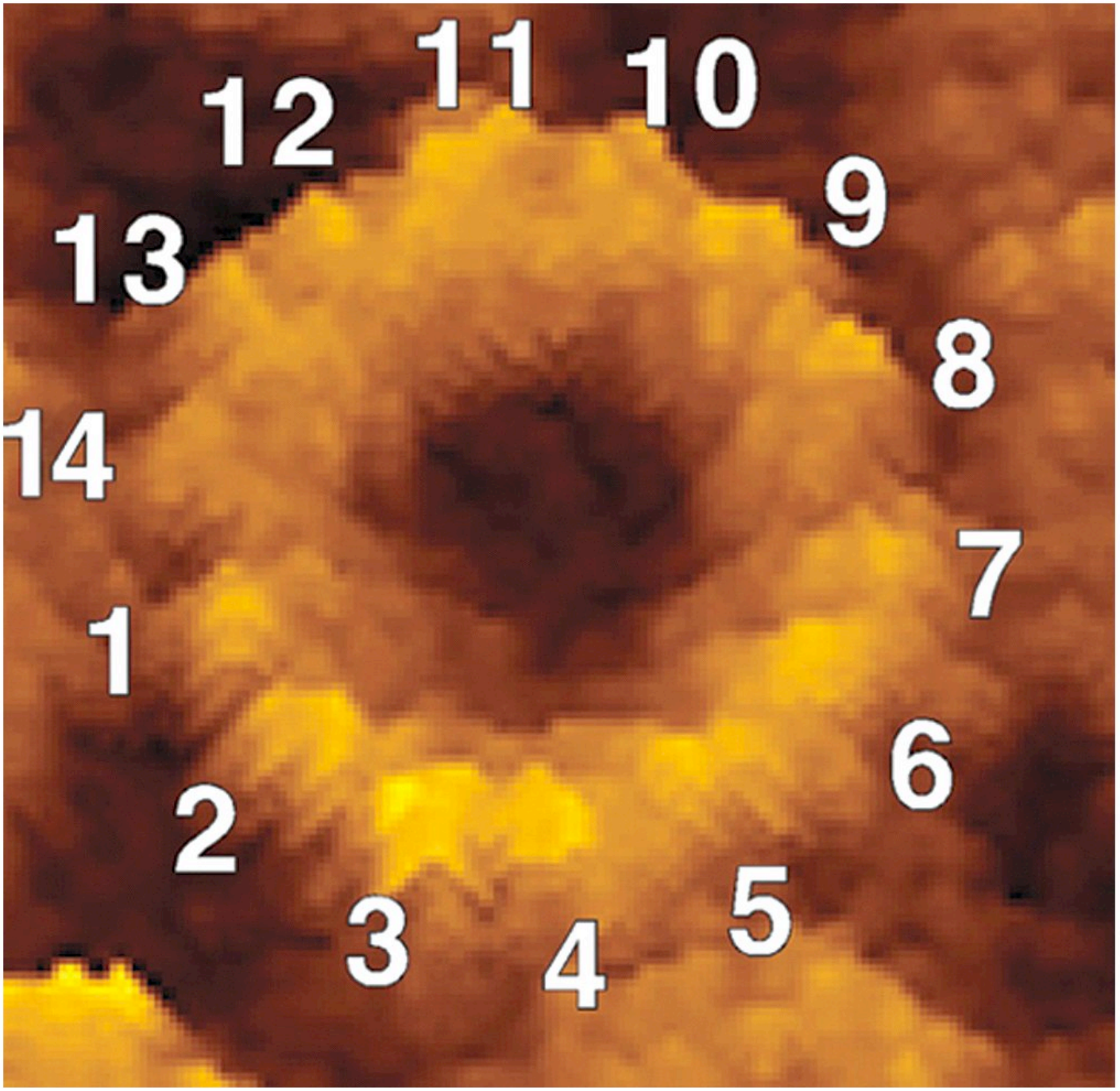


Figure 5-24b Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

The F_1-F_o ATPase

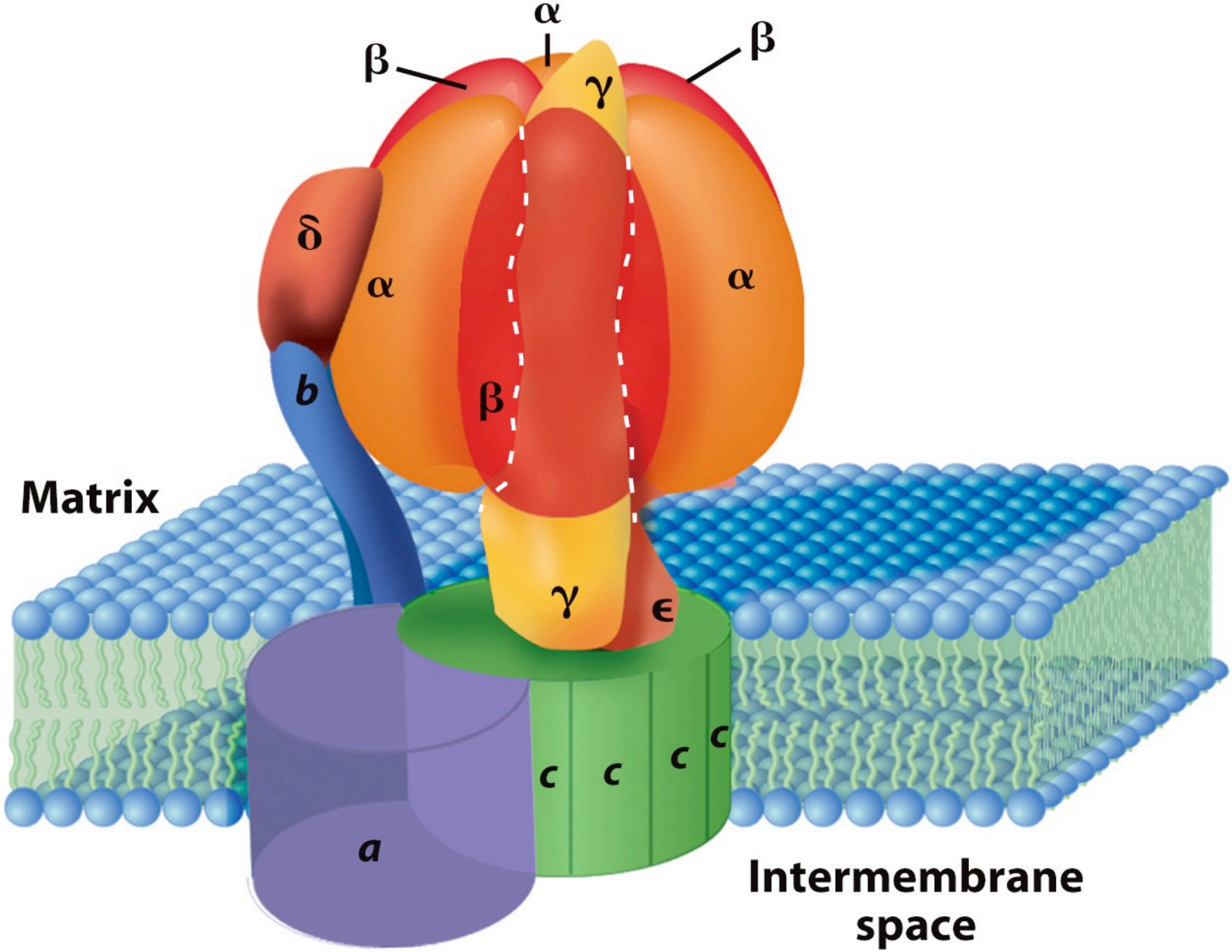


Figure 5-23b Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

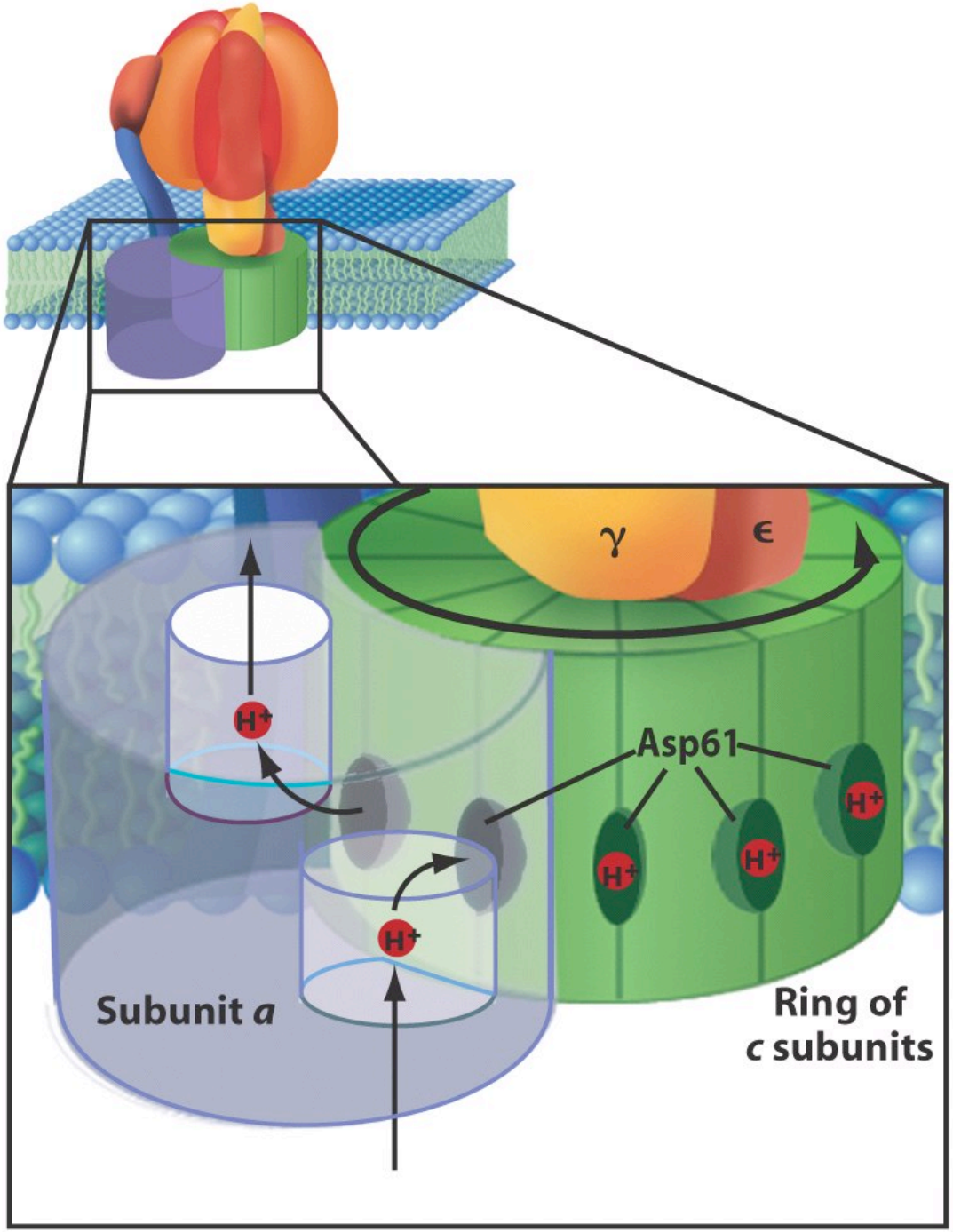
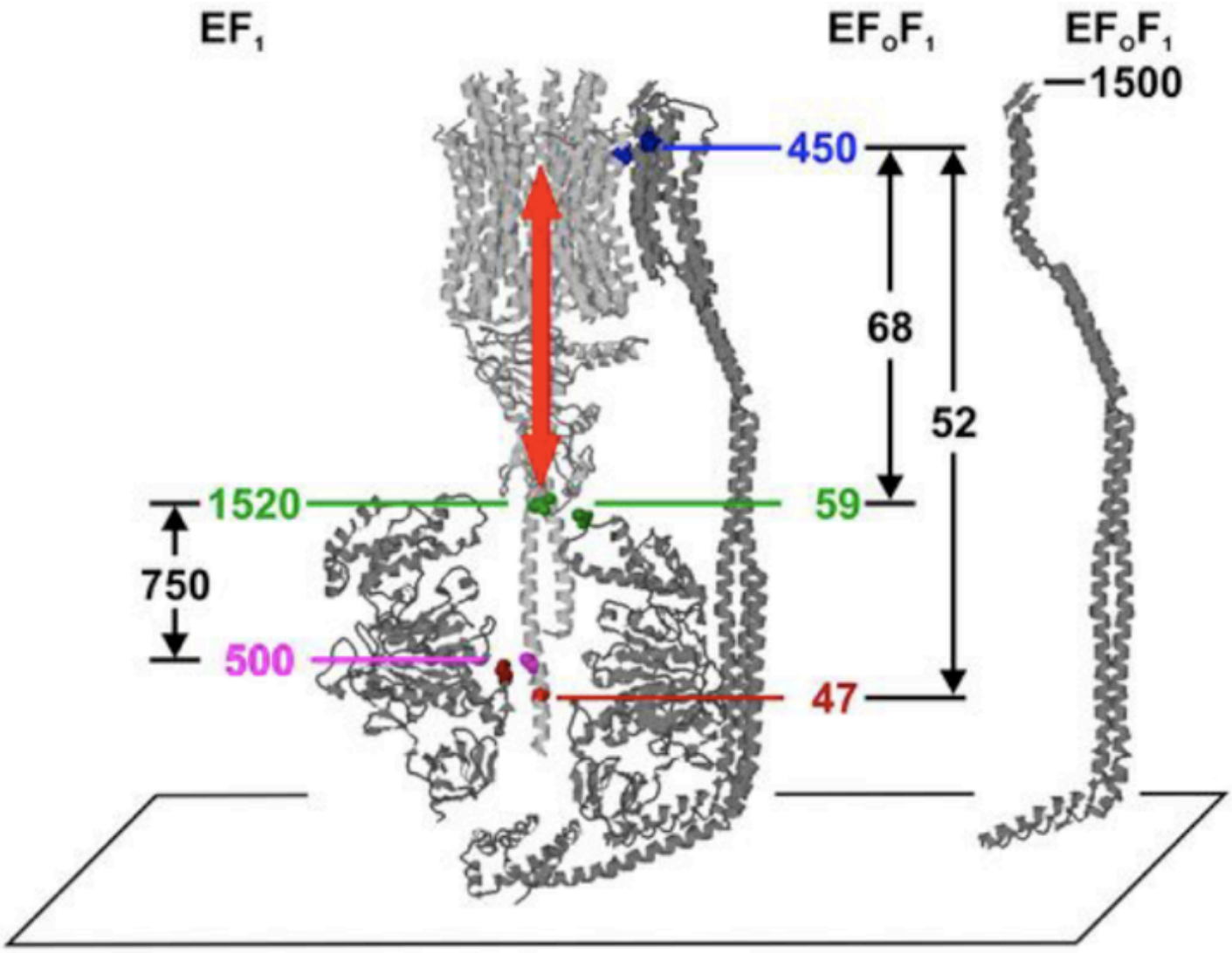
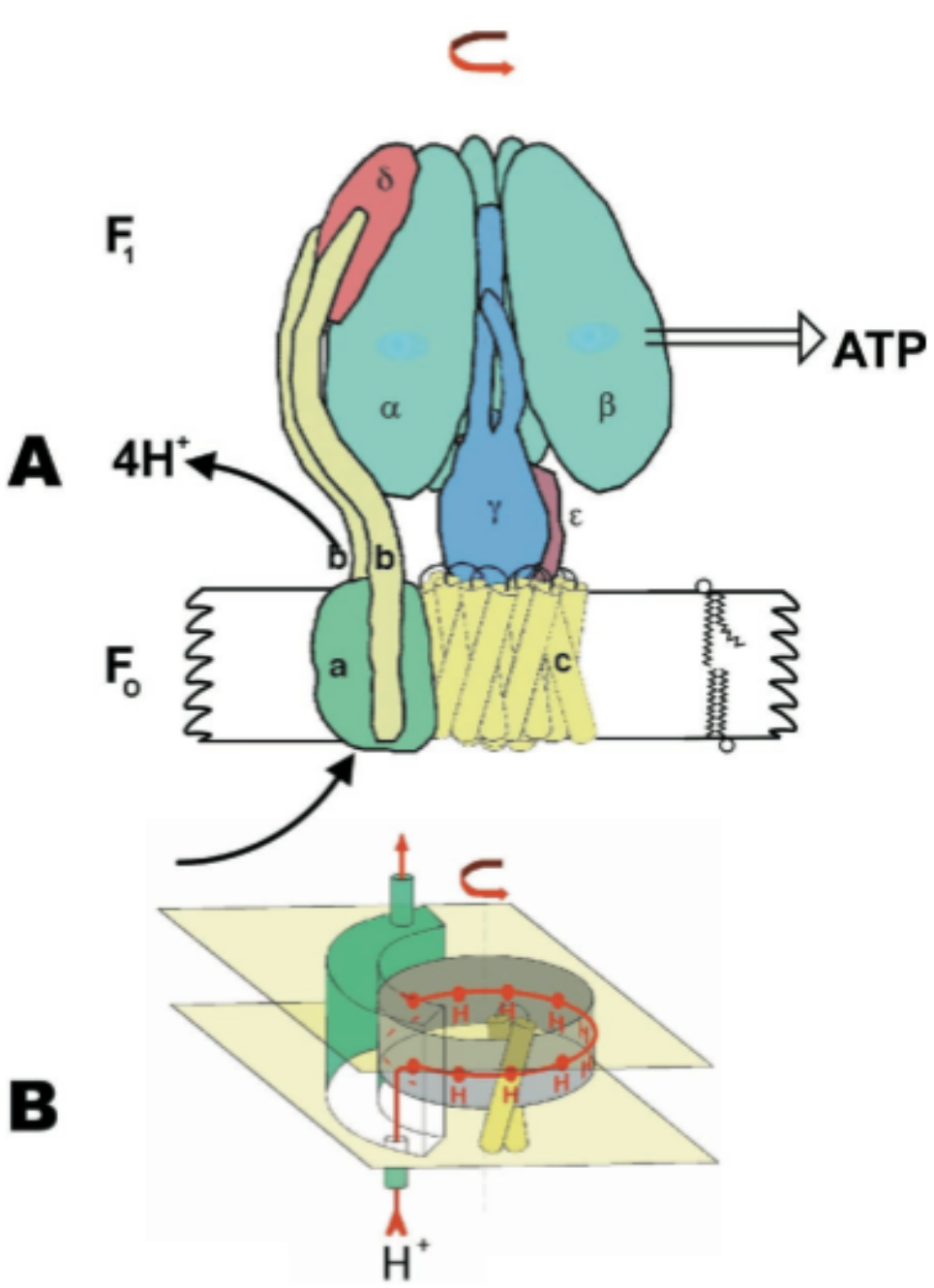


Figure 5-29 Cell and Molecular Biology, 4/e (© 2005 John Wiley & Sons)

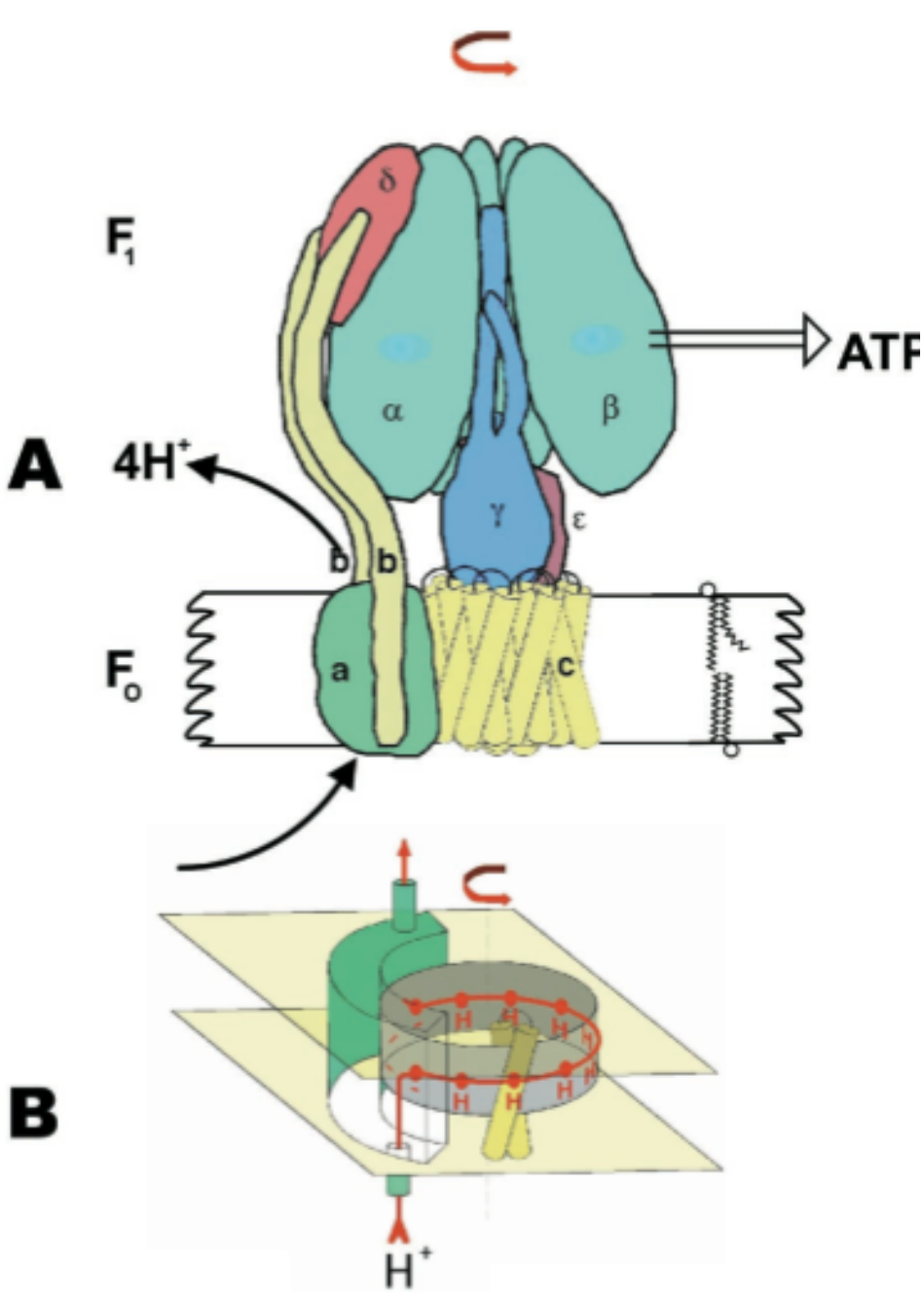


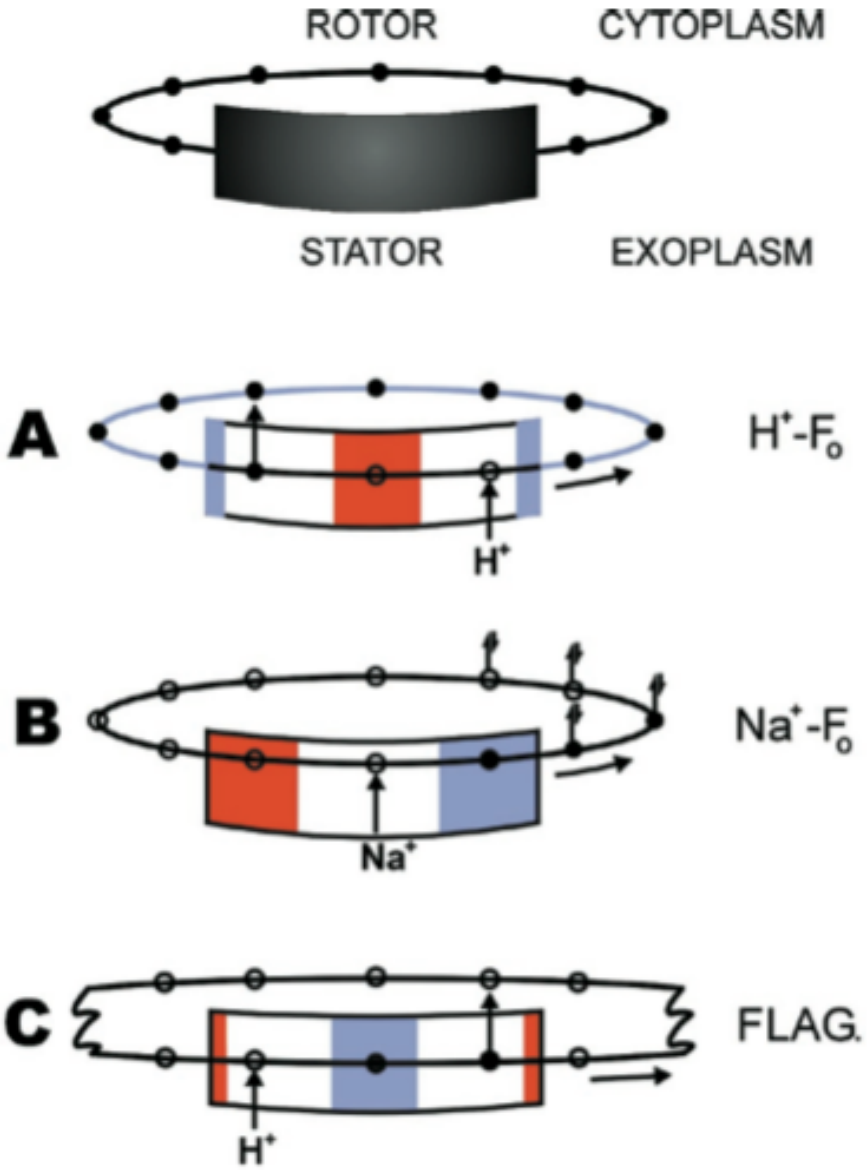
Structural model of EFoF1 (stator subunits in dark gray, rotor in light gray), and, at the very right side, of the homodimer of subunit **b,** and numbers for the torsional stiffness of various domains. Numbers given on the left side resulted from data obtained with EF1 in the set-up shown in Fig. 1A, those in the right side from EFoF1 as in Fig. 2A, and the one at the very right from EFoF1 as in Fig. 4A. The stiffness comes in units of pNnm. Numbers associated with horizontal colored lines denote the resulting stiffness *result* (see Eq. 3) as observed when the respective disulfide cross link (its two cysteines shown in the same hue, dark on the stator or light on the rotor) was closed. The numbers between the black vertical arrows denote the stiffnesses of the rotor domain lying between the respective pairs of cross link positions. The red arrow marks the region of greatest compliance in EFoF1, the dominant elastic buffer which is responsible for an elastic power transmission between Fo and F1.

Hendrik Sielaff, Henning Rennekamp, André Wächter, Hao Xie, Florian Hilbers, Katrin Feldbauer, Stanley D. Dunn, Siegfried Engelbrecht, and **Wolfgang Junge** **Domain compliance and elastic power transmission in rotary F_oF_1-ATPase** PNAS 2008 105:17760-17765; published online before print November 10, 2008, doi:10.1073/pnas.0807683105



- **Wolfgang Junge** **ATP synthase and other motor proteins** PNAS 1999 96:4735–4737



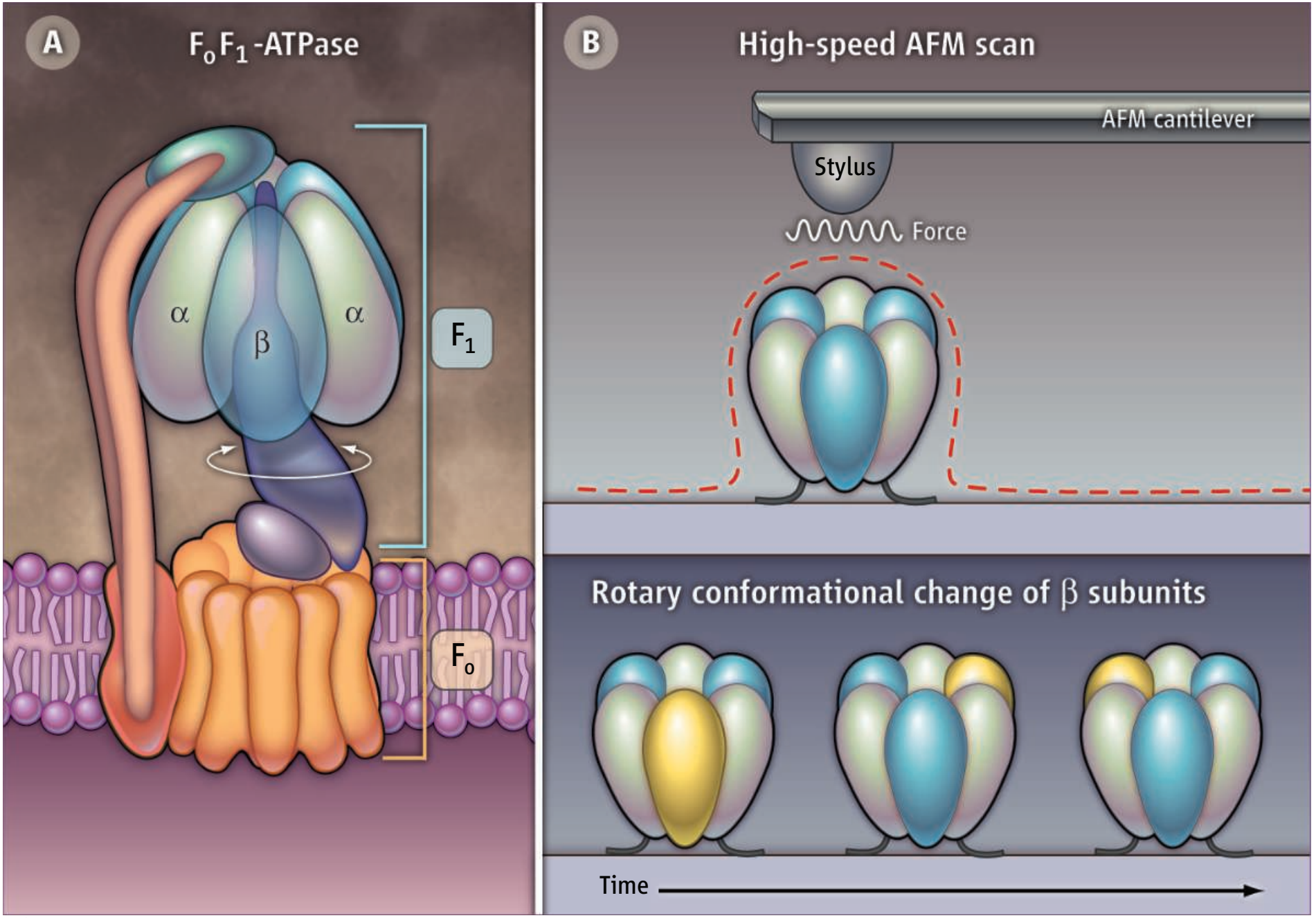


- **Wolfgang Junge** **ATP synthase and other motor proteins** PNAS 1999 96:4735–4737

Table 1. Comparison of molecular motors

Motor	Drive	Molecular mass, 10^5 Da	Processivity, %	Max. speed		Step size		Stall load	
				nm/s	rev/s	nm	deg	pN	pN·nm
Kinesin	ATP	1	100	800		8		6	
Myosin	ATP	5	1	8,000		15		4	
RNAP	NTP	7	100			0.35		30	
F_1	ATP	4	100		100		120		40
F_O	PMF	1.5	100	1,500	100	(1.00)	30	(16)	(40)
Flag	PMF	≈100	100	45,000	300	(<0.4)	<1	(300)	4,800

Myosin, kinesin, RNA polymerase (RNAP), the two drives of ATP synthase (F_O, F_1), and the flagellar motor (Flag) are driven by nucleotide triphosphates (ATP, NTP) or by an electrochemical potential difference [here named protonmotive force, (PMF)]. The processivity is almost perfect in all motors except myosin. The data for the linear motors are taken from refs. 54–57, those for the flagellar motor from refs. 35, 42, the stall load of F_1 from ref. 18, the maximum speed of F_1 from ref. 39, and the data for F_O were assumed to match those of F_1 when operating in the holoenzyme.



Seeing a Molecular Motor at Work

Wolfgang Junge[1] and Daniel J. Müller[2]

www.sciencemag.org SCIENCE VOL 333 5 AUGUST 2011 pp. 704-705

High-Speed Atomic Force Microscopy Reveals Rotary Catalysis of Rotorless F_1-ATPase

Takayuki Uchihashi,[1,2,3]* Ryota Iino,[3,4,5]* Toshio Ando,[1,2,3]† Hiroyuki Noji[3,4,5]†

F_1 is an adenosine triphosphate (ATP)–driven motor in which three torque-generating β subunits in the $\alpha_3\beta_3$ stator ring sequentially undergo conformational changes upon ATP hydrolysis to rotate the central shaft γ unidirectionally. Although extensive experimental and theoretical work has been done, the structural basis of cooperative torque generation to realize the unidirectional rotation remains elusive. We used high-speed atomic force microscopy to show that the rotorless F_1 still "rotates"; in the isolated $\alpha_3\beta_3$ stator ring, the three β subunits cyclically propagate conformational states in the counterclockwise direction, similar to the rotary shaft rotation in F_1. The structural basis of unidirectionality is programmed in the stator ring. These findings have implications for cooperative interplay between subunits in other hexameric ATPases.

www.sciencemag.org **SCIENCE** VOL 333 5 AUGUST 2011
pp. 755-757

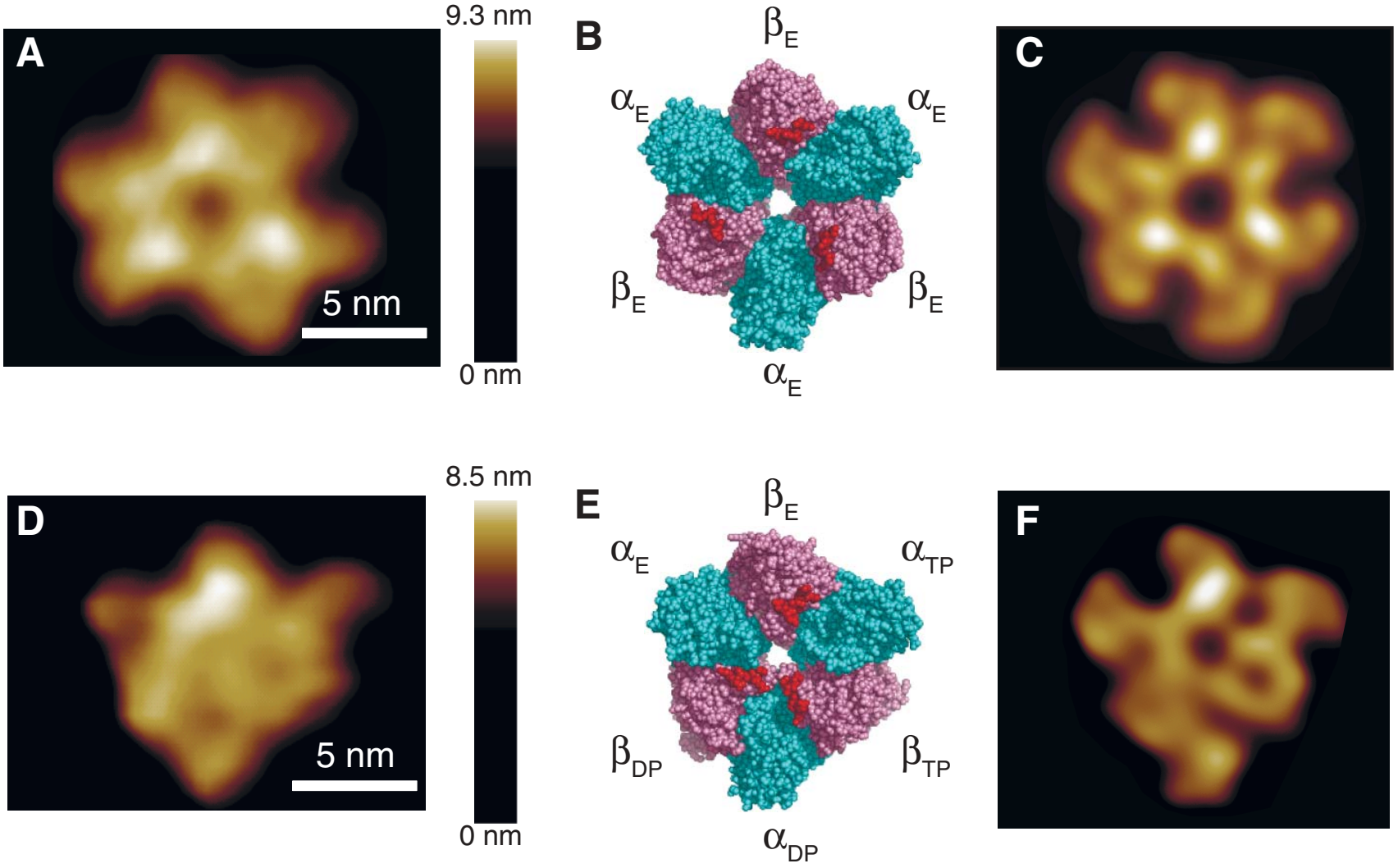
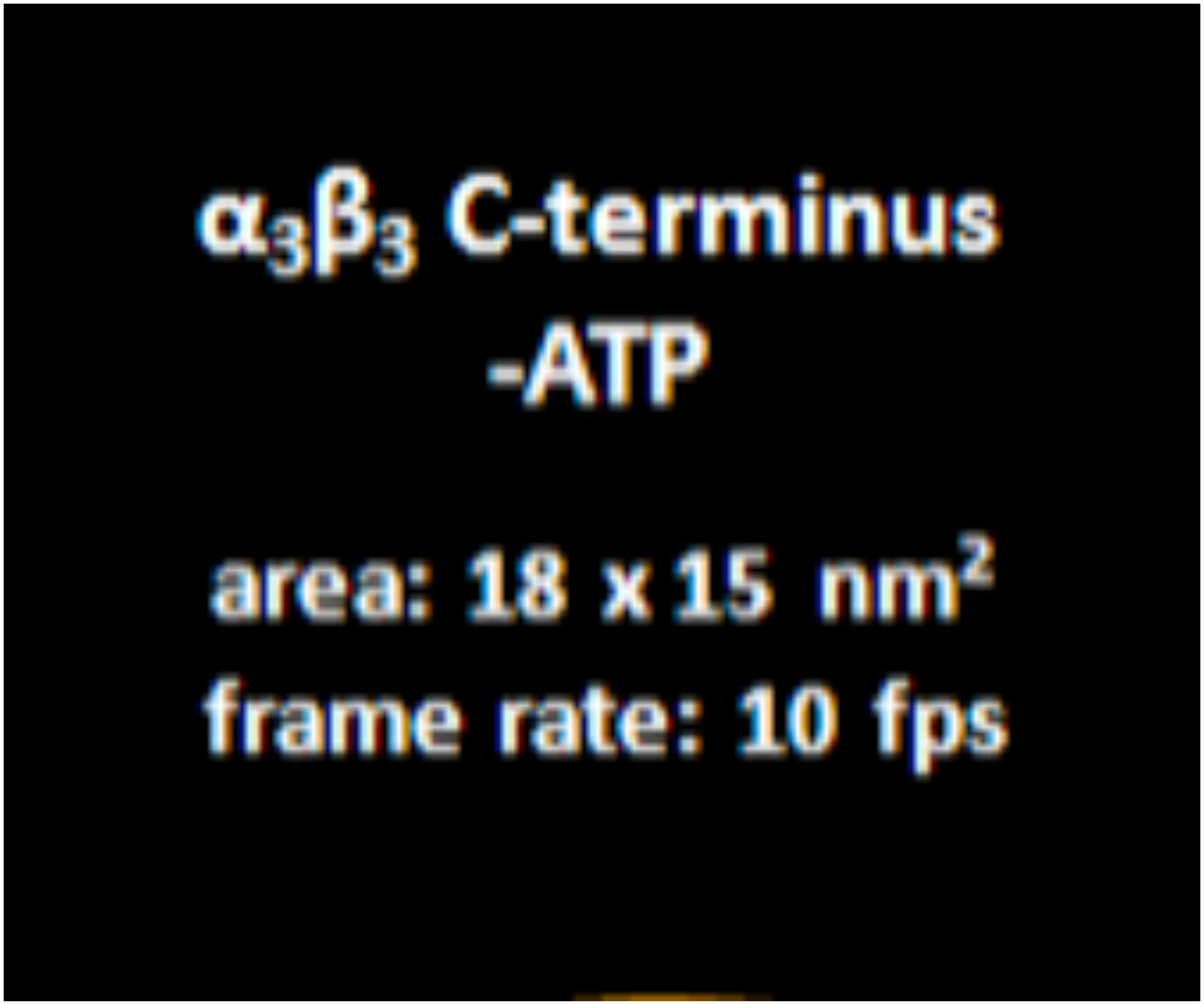


Fig. 1. (**A**) Averaged AFM image of C-terminal side of the $\alpha_3\beta_3$ subcomplex without nucleotide (movie S1). (**B**) C-terminal side of the crystal structure of the nucleotide-free $\alpha_3\beta_3$ subcomplex [Protein Data Bank (PDB) code 1SKY] (*21*). The α and β subunits are colored in cyan and pink, respectively. The C-terminal DELSEED motif of β corresponding to the high protruding portions is highlighted in red. (**C**) Simulated AFM image of the $\alpha_3\beta_3$ subcomplex constructed from the structure in (B). (**D**) Averaged AFM image of C-terminal side of the $\alpha_3\beta_3$ subcomplex in 1 mM AMPPNP. (**E**) Atomic structure of the $\alpha_3\beta_3$ subcomplex with bound nucleotides. This structure is obtained by removing γ from the crystal structure of F_1 (PDB code 1BMF) (*4*). (**F**) Simulated AFM image constructed from the structure in (E). The brightness of all AFM images in this paper represents the sample height but is not linearly set to highlight the top surface structure (fig. S4).

Movie S1

AFM movie of the C-terminal side of $\alpha_3\beta_3$ without nucleotide. Scan area, 18 x 15 nm^2; frame rate, 10 fps

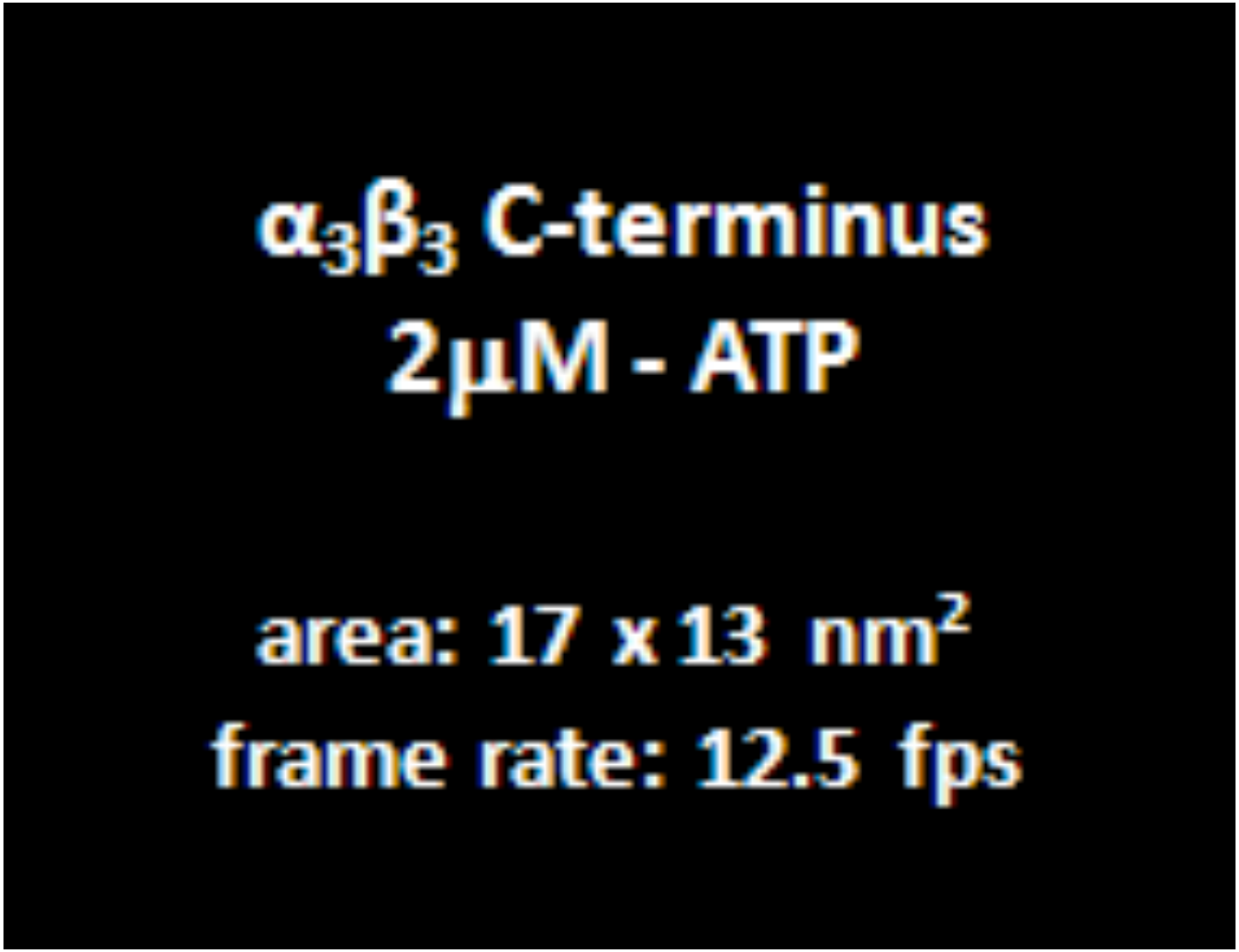


Movie S1

AFM movie of the C–terminal side of $\alpha_3\beta_3$ without nucleotide. Scan area, 18 x 15 nm^2; frame rate, 10 fps

Movie S3

AFM movie of the C-terminal side of $\alpha_3\beta_3$ in 2 μM ATP. Scan area, 17 x 13 nm^2; frame rate, 12.5 fps.

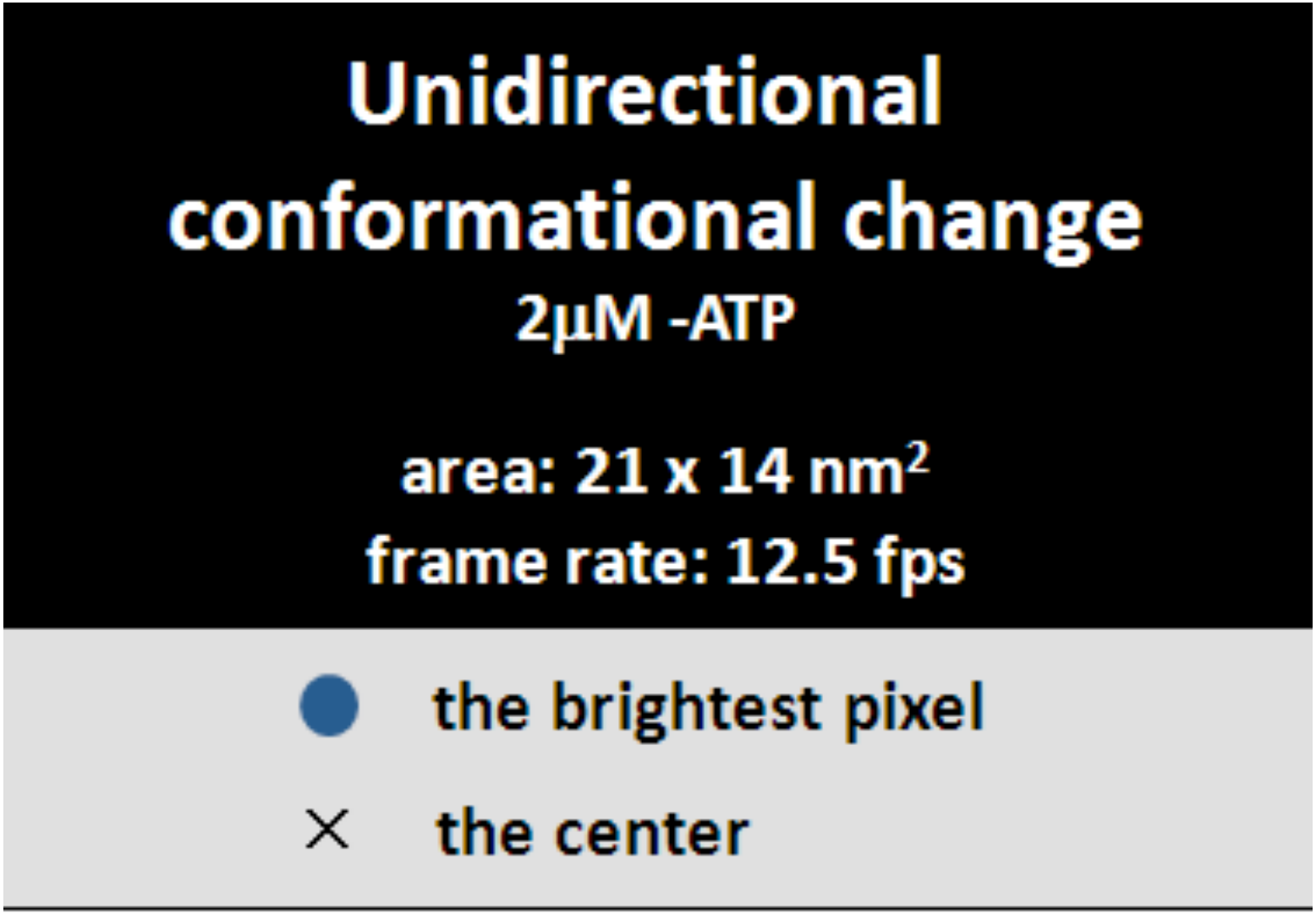


Movie S3

AFM movie of the C–terminal side of $\alpha_3\beta_3$ in 2 μM ATP. Scan area, 17 x 13 nm^2; frame rate, 12.5 fps.

Movie S6

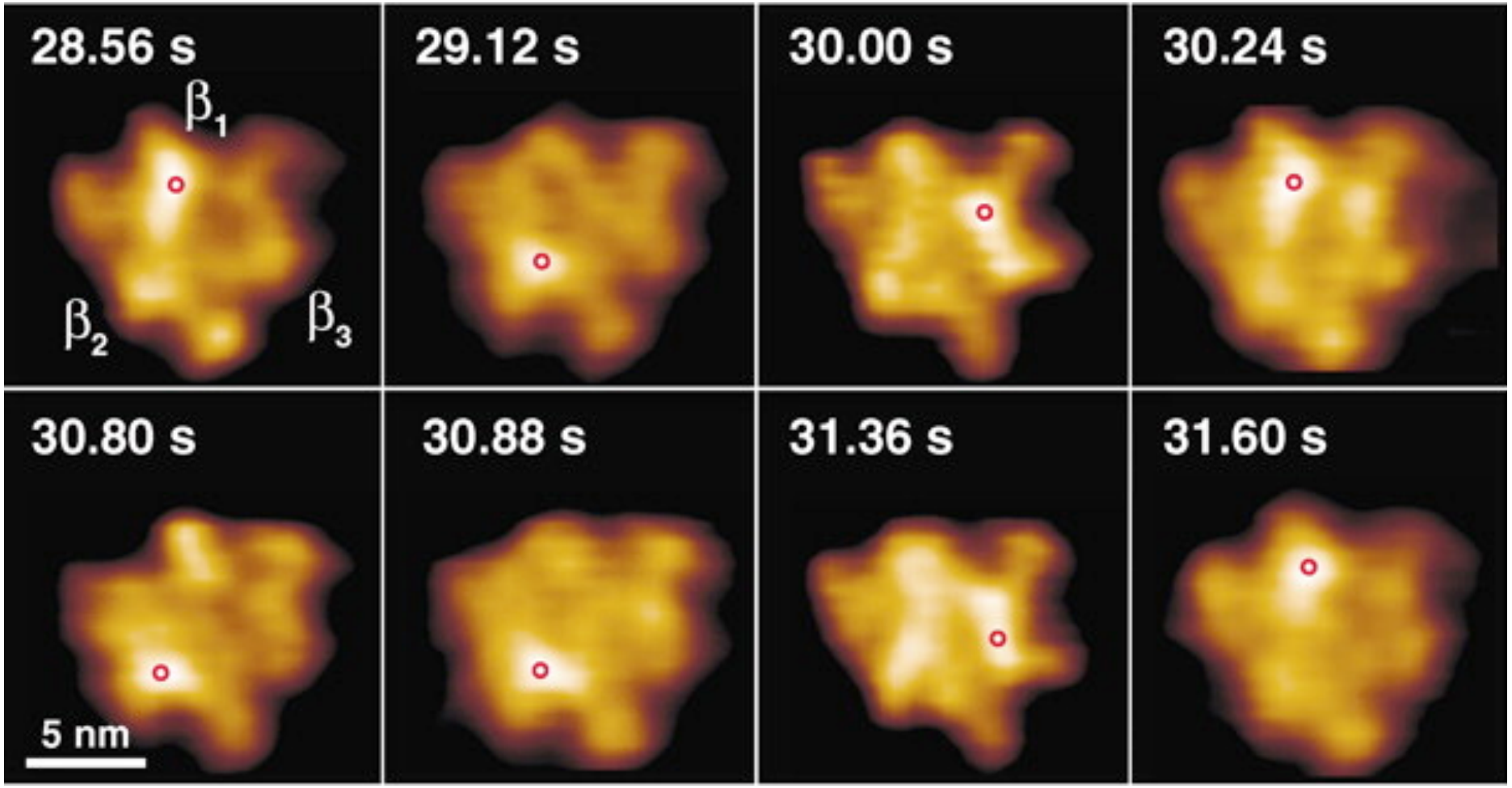
AFM movie of the C-terminal side of $\alpha_3\beta_3$ in 2 μM ATP. Scan area, 21 x 14 nm^2; frame rate, 12.5 fps. The pixel with the highest (brightest) position in each image is indicated by the blue circle. The center used for calculating the rotational angle is indicated by the cross mark.



Movie S6

AFM movie of the C–terminal side of $\alpha_3\beta_3$ in 2 μM ATP. Scan area, 21 x 14 nm^2; frame rate, 12.5 fps. The pixel with the highest (brightest) position in each image is indicated by the blue circle. The center used for calculating the rotational angle is indicated by the cross mark.

www.sciencemag.org **SCIENCE** VOL 333 5 AUGUST 2011
pp. 755-757



Successive AFM images showing the conformational change of β's in 2 μM ATP (movie S3). The highest pixel in each image is indicated by the red circle. Frame rate, 12.5 frames/s.

www.sciencemag.org **SCIENCE** VOL 333 5 AUGUST 2011
pp. 755-757

The present results prove that the stator $\alpha_3\beta_3$ ring alone possesses high cooperativity for sequential power stroking among three catalytic β's. This was also indicated by the observations that the occasional subunit dissociation completely stopped the rotary propagation of the conformational state (fig. S12). Thus, the "γ-dictator" model (*13*), which proposes that only the interaction with γ determines the conformational and catalytic states of β's (*23*, *24*), is not valid. On the other hand, the ATP-binding rate and the efficiency of unidirectionality of the $\alpha_3\beta_3$ subcomplex are distinctly lower than those of F_1 (Fig. 3 and fig. S11). Thus, the interaction with γ is dispensable but still important for the rapid and precise rotary catalysis. Our findings are not inconsistent with the observations that the rates and equilibriums of the catalytic reactions are apparently under the control of the rotary angle of γ (*10*–*12*). The intrinsic interplay among β's would reinforce catalytic control by γ; even if γ tightly interacts with only one β, it still can act on all β's through β-β interplay.

MRC Medical Research Council

Mitochondrial Biology Unit

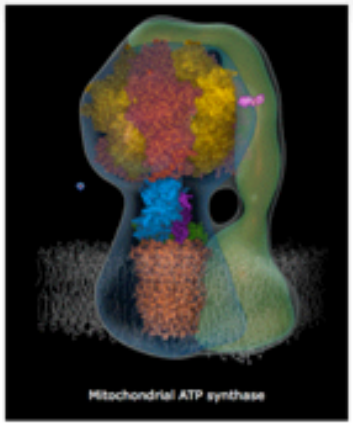
Introduction
Faculty and Research
Faculty and Topics
Research Gallery
MitoMiner
Publications
Sir Wm Dunn Scholarships
News and Events
Post-graduate Programs
Undergraduate Programs
Facilities and Technology
Jobs and Vacancies

Search
Contact Us
Directions
MBU Intranet
MBU Webmail
Medical Research Council

ATP synthase

Research area: Understanding the molecular mechanism of how ATP is made.
Group leader: John Walker

In eubacteria, chloroplasts and mitochondria, the synthesis of ATP is carried out by a highly complex molecular machine known as ATP synthase. Our aim is to understand how this machine works. We are concentrating mainly on the enzyme from mitochondria which has many features in common with the bacterial and chloroplast enzymes. It sits in the inner membranes of the organelle, where it uses the transmembrane proton motive force (pmf) generated by the oxidation of nutrients as a source of energy for making ATP. The pmf across the inner membrane of the organelle is coupled to the chemical synthesis of ATP from ADP and phosphate by a rotary mechanism illustrated in the Figure. During ATP synthesis, the central rotor turns in the direction shown about 150 times every second. In order to provide energy to sustain our lives, every day, each one us produces a quantity of ATP by this mechanism that is approximately equal to our body weights.



View from above and then below the F_1 domain along the rotating γ-subunit.

MRC | Dunn Human Nutrition Unit

How the rotating γ-subunit imposes conformational states on a β–subunit required for substrate binding, ATP formation and ATP release.

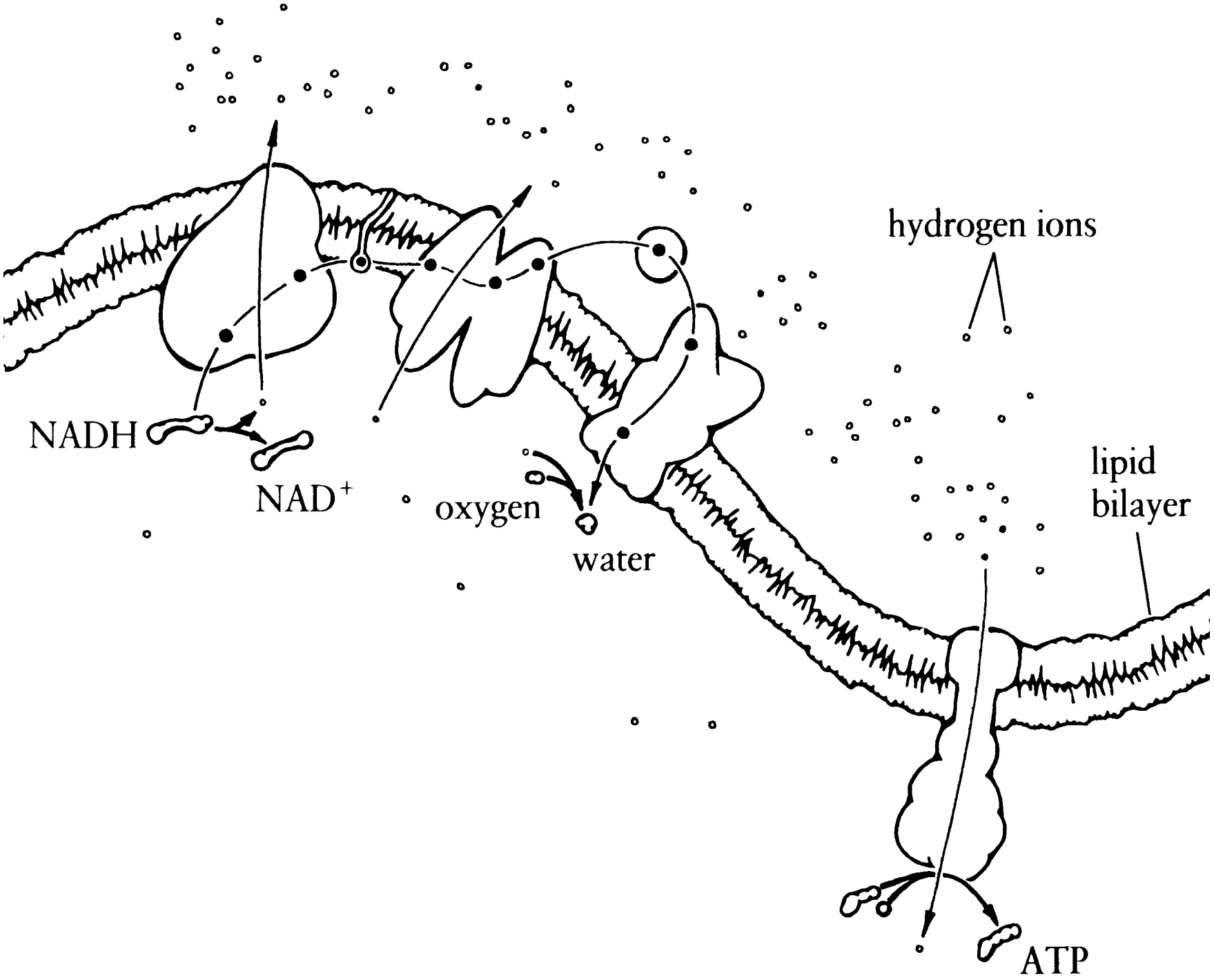
MRC | Dunn Human Nutrition Unit

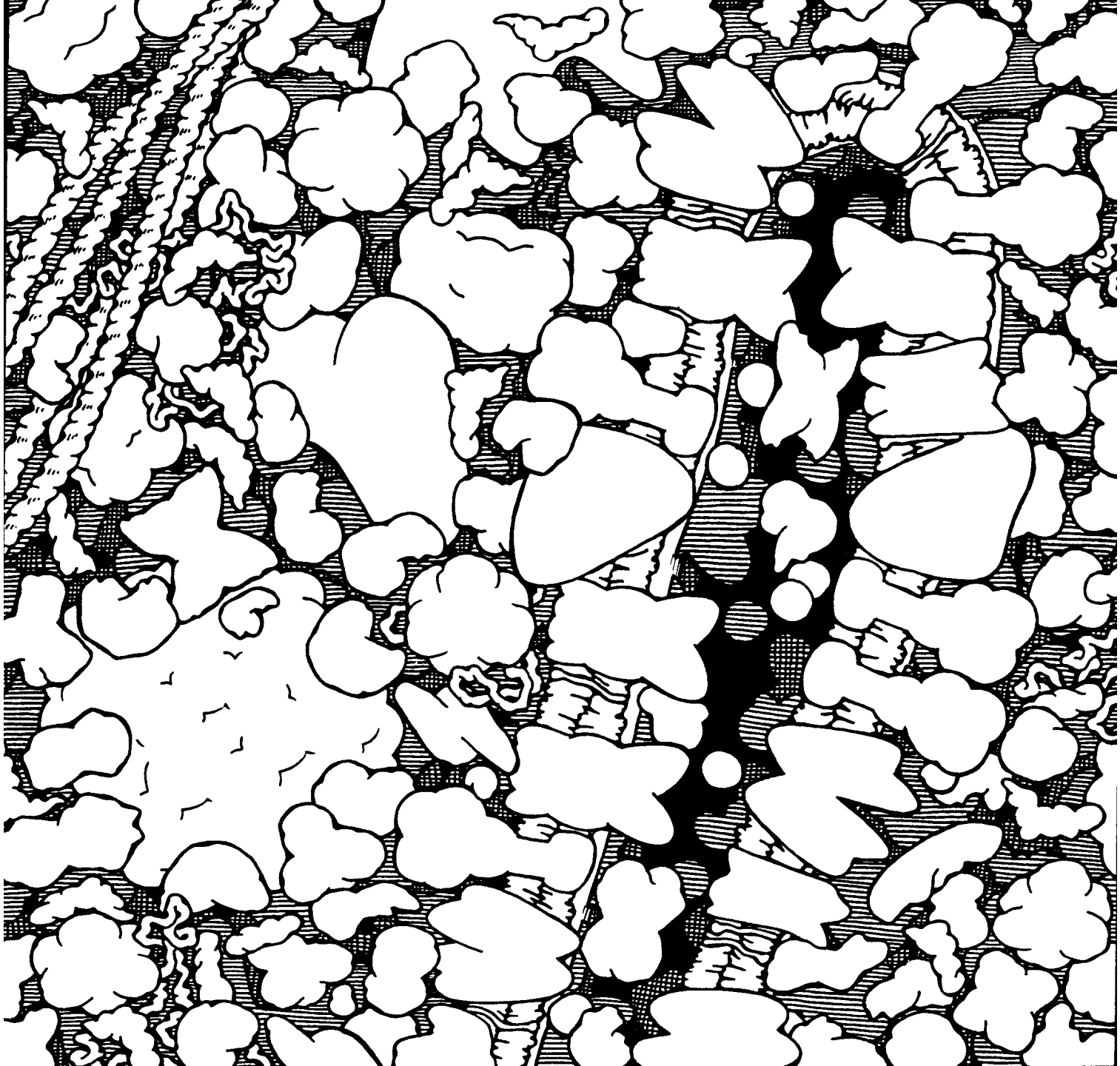
Three conformations of a catalytic β–subunit produced by 120° rotations of the central γ-subunit

MRC | Dunn Human Nutrition Unit

The rotary catalytic mechanism of mitochondrial ATP synthase.

MRC | Dunn Human Nutrition Unit


hydrogen ions
NADH
NAD+
oxygen
water
lipid
bilayer
ATP




JJK
2004


JSK
2004

The way in which mitochondria generate energy is one of the most bizarre mechanisms in biology. Its discovery has been compared with those of Darwin and Einstein. Mitochondria pump protons across a membrane to generate an electric charge with the power, over a few nanometres, of a bolt of lightning. This proton power is harnessed by the elementary particles of life—mushroom-shaped proteins in the membranes—to generate energy in the form of ATP. This radical mechanism is as fundamental to life as DNA itself, and gives an insight into the origin of life on Earth


Thank you for listening


JVK
2004

SBCS-922 Membrane Proteins

Mitochondria and respiratory chains

John F. Allen

School of Biological and Chemical Sciences,
Queen Mary, University of London

SBCS-922 Membrane Proteins

Mitochondria and respiratory chains

John F. Allen

School of Biological and Chemical Sciences,
Queen Mary, University of London

jfallen.org/lectures/