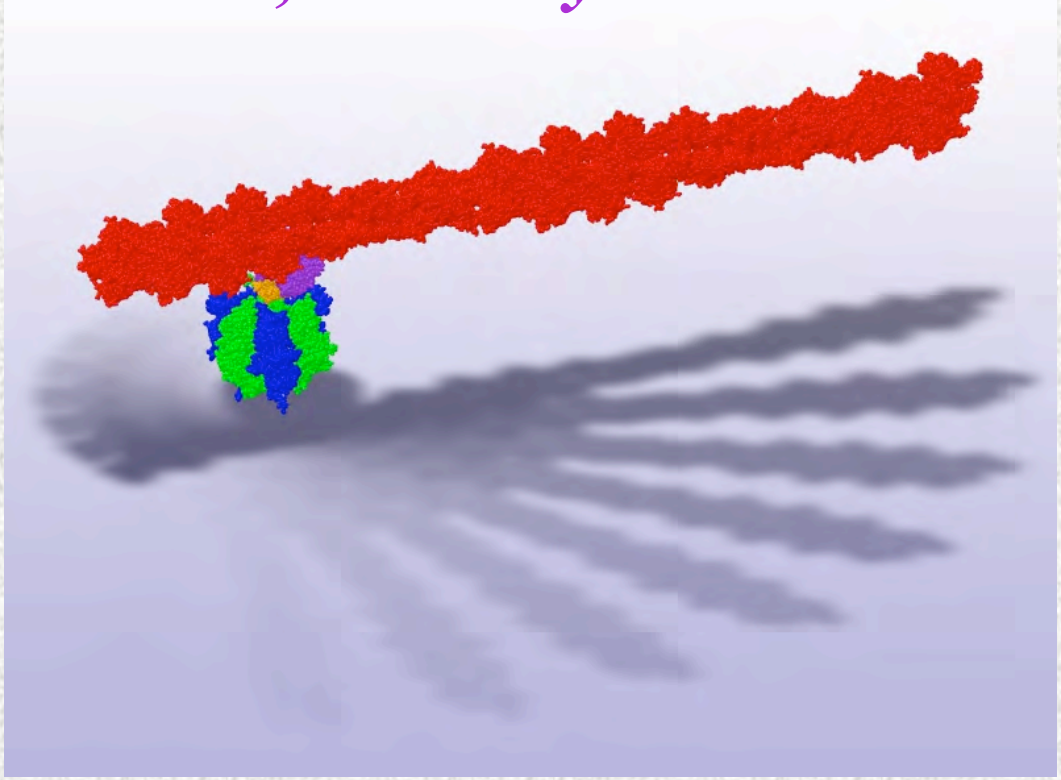
# $F_1$ - ATPase: A Molecular Transducer of Chemical and Mechanical Energies

## Why Do We Eat, and Why Do We Breathe?




Kazuhiko Kinosita, Jr.

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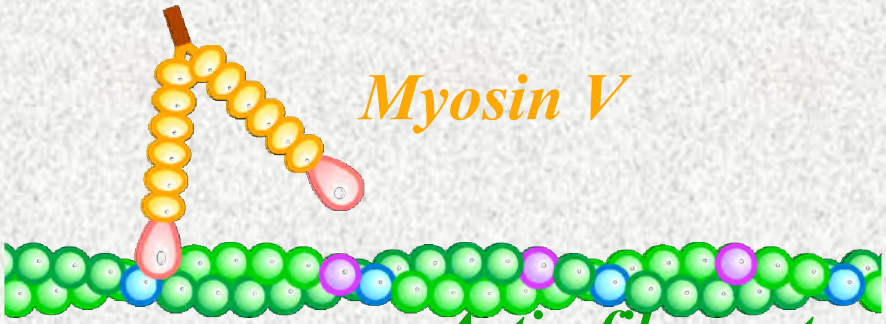
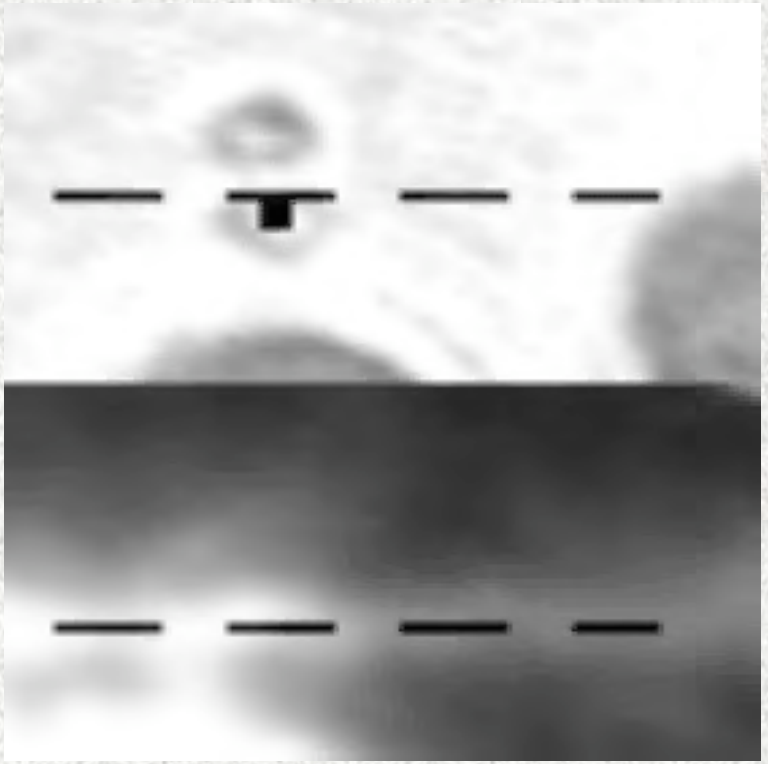
http://www.k2.phys.waseda.ac.jp

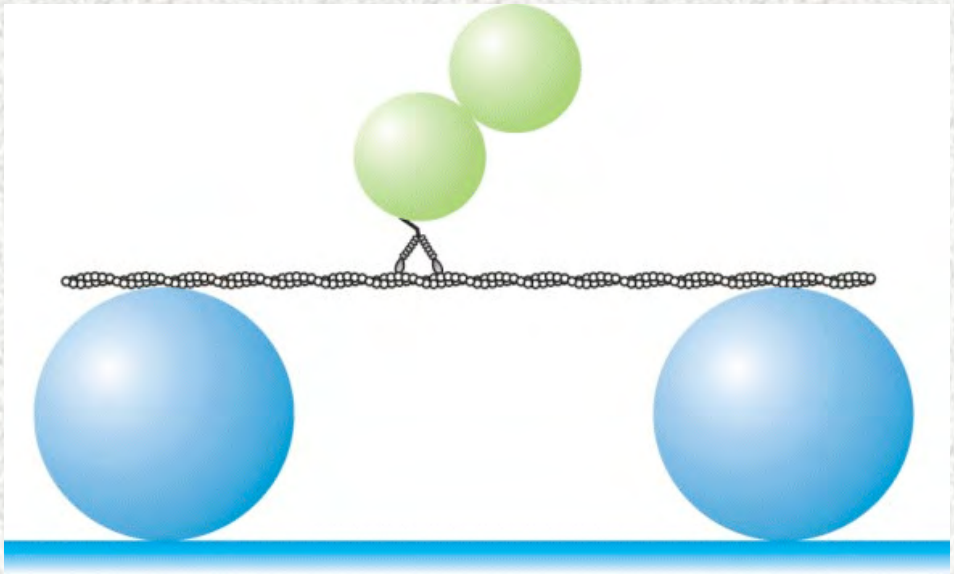
# A Two-Foot Linear Molecular Motor That Transports Nutrients in the Brain




White: closer to you
Black: away from you
4x fast replay



400 µM ATP

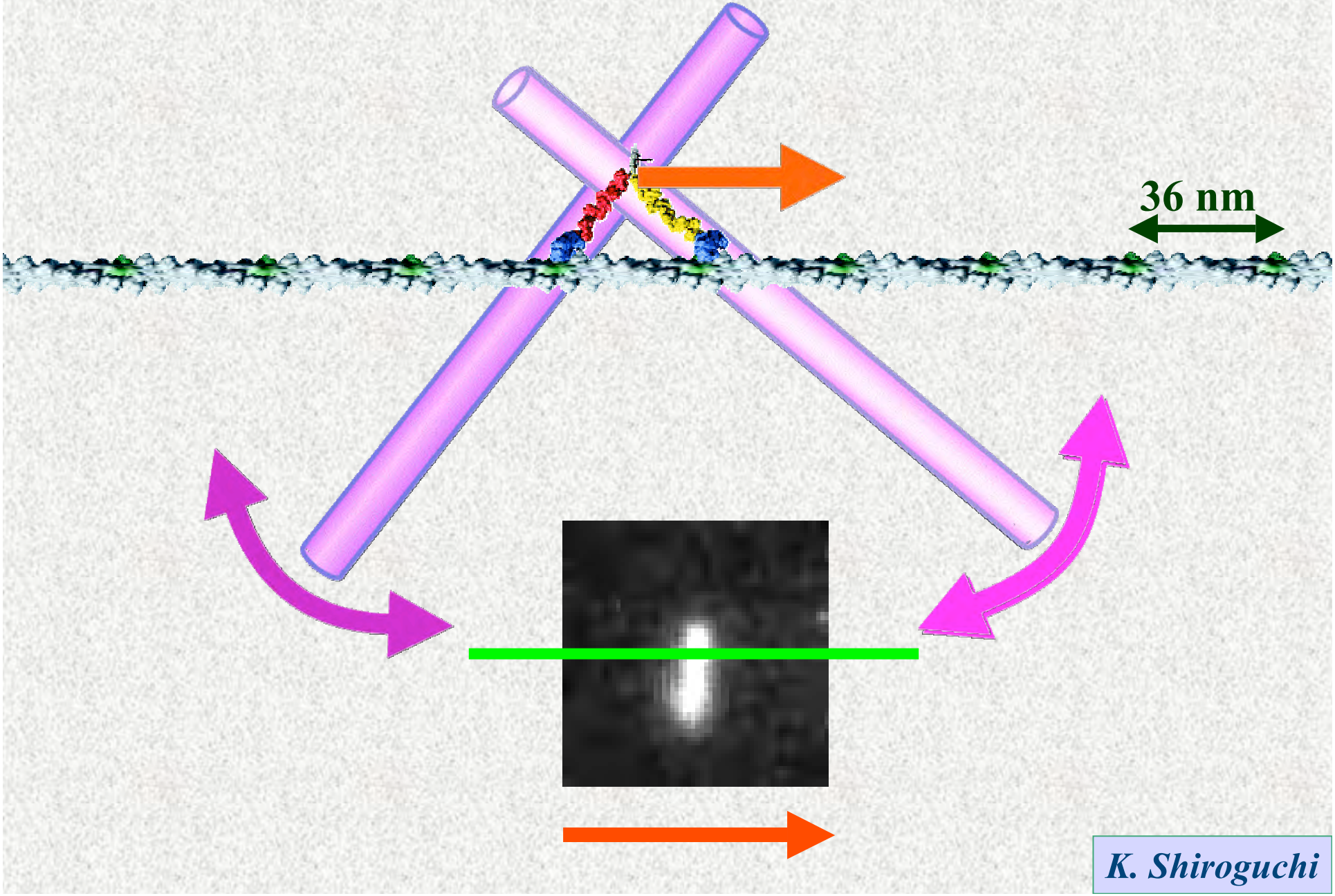


Major Players

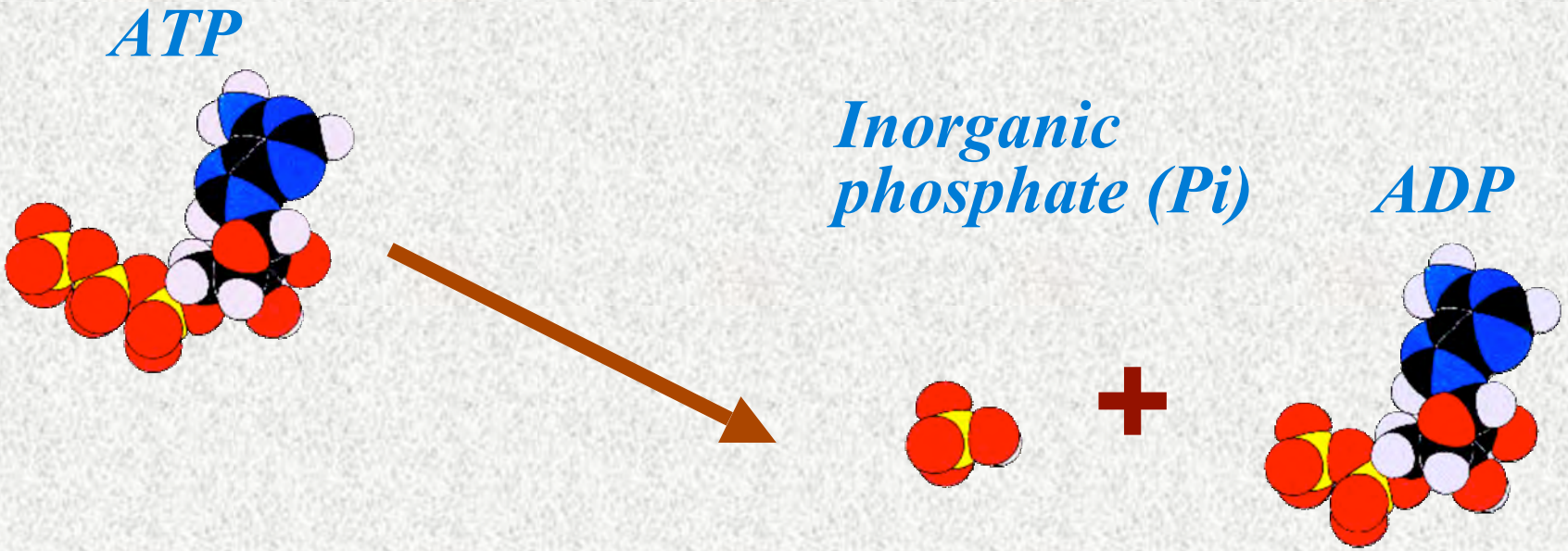
Literature quotation

M. Y. Ali, S. Uemura, S. Ishiwata

# *Watching How Myosin May Walk*



# *ATP (Adenosine Triphosphate): A Universal Currency of Energy in the Biological World*




*Free energy drop:*

$\Delta G = \Delta G_0 + k_B T \ln[ADP][Pi]/[ATP]$

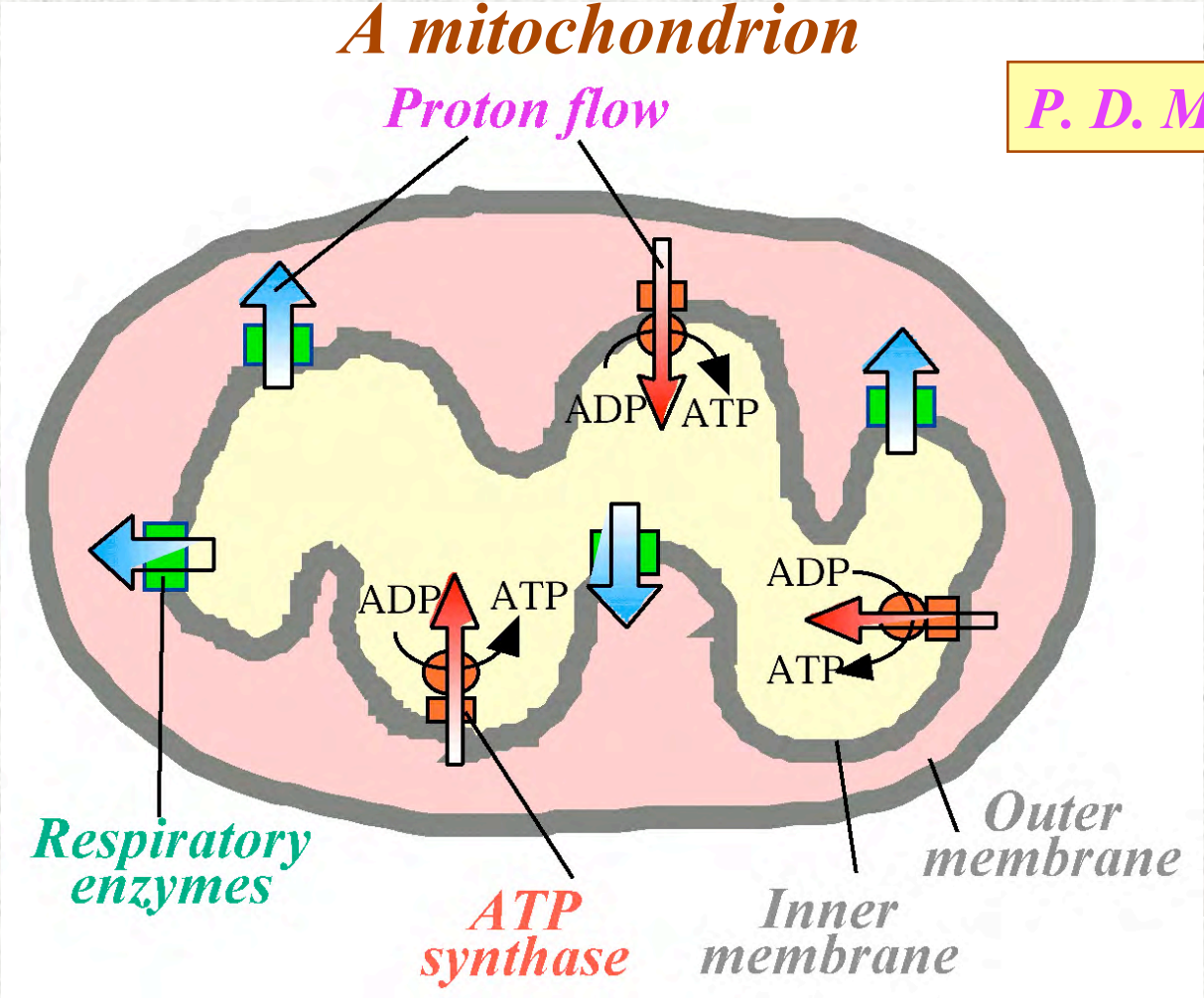
$\Delta G_0 = -50$ pN·nm (@pH 7)

$\Delta G = -(80\sim100)$ pN·nm *in cells*

$= -(20\sim25)\ k_B T$

# *Why do We Eat, and Why do We Breathe?*

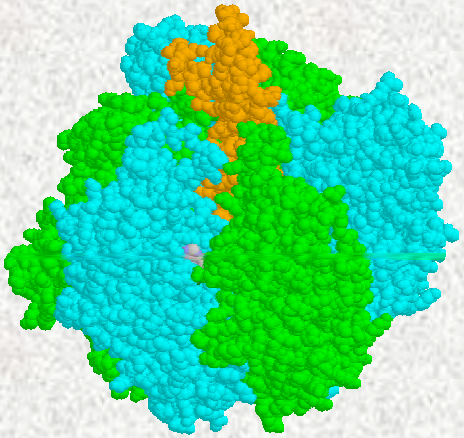
## *To obtain energy (= to synthesize ATP)*
## *by slowly burning the food we ingest with oxygen we inhale.*



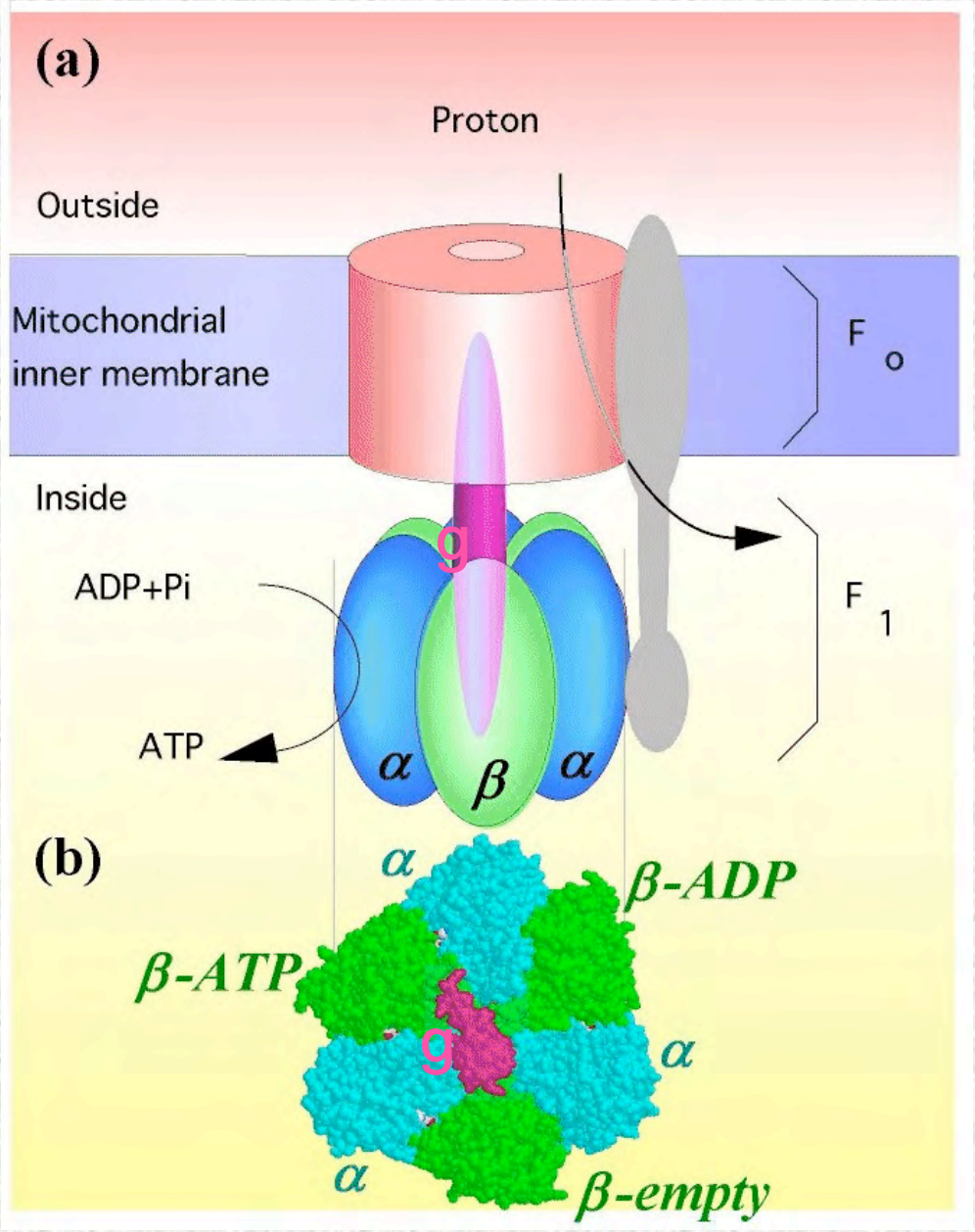
# ATP Synthase

***Proton-driven and ATP-driven motors connected by a common shaft (γ).***

***ATP synthesis/hydrolysis on three βs.***

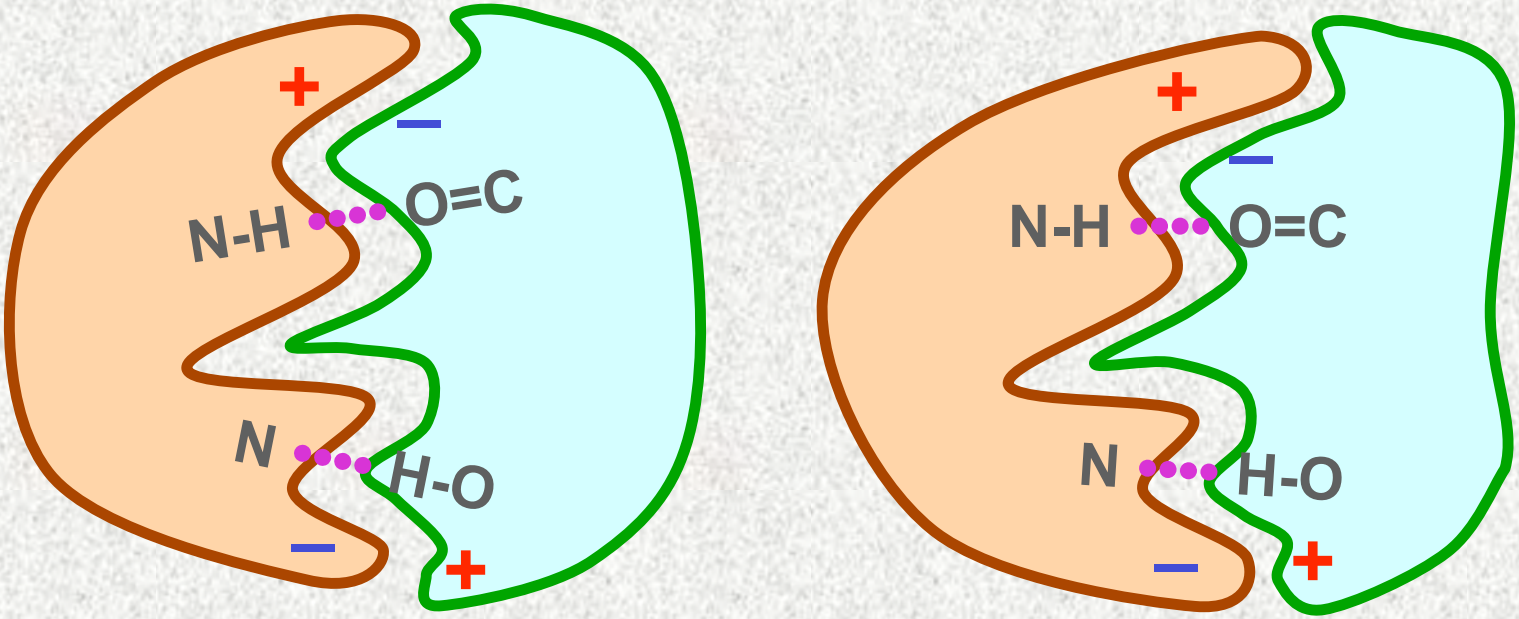


***Isolated $F_1$ only hydrolyzes ATP; hence it is called $F_1$-ATPase***

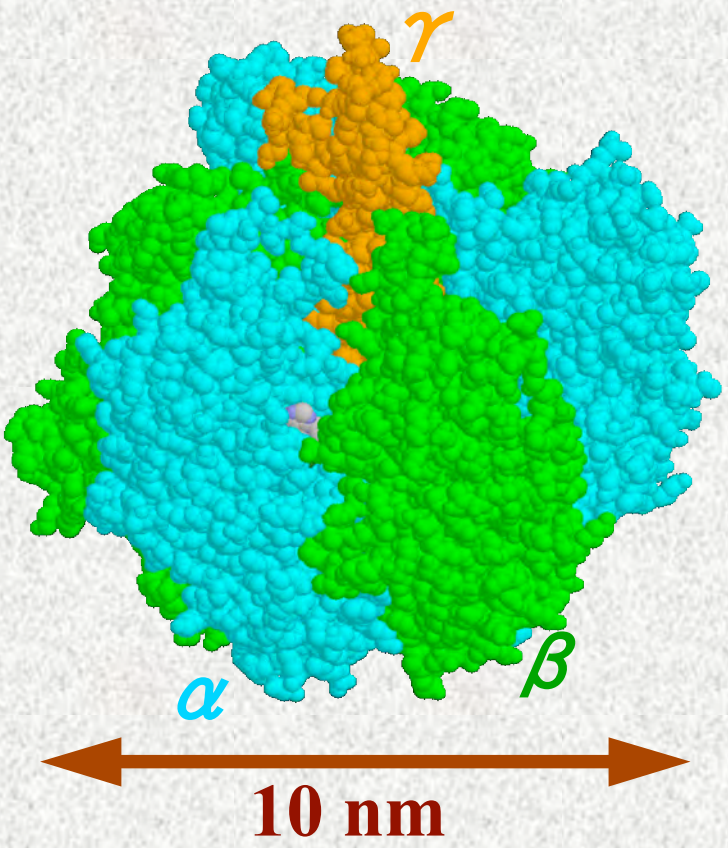


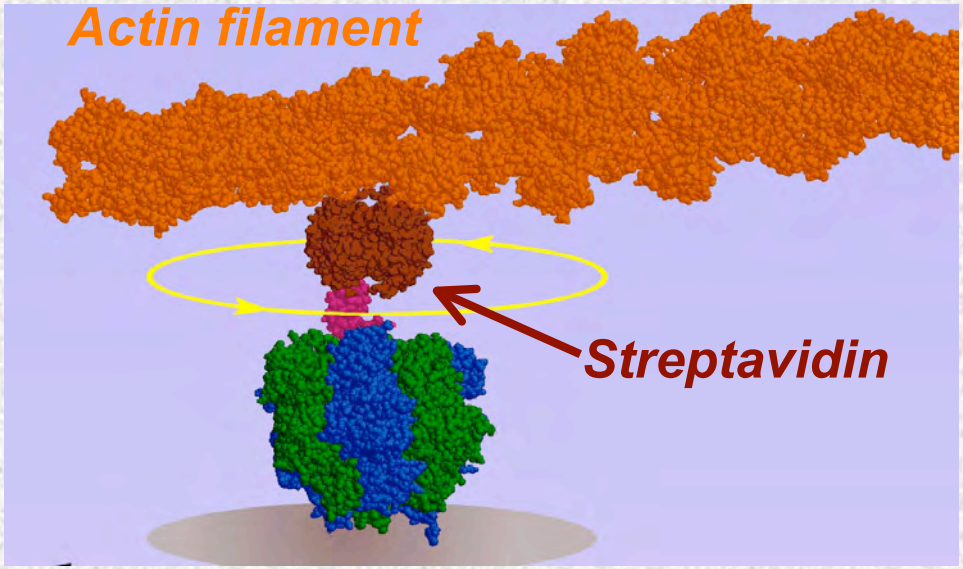

*D. Boyer* | *F. Oosawa & S. Hayashi* | *J. E. Walker & colleagues*

# *A Protein Molecule Is Made by Lock-and-Key Mechanisms*



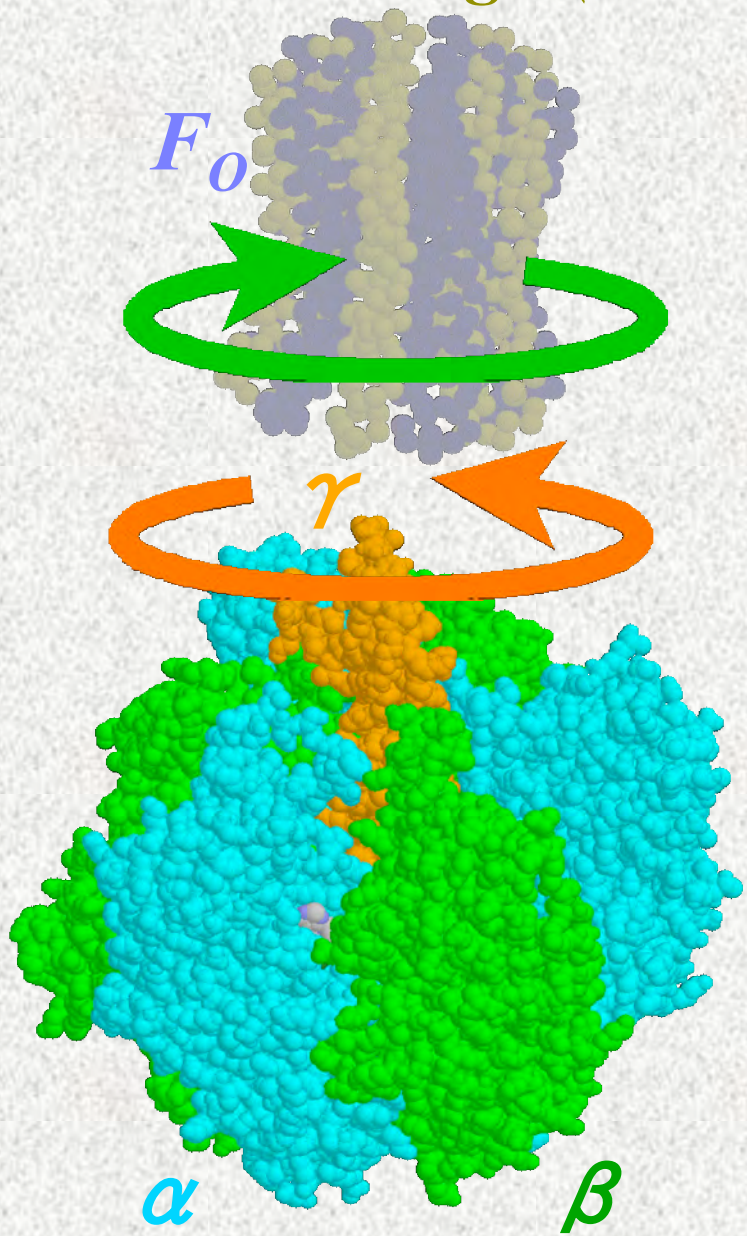
# *$F_1$-ATPase:*
# *A Rotary Motor Made of a Single Molecule*




*H. Noji, R. Yasuda & M. Yoshida*

# *Physiological Function of $F_1$ Is to Synthesize ATP through (Forced) Clockwise Rotation*




***Isolated $F_1$ :***

***CCW rotation powered by ATP hydrolysis in the three □ subunits***

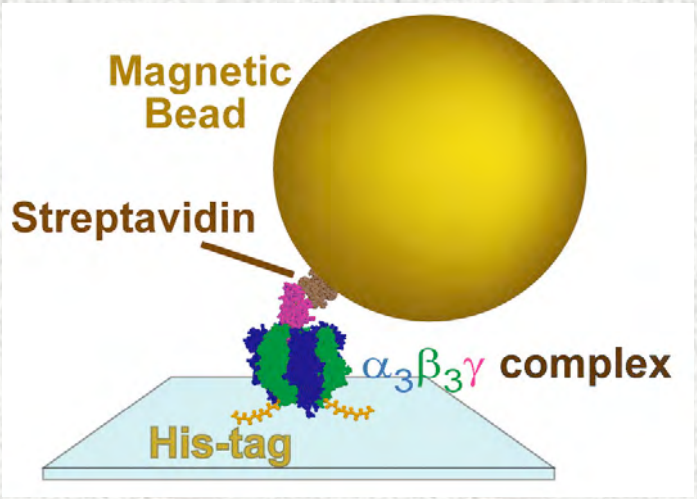
***$F_1$ in vivo:***

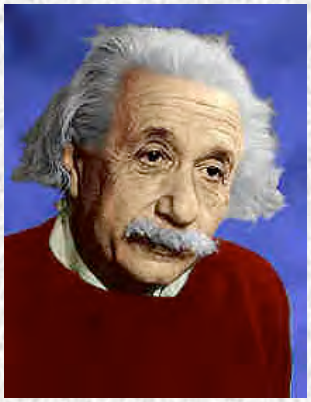
***CW rotation driven by proton flow through the $F_o$ motor***

↓

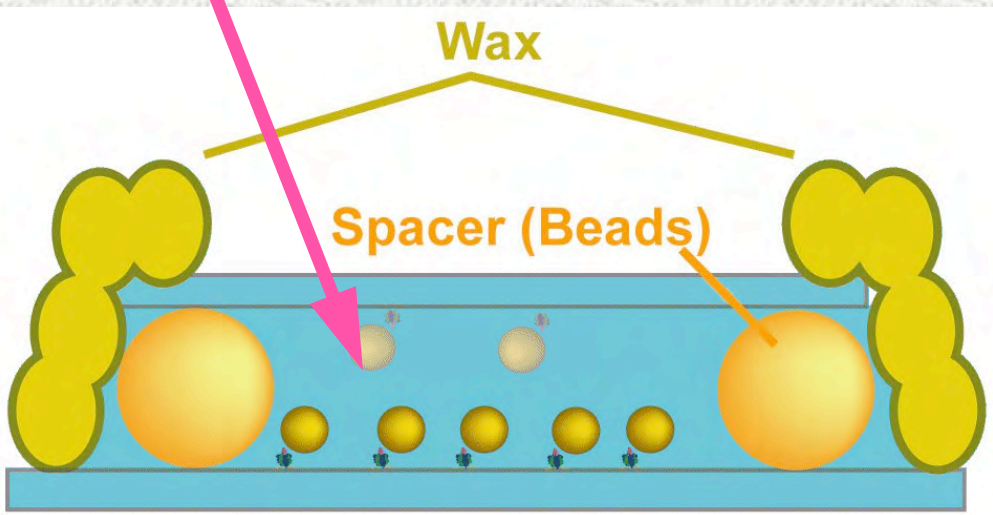
***ATP synthesis in the three □ subunits***

# *Attempt at Mechanical Synthesis of ATP*



*Luciferin/Luciferase*



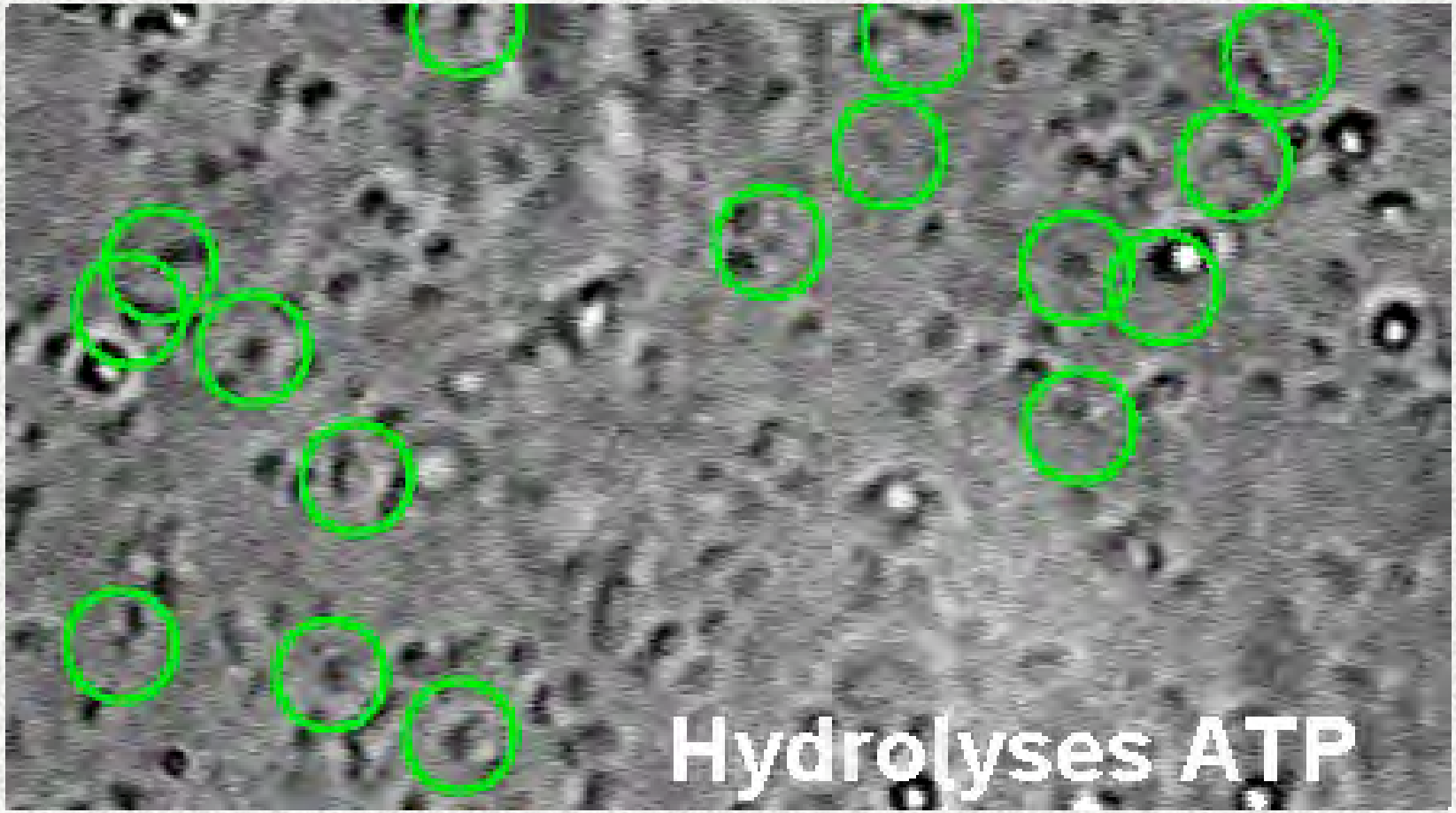




*A. Einstein*

*H. Itoh*

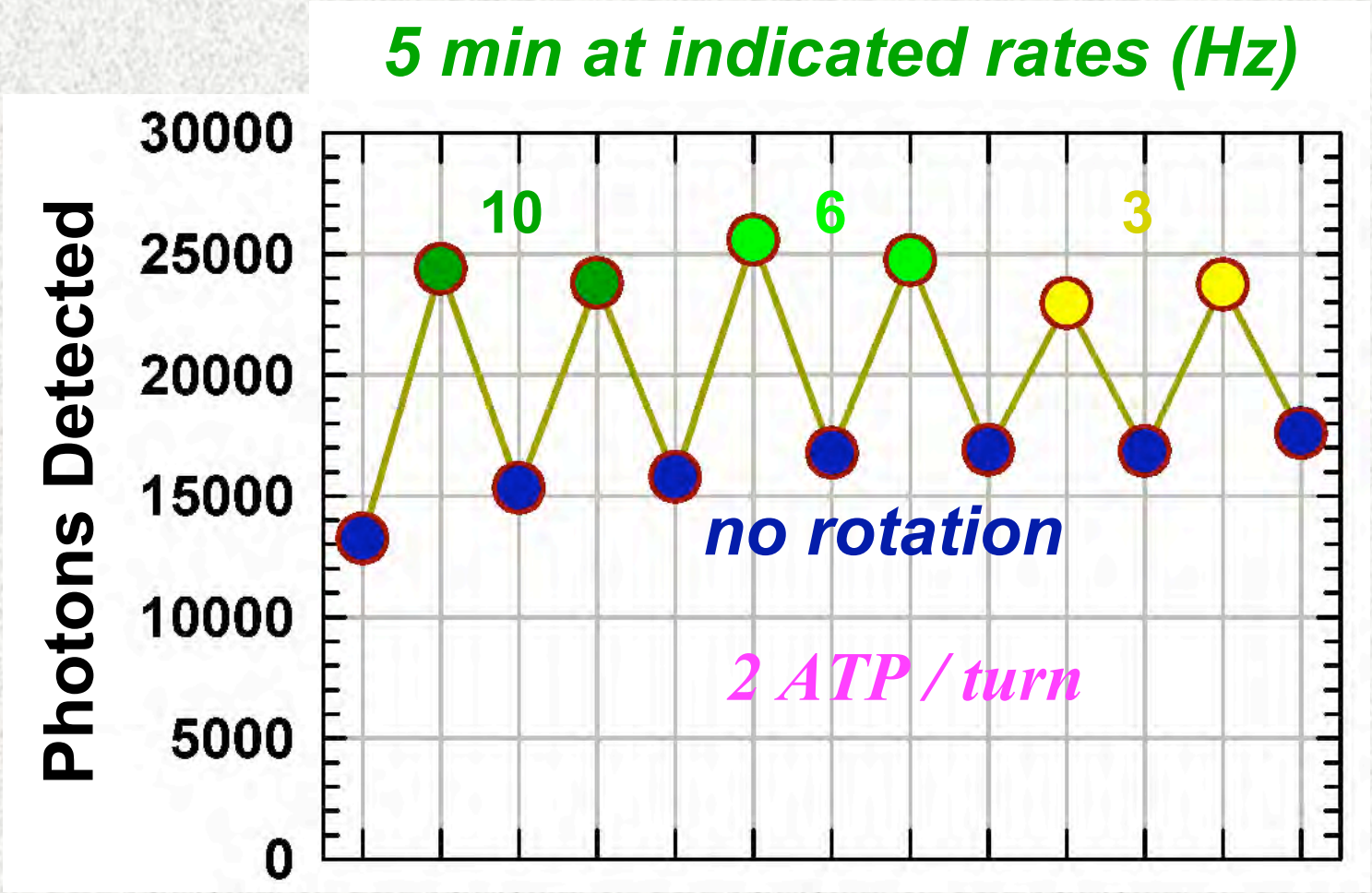
# *Manipulating Many Motors Simultaneously*




*Magnet rotated at 10 Hz*

*H. Itoh*

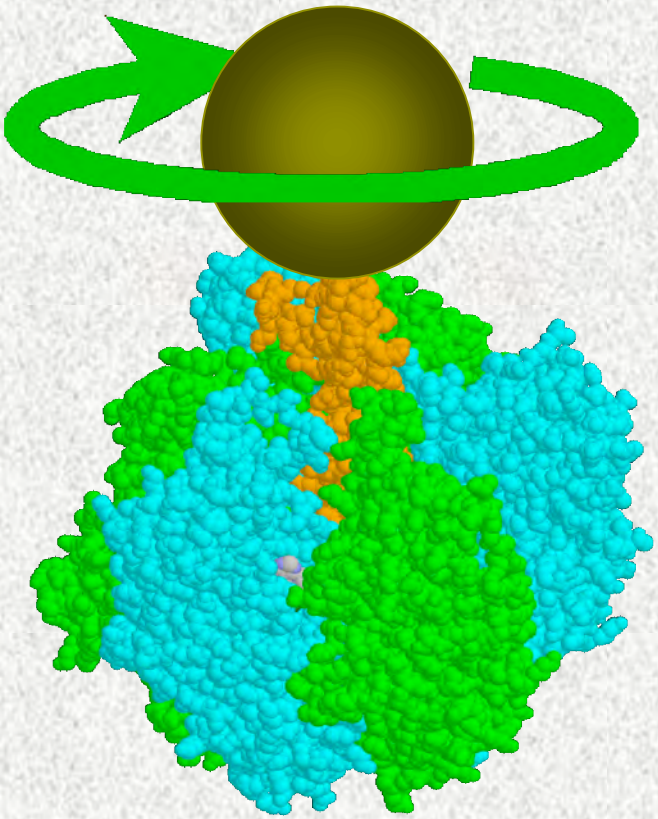
# *Reverse Rotation Led to ATP Synthesis!!*




*First chemical synthesis driven by force*

*Hiro Itoh @Hamamatsu Photonics Co., Ltd.*

# *Chemical Synthesis by Force (Torque)!*



***Free energy of ATP hydrolysis:***

$$\Delta G = \Delta G_0 + k_B T \ln [ADP][Pi]/[ATP]$$

$\Delta G_0 = -58$ pN·nm *(pH7.6)*

$\Delta G = -$ (80~100) pN·nm *(in cells)*

$= -$ (20~25) $k_B T$

$\Delta G \sim -$ 30 pN·nm *(this experiment)*

$\sim -$ 7 $k_B T$

[ADP]=200μM,[Pi]=10mM,[ATP]~1nM

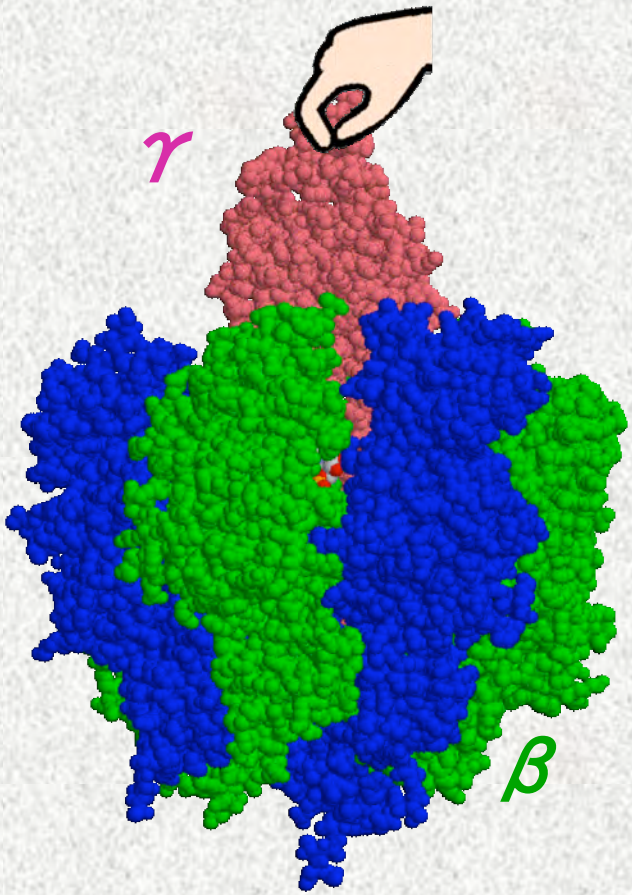
***Hiro Itoh @Hamamatsu Photonics Co., Ltd.***

# *A Force (Torque) Applied to One Point Can Reverse the Operation of $F_1$!!*

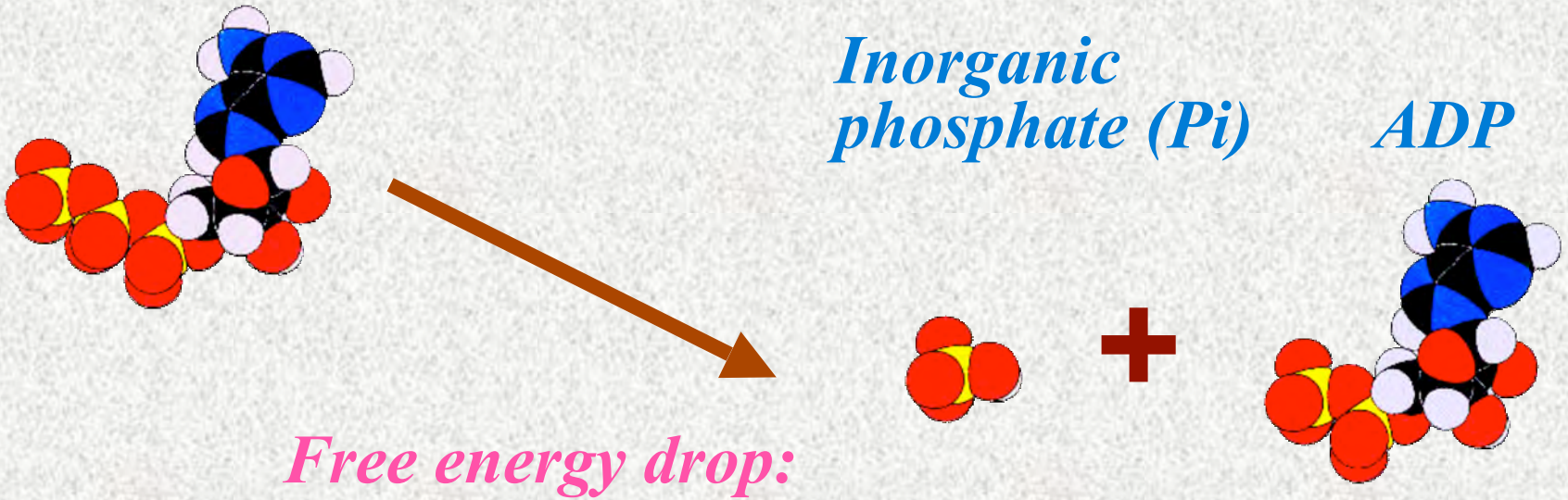
*□- Dictator Mechanism:*

*The □angle dictates how chemical reactions proceed in □'s.*

*In hydrolysis, three □'s cooperate through the □angle.*



# *How Can a Molecular Machine Convert Chemical Energy of ATP Hydrolysis into Mechanical Work?*




*Free energy drop:*

$\Delta G = \Delta G_0 + k_B T \ln [ADP][Pi]/[ATP]$

$\Delta G_0 = -50$ pN·nm (@pH 7)

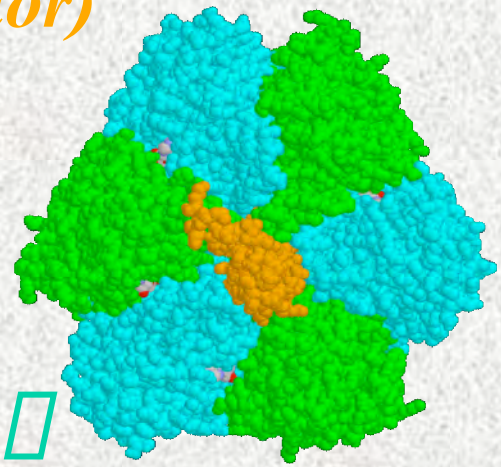
$\Delta G = -(80\sim100)$ pN·nm *in cells*

$= -(20\sim25)\ k_B T$

***Liberation of free energy == Reaction goes toward right***

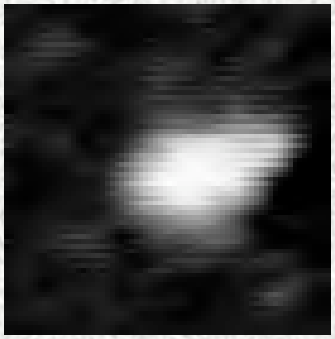
# *Stepwise Rotation of $F_1$*

*□(rotor)*



*□(catalytic)*

*Watch!!*



**[ATP] = 20 nM**

*R. Yasuda & H. Noji*