List of major papers and books and their overview

PAPER

1. **T. Yanagida:** Angles of nucleotides bound to cross-bridges in glycerinated muscle fiber at various concentrations ε-ATP, ε-ADP and ε-AMPPNP detected by polarized fluorescence. **J. Mol. Biol**., **146**, 539-560 (1981)
   For the first time, succeeded in capturing the movement of the head of the myosin molecule during muscle contraction by the polarized fluorescence method, and reviewed the widely accepted "Cross-bridge tilting theory". The research on the mechanism of muscle contraction returned to the starting point and became a big topic.

2. **T. Yanagida**, M. Nakase, K. Nishiyama and F. Oosawa: Direct observation of motion of single F-actin filaments in the presence of myosin. **Nature**. 307, 58-60 (1984)
   Succeeded in visualizing one actin filament in the solution with a fluorescence microscope. We have made it possible to visualize the sliding motion of muscles at the molecular level and observe the dynamics of actin filaments in cells. (1996 Nobel Prize in Chemistry Used for experiments to prove rotation model of ATP synthase F1F0

3. **T. Yanagida**, T. Arata and F. Oosawa: Sliding distance of actin filament induced by a myosin crossbridge during one ATP hydrolysis cycle. **Nature**. 316, 366-369 (1985)
   The sliding distance of actin filaments and the amount of ATP hydrolysis were measured in muscle. Proposed the loose coupling theory (Bias Brownian movement) in which the chemical reaction (ATPhydrolysis) and the movement (structure change) of myosin are not rigidly coupled in the manner of 1:1.

4. Y. Harada, A. Noguchi, A. Kishino and **T. Yanagida**: Sliding movement of single actin filaments on one-headed myosin filaments. **Nature**. 326, 805-808 (1987)
   Shown that even one head can move actin fragments using the in vitro movement assay system., although muscle myosin has a structure with two heads.

5. Kishino and **T. Yanagida**: Force measurements by micromanipulation of a single actin filament by glass needles. **Nature**. 334, 74-76 (1988)
   Succeeded in direct manipulation of one actin filament with a microneedle and measuring the displacement and force generated by the actin-myosin interaction in vitro.

6. Ishijima, T. Doi, K. Sakurada and **T. Yanagida**: Sub-piconewton force fluctuations of actomyosin in vitro. **Nature (Article)**. 352, 301-306 (1991)
   Succeeded in measuring the displacement and force of muscle myosin with nanometer and pico-Newton accuracy, respectively. For the first time, it was shown directly that a force per one myosin molecule is 2 pN (2 g (heavy)/10 billion). Development of nano measurement operation technology

7. T. Funatsu, Y. Harada, M. Tokunaga, K. Saito and **T. Yanagida**: Imaging of single fluorescent molecules and individual ATP turnovers by single myosin molecules in aqueous solution. **Nature**. 374, 555-559 (1995)
   Succeeded in imaging a single molecule in an aqueous solution. This has opened the way of biological use of single molecule technique, allowing direct visualization of molecular movement, structural changes, enzyme reactions and signaling in living cells, DNA sequence for next-generation ultrafast DNA single molecule sequencer, etc. It laid the foundation for the field of "Single Molecule Biophysics". (Became the basis of the 2014 Nobel Prize in Chemistry Super Resolution Microscope)

8. R. D. Vale, T. Funatsu, D. W. Pierce, L. Romberg, Y. Harada and **T. Yanagida**: Direct observation of single kinesin molecules moving along. **Nature**. 380, 451-453 (1996)

   The first report to directly observe the processive movement of single molecular motor, kinesin molecules. This method has opened a new era of the study of transport-type molecular motors, such as kinesin, dynein, non-muscle myosin.

9. C. Shingyoji, H. Higuchi, M. Yoshimura, E. Katayama and **T. Yanagida:** Dynein arms are oscillating force generators. **Nature**. 393, 711-714 (1998)

   The displacement and force of one dynein molecule, a molecular motor responsible for the waving movement of sperm flagella, were measured.

10. Ishijima, H. Kojima, T. Funatsu, M. Tokunaga, H. Higuchi, H. Tanaka and **T. Yanagida**: Simultaneous observation of individual ATPase and mechanical events by a single myosin molecule during interaction with actin. **Cell**. 92, 161-171 (1998)

    Invited paper from Cell magazine. This first experiment in which the mechanical reaction (displacement, force) and the chemical reaction (ATPase reaction cycle) of one muscle myosin molecule were simultaneously measured in real time.

11. H. Yokota, K. Saito and **T. Yanagida**: Single molecule imaging of fluorescently labeled proteins on metal by surface plasmons in aqueous solution. **Phys. Rev. Letter.** 80(20), 4606-4609 (1998)

    Succeeded in imaging one molecule of fluorescently labeled protein in an aqueous solution with plasmons generated on the metal surface. A symbolic study of interdisciplinary research that published a paper in the same year (1998) in the top journals of physics and biology (Cell).

12. K. Kitamura, M. Tokunaga, A. H. Iwane and **T. Yanagida**: A single myosin head moves along an actin filament with regular steps of ~5.3nm. N**ature (Article)**. 397, 129-134 (1999)

    Succeeded in measuring the movement of one head of the muscle myosin molecule with millisecond and nm accuracy. Directly proved that myosin is moving (biased in one direction) by making good use of Brownian motion (thermal fluctuation) (biased Brownian motion).

13. Y. Sambongi , Y. Iko, M. Tanabe, H. Omote, A. Iwamoto-Kihara, I. Ueda, **T. Yanagida**, Y. Wada and M. Futai: Mechanical Rotation of the c Subunit Oligomer in the ATP Synthase (FoF1): Direct Observation. **Science.** 286, 1722-1724 (1999)

    Using a single-molecule imaging method, showed that rotation occurs in a complex with F0, which drives the rotation of ATP synthase F1.

14. Y. Harada, T. Funatsu, K. Murakami, Y. Nonoyama, A. Ishihama, T. Yanagida, Single molecule imaging of RNA polymerase-DNA interactions in real time. **Biophys. J.,** 76, 709-715 (1999)

    The first research that has been carried out recently on single-molecule imaging of DNA-protein interactions. Found that RNA polymerase searches the promoter position along the DNA by thermal diffusion.

15. Y. Sako, S. Minoguchi and **T. Yanagida**: Single-molecule imaging of EGFR signaling on the surface of living cells. **Nature Cell Biology** 2, 168-172 (2000)

    The first paper to directly observe the signal transduction process in living cells by single molecule imaging method. Direct observation of how EGF binds to the EGF receptor in living cells and how these complexes form dimers and transmit signals downstream

16. M. Ueda, Y. Sako, T. Tanaka, P. Devreotes and **T. Yanagida**: Single molecule analysis of chemotactic signaling in *Dictyostelium* cells. **Science** 294, 864-867 (2001)

Single-molecule imaging method was used to observe the cAMP signal transduction process related to the chemotaxis of amoebar in real time, and showed how amoeber detects minute cAMP concentration difference in a noisy environment.

17. M. Nishiyama, E. Muto, Y. Inoue, T. Yanagida, H. Higuchi, Substeps within the 8-nm step of the ATPase cycle of single kinesin molecules. **Nature Cell Biology**, 3, 425-428 (2001)
    Shown that there is a 4 nm substructure in the 8 nm step of kinesin.

18. H. Tanaka, K. Homma, A. H. Iwane, E. Katayama, R. Ikebe, J. Saito, **T. Yanagida** and M. Ikebe: The motor domain determines the large step of myosin-V. **Nature** 415, 192-195 (2002)
    Shown that the movement occurs even if the structure (lever arm) thought to cause the movement of myosin is removed, demonstrating that not only structural changes but also Brownian movements were working

19. M. Nishiyama, H. Higuchi and **T. Yanagida**: Chemomechanical coupling of the ATPase cycle to the forward and backward movements of single kinesin molecules. **Nature Cell Biology**. 4, 790-797 (2002).
    Proof that molecular motor, kinesin, uses Brownian motion to repeat 8nm steps back and forth on microtubules, and proceed with fluctuation

20. T. Murata, N. Matsui, S. Miyauchi, Y. Kakita, T. Yanagida, _Discrete stochastic process underlying perceptual rivalry. **Neuroreport**, 14, 1347-1352 (2003)
    In the process of perception of ambiguous figures, it was shown that the transition of appearance does not occur at once but through discrete states.

21. J. Kozuka, H. Yokota, Y. Arai, Y. Ishii, **T. Yanagida**, _Dynamic polymorphism of single actin molecules in the actin filament, **Nature Chem. Biol.,** 2, 83-86 (2006)
    By single molecule fluorescence energy transfer (FRET) showed that actin transits between two states. A noteworthy paper directly showing that proteins do not exist stably in one state but thermally fluctuate in multiple states (dynamic polymorphism)

22. M. Nishikawa, H. Takagi, T. Shibata, A. H. Iwane, **T. Yanagida**, _Fluctuation Analysis of Mechanochemical Coupling Depending on the Type of Biomolecular Motors, **Phys. Rev. Lett.,** 101(12), 128103 (2)
    Experiments and theoretical analysis showed that myosin uses Brownian motion to control the motion mode (loose coupling degree) depending on the load.

23. M. Iwaki, A. H. Iwane, T. Shimokawa, R. Cooke, **T. Yanagida**. Brownian search-and-catch mechanism for myosin-VI steps. **Nature Chem. Biol**., 5(6), 403-405 (2009)
    The myosin head acts as a strain sensor, which binds more strongly when interacting with actin in the forward direction, and dissociates in the opposite direction, which biases Brownian motion forward with an asymmetric bond

24. T. Fujii, A. H. Iwane, **T. Yanagida,** K. Namba. Direct visualization of secondary structures of F-actin by electron cryomicroscopy. **Nature** 467(7316), 724-8 (2010)
    Observation of the secondary structure of actin filaments with a cryo-electron microscope

25. S. Nishikawa, I. Arimoto, K. Ikezaki, M. Sugawa, H. Ueno, T. Komori, A. H Iwane, **T. Yanagida.** Switch between large hand-over-hand and small inchworm-like steps in myosin VI. **Cell** 142(6),879-88 (2010)

Developed single molecule nano-imaging method to see the movement of molecules at ultra high speed of 30 μsec. It was discovered that non-muscle myosin VI switches the motion pattern from hand-over hand to inchworm-like according to the load

26. K. Fujita, M. Iwaki, A. H. Iwane, L. Marcucci, **T. Yanagida** "Switching of myosin-V motion between the lever-arm swing and Brownian search-and-catch", **Nature Commun**., 3, 956 (2012)
Measured the work of myosin V generated by structural changes (lever arm swing) and bias Brownian motion. It was found that the structural change was 30% and the bias Brownian motion was 70%.

27. L.Marcucci, T. Yanagida , "From Single Molecule Fluctuations to Muscle Contraction: A Brownian Model of A.F. Huxley's Hypotheses", **PLoS One**.7, e40042,(2012)
Proved by computer simulation that the Bias Brownian motion model successfully explains the basic motion characteristics of muscles, the relationship between speed and force, energy consumption, and power, and the flexible response to external mechanical stimuli (length and load changes).

28. Murata T, Hamada T, Shimokawa T, Tanifuji M, Yanagida T. "Stochastic process underlying emergent recognition of visual objects hidden in degraded images.", **PLoS One**, 9(12): e115658 (2014)
The inspiration of a hidden picture is caused by the spontaneous emergence of a few discrete elements contained in the hidden picture

29. K. Fujita , M. Iwaki , T. **Yanagida ,**"Transcriptional bursting is intrinsically caused by interplay between RNA polymerases on DNA.", **Nature Commun.**, 7, 13788 (2016)
Single molecule imaging of the interaction between DNA and RNA polymerase and the transcriptional reaction showed directly that the transcription fluctuates greatly instead of uniformly. Suggested that cell diversity is caused by spontaneous fluctuations in transcription

30. M. Iwaki, S. Wickham , K. Ikezaki, T. **Yanagida**, W. Shih, "A programmable DNA origami nanospring that reveals force-induced adjacent binding of myosin VI heads.", **Nature Commun.**, 7, 13715 (2016)
We developed a method to make nano-sized springs using DNA origami and measure the movement and force of motor molecules simultaneously.

31. L. Marcucci , T. Washio , **T.Yanagida** , "Including Thermal Fluctuations in Actomyosin Stable States Increases the Predicted Force per Motor and Macroscopic Efficiency in Muscle Modelling.", **PLoS Comput Biol.** 12, e1005083, (2016)
Computer simulation showed that Bias Brownian motion mechanism successfully explains the flexible and highly efficient mechanical properties of heart beat

32. K. Fujita , M. Ohmachi , K. Ikezaki , **T. Yanagida** , M. Iwaki, Direct visualization of human myosin II force generation using DNA origami-based thick filaments. **Commun. Biol.**, 2(1):437(2019)
First direct evidence that muscle contraction is generated by both of bias Brownian movement and structural change (lever arm swing).

BOOK

33. **T. Yanagida**, K. Kitamura, H. Tanaka, A. H. Iwane and S. Esaki: Single molecule analysis of the actomyosin motor. **Current Opinion in Cell Biology**. 12, 20-25 (2000)

34. Y. Ishii and **T. Yanagida**: Single Molecule Detection in Life Science. **Single Molecules.** 1, 5-14 (2000)

35. Y. Sako and **T.Yanagida,** (2003) :Single-molecule visualization in cell biology. **Nature Rev. Mol. Cell Biol**. 4, s1-6 (2003)

36. Ishijima and **T. Yanagida**: Single Molecule Nano-Bioscience. **Trends in Biochemical Sciences**. 26, 438-444(2001) .

37. Y. Ishii, Kitamura K, Tanaka H, **Yanagida T**: Molecular motors and s ingle-molecule enzymology. **Methods in Enzymol**. 361:228-245 (2003).

38. **T. Yanagida** and Y. Ishii (ed) Single Molecule Dynamics in Life Science **Book (Wiley-VCH)** (2009)

39. Peter Karagiannis, Yoshiharu Ishii, **Toshio Yanagida** "Myosin Uses Randomness to Behave Predictably" **Chemical Review (ACS)** 114:3318-3334 (2014)

40. **Yanagida T**, Ishii Y. "Single molecule detection, thermal fluctuation and life.", **Proc Jpn Acad Ser B Phys Biol Sci.** 10; 93(2): 51–63 (2017)

Major invited lectures（2002～）

1. **Yanagida ,T**. (June,2002), Single Molecule Nano-Bioscience, **Plenary Lecture**, 5th International Symposium on Functionalπ-electron Systems, Germany

2. **Yanagida, T**.(June,2002), The acto-myosin motor: theoretical and experimental finding, **Plenary Lecture**, BIOCOMP2002, Italy

3. **Yanagida, T**.(August,2002), How do biological motors work?, **Plenary Lectur**e, IVWorld Congress on Biomechanics, Canada

4. **Yanagida, T**.(June,2003), Single Molecule Nano-Bioscience, **Plenary Lecture**, TRANSDUCERS'03, USA

5. **Yanagida, T**.(August,2003), Single Molecule Nano-Bioscience, **Plenary Lecture**, 11th European Congress on Biotechnology, Switzerland

6. **Yanagida, T**.(September,2004), Single Molecule Nano-Bioscience, **Plenary Lecture**, Micro TAS (Total Analysis Systems) 2004 Conference, Sweden

7. **Yanagida, T**.(June,2008), A strain-dependent search and catch mechanism to describe direction movement in myosin, **Invited Speaker**, Novel Symposium on single Molecule Spectroscopy in Chemistry, Physics and Biology, Sweden

8. **Yanagida, T**.(September,2008), Single-Molecule Nanobiology, **Plenary Lecture**, XIV International Symposium on Small Particles and Inorganic Clusters, Spain

9. **Yanagida, T**.(September,2009), Single Molecule Nano-biology: Fluctuation and Function of Life, **Plenar**y **Lecture**, 15th Anniversary International Workshop on "Single Molecule Spectroscopy and Ultra Sensitive Analysis in the Life Sciences", Germany

10. **Yanagida, T**.(May,2010), Single Molecule Imaging and Nanometry: Fluctuation and Function of Life, **Plenary Lecture**, Symposium on Frontiers of Biophysics, Korea

11. **Yanagida, T**.(July,2010), Single Molecule Nanobioscience: Fluctuation and Function of Life, **Plenary Lecture**, International Symposium on Advancing the Chemical Sciences, Hungary

12. **Yanagida, T**. (June,2011), Single Molecule imaging and nanometry :Fluctuation and the Function of life, **Plenary Lecture**, The 85th ACS Colloid and Surface Science Symposium, Canada

13. **Yanagida, T**.(July,2011), Single molecule nanoscale imaging: Fluctuation and the function of life, **Plenary Lecture**, Engineering of Chemical Complexity, Germany

14. **Yanagida, T**.(July,2012), Single molecule in vitro and vivo, **Keynote Lecture**, Gordon Research Conferences -Single Molecule Approaches to Biology, USA

15. **Yanagida, T**.(May,2013), What is a biological principle to control complex systems with extremely low energy consumption and high robustness?, **Plenary Lecture**, 8th Symposium of Asian Biophysics Association, Korea

16. **Yanagida, T**.(Octorber,2014), Single Molecule Imaging and Nanometry: Fluctuation and Function of Life, **Plenary Lecture**, 2014 IEEE Photonics Conference, USA

17. **Yanagida, T**.(July,2014), **Discussion leader & Conference Vice Chairman**, Gordon Research Conference /Seminar, Single Molecule Approaches to Biology, Italy

18. **Yanagida, T**.(May,2015), Role of fluctuations for driving bio-molecular machines, **Invited Speaker**, Novel Workshop Molecules in life science research, Sweden

19. **Yanagida, T**.(July,2016), **Conference Chair**, Gordon research conference, Hong Kong

20. **Yanagida, T**.(March,2018), Role of Fluctuations for driving bio-machines, **Keynote Lecture**, 2nd Plenary ARBRE-MOBIEU meeting, Poland

21. **Yanagida, T**.(September,2019), Single molecule study on how muscle works, **Keynote Lecture**, Single Molecule and Superresolution Microscopy Workshop, Germany

22. **Yanagida, T**.(September,2019), Single Molecule Nano-Science: Noise and Function of Life, **Keynote Lecture**, 49th ESSCIRC/45th ESSCERC joint conference, Poland

23. **Yanagida, T**.(August, 2020), Single Molecule Nano-Science: Role of fluctuation of biological molecular machine, **Keynote Lecture,** SPIE (Optics ＋ Photonics) Conference, USA