CHAPTER 1

An introduction

Jian Zhong[1,2], Hongshun Yang[3] and Claire Gaiani[4,5]
[1]Xinhua Hospital, Shanghai Institute for Pediatric Research, Shanghai Key Laboratory of Pediatric Gastroenterology and Nutrition, Shanghai Jiao Tong University School of Medicine, Shanghai, P. R. China
[2]National R&D Branch Center for Freshwater Aquatic Products Processing Technology (Shanghai), Integrated Scientific Research Base on Comprehensive Utilization Technology for By-Products of Aquatic Product Processing, Ministry of Agriculture and Rural Affairs of the People's Republic of China, Shanghai Engineering Research Center of Aquatic-Product Processing and Preservation, College of Food Science & Technology, Shanghai Ocean University, Shanghai, P. R. China
[3]Department of Food Science and Technology, National University of Singapore, Singapore, Singapore
[4]LIBio (Laboratoire d'Ingénierie des Biomolécules), Université de Lorraine, Vandoeuvre-lès-Nancy Cedex, France
[5]Ministry of Higher Education, Research and Innovation, IUF (Institut Universitaire de France), Paris, France

Atomic force microscope (AFM) was developed in 1985 by Binnig and Quate at IBM San Jose Research Laboratory, Stanford and Gerber (Binnig, Quate, & Gerber, 1986). It is a member of the family of scanning probe microscopes, which analyze the surface characteristics based on a variety of tip—sample interactions. Generally, AFM uses a sharp nanoscale tip to sense the surface characteristics (topographical, mechanical, electrical, and magnetic information) or to manipulate surface substances of a sample of interest at nanoscale (Collins, Liu, Ovchinnikova, & Proksch, 2019; Dufrêne et al., 2017; Gross et al., 2018; Krieg et al., 2019; Pavliček & Gross, 2017). AFM has been widely applied in the field of materials, energy, biology, chemistry, physics, medicine, etc. (Bellon, 2020; Chen & Xu, 2020; Efremov, Okajima, & Raman, 2020; Kiio & Park, 2020; Li, Liu, Yuan, & Huang, 2021; Li, Xi, Wang, & Liu, 2021; Liu & Vancso, 2020; Nandi & Ainavarapu, 2021; Si et al., 2020; Yadavalli & Ehrhardt, 2021). Moreover, with the boom in nanotechnology, AFM will attract more and more attention in the scientific and engineering fields due to its advantages such as multifunction and high resolution.

In the field of biology, AFM has been widely applied to image biomolecule structures (Kuchuk & Sivan, 2018; Main et al., 2021) and the morphologies of biological aggregates (Ma et al., 2013; Nievergelt, Banterle, Andany, Gönczy, & Fantner, 2018; Zhong & He, 2012) to analyze the effects of processing conditions on biological substances (Zhong et al., 2015; Zhong, Ma, et al., 2014), to observe biological dynamic process in liquid (Uchihashi & Scheuring, 2018; Zhong et al., 2007, 2009;

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Zhong, 2011), to measure the force of biomolecular interaction (Martines et al., 2012; Sapra, Spoerri, Engel, Alsteens, & Müller, 2019), to manipulate biomolecules (Fukui et al., 2018; Zhao, Liu, & Gao, 2018), to analyze cell nanomechnics (Kilpatrick, Revenko, & Rodriguez, 2015; Zhou, Zhang, Tang, Yu, & Galluzzi, 2021), and to mechanically fabricate 3D bionanostructures (Zhong et al., 2013; Zhong, Sun, & He, 2014). Thus, AFM has proven to be a powerful technique for the studies of biological processes and biological nanomaterials.

AFM has been successfully and broadly explored in the field of food science and technology (Gunning & Morris, 2018; Jones, 2016; Obeid & Guyomarc'h, 2020; Wen, Xu, Liu, Corke, & Sui, 2020; Zhong, Finglas, Wang, & Wang, 2019). Foods and their production processes can be considered as typical biological nanomaterials and biological processes. With more research going into food science, the use of AFM has been expanded to analyzing different food samples ranging from the smallest biomolecules such as food proteins (Shi, He, Ding, Wang, & Zhong, 2019a,b), food carbohydrates (Wang & Nie, 2019), and food toxins (Alexander Reese & Xu, 2019) to food-related microorganisms and pathogens (Kuda, Shibata, Takahashi, & Kimura, 2015; Liu & Yang, 2019) and food cell wall structures (Posé et al., 2019) to all the way up to food materials (Cárdenas-Pérez et al., 2019), food packaging materials (Marinello, La Storia, Mauriello, & Passeri, 2019), and food emulsion (Ho, Abik, & Mikkonen, 2022). Hence, AFM has also proven to be a powerful technique for the studies of food production processes and food analyses.

As an increasingly popular nanotechnological tool, AFM has many advantages for food research. (1) AFM has many primary (e.g., contact, noncontact, and tapping) and secondary (e.g., phase imaging and deflection) imaging modes for sample surface analysis (Zhong & Yan, 2016), which are useful for analyzing many properties of food substances. (2) Compared with optical imaging techniques (e.g., general optical microscopy and fluorescence microscopy), AFM has higher spatial resolution (Z direction: subnanometer scale; X−Y direction: nanometer scale), and so the substructures of food substances can be observed (Fukuma, 2020). (3) Compared with electron imaging techniques (e.g., scanning electron microscopy and transmission electron microscopy), the sample preparation of AFM does not require complicated preparations or chemical modifications, which might result in possible artifacts. (4) Compared with other imaging techniques, AFM images the samples in a true three-dimensional surface profile way, which can be applied to measure the height of the food substances and the surface roughness of food tissues and materials. (5) The samples can be analyzed in atmosphere and liquid environments (no need of dehydration like other electron microscopy imaging techniques), which is useful for analyzing the behaviors of food substances in simulated working and physiological conditions. (6) The samples can be analyzed in some special environments (e.g., vacuum, cryo, and controlled humidity and temperature), which is useful for analyzing the behaviors of food substances in simulated food processing and storage conditions (Zhao, Kristi, & Ye, 2021). (7) The samples can be in situ observed by normal and high-speed AFM, which is useful for obtaining a nanoscale topographic "movie" of the nanomaterial-related food processing and preservation processes. (8) AFM can be combined with other techniques such as optical microscopy (Gómez-Varela et al., 2020; Miranda et al., 2021), infrared spectroscopy (Dazzi & Prater, 2017), Raman (Fernandes, Mareau, & Gonon, 2018; Prats-Mateu & Gierlinger, 2017), mass spectrometry (Thiruvallur Eachambadi et al., 2021), and X-ray technique (Slobodskyy et al., 2015) to simultaneously analyze the different samples of interests. (9) AFM can be applied to measure the force—distance curves when AFM tip approaches to and retracts from the sample surfaces, which is useful for analyzing single-molecule interaction and nanomechanical properties of food materials (Alexander Reese & Xu, 2019; Cárdenas-Pérez et al., 2019). (10) AFM can be used as a mechanical nanomachining tool to manipulate and fabricate biological samples (Pavliček & Gross, 2017; Zhao et al., 2018), which is useful for analyze the behaviors of food substances during mechanical processing. Due to these specific advantages, AFM will undoubtedly attract the attention of food scientists and engineers in the future.

It should be noted that the application of AFM for food research has several disadvantages: (1) The poor temporal resolution (in minute range) of normal AFM greatly limits their application in biological research. To overcome these limitations, scientists have tried to develop high-speed AFM (Feuillie et al., 2020; Jiao, Cannon, Lin, Gladfelter, & Scheuring, 2020) and large-scan area high-speed AFM (Marchesi et al., 2021), which increases the temporal resolution to milliseconds. In addition, commercial high-speed AFMs have been developed recently. (2) Sample height compression effect may occur because of the elastic deformation of biological samples (Zhong & Yan, 2016) and the measured heights are lower than the real heights of biological samples. (3) Tip-broadening effect may occur because of the tip–sample convolution (Yuan, Liang, Liang, Pang, & Jia, 2021), and the measured widths are larger than the real widths of biological samples. (4) Under liquid, the possible electrostatic repulsion between AFM tip and the sample surface may affect the AFM tip approach and retract process, which, in turn, may affect the measurement of the real morphology of biological samples (Müller & Engel, 1997; Zhong et al., 2010). We should be careful in eliminating the possible electrostatic repulsion by optimizing the liquid conditions such as the ionic strength. (5) It results in many possible image artifacts during the AFM operation process, which should be minimized to obtain reliable data.

We suggest food scientists and engineers to master the basic knowledge of AFM prior to using it. AFM is a very professional instrument and the operators should be very careful during the AFM work process. Thorough learning and training are imperative for new users. There is a steep learning curve for new users who hope to master AFM application. There are several books published on AFM application for biologists such as *Atomic force microscopy in cell biology* (Wilson, Matsudaira, Jena, & Horber, 2002), *Atomic force microscopy for biologists* (Morris, Kirby, & Gunning, 2009), *Atomic force microscopy in biomedical research: methods and protocols (methods in molecular biology)* (Braga & Ricci, 2011), *Atomic force microscopy in nanobiology* (Takeyasu, 2014), *Cellular analysis by atomic force microscopy* (Lekka, 2017), and *Atomic force microscopy in molecular and cell biology* (Cai, 2018). The interested readers could read these books for more detail. However, until now, no such book has systematically described the application of AFM for food research.

The purpose of this book is to introduce the reader to the fundamentals of application of AFM for food research. The book consists of three parts: Part I: Introduction of AFM for food research (Chapter 1); Part II: Fundamentals of AFM for food research (Chapters 2–3); and Part III: Application of AFM for food research (Chapters 4–10). Chapter 1 mainly discusses why this book is indispensable for the food community. Chapter 2 introduces the basic principles of AFM. Chapter 3 describes the operation procedure of AFM. Chapters 4–8 presente the application of AFM for food proteins, food polysaccharides, food microorganisms, food foams and emulsions, and food powders and contact materials, respectively. Chapter 9 introduces AFM nanomechanics for food research. Chapter 10 discusses current and potential integration of AFM with other techniques for food science. This book does not discuss AFM application for food cells and tissues because very few studies have been published on these two topics so far. The interested readers could read the books mentioned in the above paragraph or reviews on AFM application for biological cells (Bitler, Dover, & Shai, 2018; Chtcheglova & Hinterdorfer, 2018; Guillaume-Gentil et al., 2014; Kasas, Stupar, & Dietler, 2018; Sokolov, Dokukin, & Guz, 2013) and tissues (Han et al., 2017; Stylianou, Lekka, & Stylianopoulos, 2018). In summary, this book serves as a guide for understanding the application of AFM for food research. It can facilitate in understanding AFM application easily and thus shortening the learning time for new hands.

The target audience of this book is broad. This book is ideal for professional food scientists and engineers who are interested in food formulation and structuration. It is also ideal for AFM operators in instrumental analysis centers who are required to measure and analyze food samples. In addition, it is ideal for students pursuing undergraduate and postgraduate courses on food structures. It may also prove useful for AFM developers and application experts who want to develop and popularize AFM in the field of food science and technology.

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References

Alexander Reese, R., & Xu, B. (2019). Single-molecule detection of proteins and toxins in food using atomic force microscopy. *Trends in Food Science & Technology*, *87*, 26−34.

Bellon, L. (2020). Atomic force microscopy. *Physics Today*, *73*, 57−58.

Binnig, G., Quate, C. F., & Gerber, C. (1986). Atomic force microscope. *Physical Review Letters*, *56*, 930−933.

Bitler, A., Dover, R. S., & Shai, Y. (2018). Fractal properties of cell surface structures: A view from AFM. *Seminars in Cell & Developmental Biology*, *73*, 64−70.

Braga, P. C., & Ricci, D. (2011). *Atomic force microscopy in biomedical research: Methods and protocols*. Springer.

Cai, J. (2018). *Atomic force microscopy in molecular and cell biology*. Springer.

Chen, J., & Xu, K. (2020). Applications of atomic force microscopy in materials, semiconductors, polymers, and medicine: A minireview. *Instrumentation Science & Technology*, *48*, 667–681.

Chtcheglova, L. A., & Hinterdorfer, P. (2018). Simultaneous AFM topography and recognition imaging at the plasma membrane of mammalian cells. *Seminars in Cell & Developmental Biology*, *73*, 45–56.

Collins, L., Liu, Y., Ovchinnikova, O. S., & Proksch, R. (2019). Quantitative electromechanical atomic force microscopy. *ACS Nano*, *13*, 8055–8066.

Cárdenas-Pérez, S., Chanona-Pérez, J. J., Méndez-Méndez, J. V., Arzate-Vázquez, I., Hernández-Varela, J. D., & Vera, N. G. (2019). Recent advances in atomic force microscopy for assessing the nanomechanical properties of food materials. *Trends in Food Science & Technology*, *87*, 59–72.

Dazzi, A., & Prater, C. B. (2017). AFM-IR: Technology and applications in nanoscale infrared spectroscopy and chemical imaging. *Chemical Reviews*, *117*, 5146–5173.

Dufrêne, Y. F., Ando, T., Garcia, R., Alsteens, D., Martinez-Martin, D., Engel, A., ... Müller, D. J. (2017). Imaging modes of atomic force microscopy for application in molecular and cell biology. *Nature Nanotechnology*, *12*, 295–307.

Efremov, Y. M., Okajima, T., & Raman, A. (2020). Measuring viscoelasticity of soft biological samples using atomic force microscopy. *Soft Matter*, *16*, 64–81.

Fernandes, J. P. C., Mareau, V. H., & Gonon, L. (2018). AFM-Raman colocalization setup: Advanced characterization technique for polymers. *International Journal of Polymer Analysis and Characterization*, *23*, 113–119.

Feuillie, C., Lambert, E., Ewald, M., Azouz, M., Henry, S., Marsaudon, S., ... Molinari, M. (2020). High speed afm and nanoinfrared spectroscopy investigation of Aβ1–42 peptide variants and their interaction with POPC/SM/Chol/GM1 model membranes. *Frontiers in Molecular Biosciences*, *7*, 571696.

Fukui, T., Uchihashi, T., Sasaki, N., Watanabe, H., Takeuchi, M., & Sugiyasu, K. (2018). Direct observation and manipulation of supramolecular polymerization by high-speed atomic force microscopy. *Angewandte Chemie International Edition*, *57*, 15465–15470.

Fukuma, T. (2020). Subnanometer-scale imaging of nanobio-interfaces by frequency modulation atomic force microscopy. *Biochemical Society Transactions*, *48*, 1675–1682.

Gross, L., Schuler, B., Pavliček, N., Fatayer, S., Majzik, Z., Moll, N., ... Meyer, G. (2018). Atomic force microscopy for molecular structure elucidation. *Angewandte Chemie International Edition*, *57*, 3888–3908.

Guillaume-Gentil, O., Potthoff, E., Ossola, D., Franz, C. M., Zambelli, T., & Vorholt, J. A. (2014). Force-controlled manipulation of single cells: From AFM to FluidFM. *Trends in Biotechnology*, *32*, 381–388.

Gunning, A. P., & Morris, V. J. (2018). Getting the feel of food structure with atomic force microscopy. *Food Hydrocolloids*, *78*, 62–76.

Gómez-Varela, A. I., Stamov, D. R., Miranda, A., Alves, R., Barata-Antunes, C., Dambournet, D., ... De Beule, P. A. A. (2020). Simultaneous co-localized super-resolution fluorescence microscopy and atomic force microscopy: Combined SIM and AFM platform for the life sciences. *Scientific Reports*, *10*, 1122.

Han, B., Nia, H. T., Wang, C., Chandrasekaran, P., Li, Q., Chery, D. R., ... Han, L. (2017). AFM-nanomechanical test: An interdisciplinary tool that links the understanding of cartilage and meniscus biomechanics, osteoarthritis degeneration, and tissue engineering. *ACS Biomaterials Science & Engineering*, *3*, 2033–2049.

Ho, T. M., Abik, F., & Mikkonen, K. S. (2022). An overview of nanoemulsion characterization via atomic force microscopy. *Critical Reviews in Food Science and Nutrition*, *62*, 4908–4928.

Jiao, F., Cannon, K. S., Lin, Y.-C., Gladfelter, A. S., & Scheuring, S. (2020). The hierarchical assembly of septins revealed by high-speed AFM. *Nature Communications*, *11*, 5062.

Jones, O. G. (2016). Developments in dynamic atomic force microscopy techniques to characterize viscoelastic behaviors of food materials at the nanometer-scale. *Current Opinion in Food Science*, *9*, 77–83.

Kasas, S., Stupar, P., & Dietler, G. (2018). AFM contribution to unveil pro- and eukaryotic cell mechanical properties. *Seminars in Cell & Developmental Biology*, *73*, 177–187.

Kiio, T. M., & Park, S. (2020). Nano-scientific application of atomic force microscopy in pathology: From molecules to tissues. *International Journal of Medical Sciences*, *17*, 844–858.

Kilpatrick, J. I., Revenko, I., & Rodriguez, B. J. (2015). Nanomechanics of cells and biomaterials studied by atomic force microscopy. *Advanced Healthcare Materials*, *4*, 2456–2474.

Krieg, M., Fläschner, G., Alsteens, D., Gaub, B. M., Roos, W. H., Wuite, G. J. L., ... Müller, D. J. (2019). Atomic force microscopy-based mechanobiology. *Nature Reviews Physics*, *1*, 41–57.

Kuchuk, K., & Sivan, U. (2018). Hydration structure of a single DNA molecule revealed by frequency-modulation atomic force microscopy. *Nano Letters*, *18*, 2733–2737.

Kuda, T., Shibata, G., Takahashi, H., & Kimura, B. (2015). Effect of quantity of food residues on resistance to desiccation of food-related pathogens adhered to a stainless steel surface. *Food Microbiology*, *46*, 234–238.

Lekka, M. (2017). *Cellular analysis by atomic force microscopy*. CRC Press.

Li, J., Liu, Y., Yuan, Y., & Huang, B. (2021). Applications of atomic force microscopy in immunology. *Frontiers of Medicine*, *15*, 43–52.

Li, M., Xi, N., Wang, Y.-c., & Liu, L.-q. (2021). Atomic force microscopy for revealing micro/nanoscale mechanics in tumor metastasis: From single cells to microenvironmental cues. *Acta Pharmacologica Sinica*, *42*, 323–339.

Liu, Q., & Yang, H. (2019). Application of atomic force microscopy in food microorganisms. *Trends in Food Science & Technology*, *87*, 73–83.

Liu, Y., & Vancso, G. J. (2020). Polymer single chain imaging, molecular forces, and nanoscale processes by Atomic Force Microscopy: The ultimate proof of the macromolecular hypothesis. *Progress in Polymer Science*, *104*, 101232.

Ma, M., Zhong, J., Li, W., Zhou, J., Yan, Z., Ding, J., & He, D. (2013). Comparison of four synthetic model peptides to understand the role of modular motifs in the self-assembly of silk fibroin. *Soft Matter*, *9*, 11325–11333.

Main, K. H. S., Provan, J. I., Haynes, P. J., Wells, G., Hartley, J. A., & Pyne, A. L. B. (2021). Atomic force microscopy-A tool for structural and translational DNA research. *APL Bioengineering*, *5*, 031504.

Marchesi, A., Umeda, K., Komekawa, T., Matsubara, T., Flechsig, H., Ando, T., ... Franz, C. M. (2021). An ultra-wide scanner for large-area high-speed atomic force microscopy with megapixel resolution. *Scientific Reports*, *11*, 13003.

Marinello, F., La Storia, A., Mauriello, G., & Passeri, D. (2019). Atomic force microscopy techniques to investigate activated food packaging materials. *Trends in Food Science & Technology*, *87*, 84–93.

Martines, E., Zhong, J., Muzard, J., Lee, A. C., Akhremitchev, B. B., Suter, D. M., & Lee, G. U. (2012). Single-molecule force spectroscopy of the Aplysia cell adhesion molecule reveals two homophilic bonds. *Biophysical Journal*, *103*, 649–657.

Miranda, A., Gómez-Varela, A. I., Stylianou, A., Hirvonen, L. M., Sánchez, H., & DeBeule, P. A. A. (2021). How did correlative atomic force microscopy and super-resolution microscopy evolve in the quest for unravelling enigmas in biology? *Nanoscale*, *13*, 2082–2099.

Morris, V. J., Kirby, A. R., & Gunning, P. A. (2009). *Atomic force microscopy for biologists*. World Scientific.

Müller, D. J., & Engel, A. (1997). The height of biomolecules measured with the atomic force microscope depends on electrostatic interactions. *Biophysical Journal*, *73*, 1633–1644.

Nandi, T., & Ainavarapu, S. R. K. (2021). Applications of atomic force microscopy in modern biology. *Emerging Topics in Life Sciences*, *5*, 103−111.

Nievergelt, A. P., Banterle, N., Andany, S. H., Gönczy, P., & Fantner, G. E. (2018). High-speed photothermal off-resonance atomic force microscopy reveals assembly routes of centriolar scaffold protein SAS-6. *Nature Nanotechnology*, *13*, 696−701.

Obeid, S., & Guyomarc'h, F. (2020). Atomic force microscopy of food assembly: Structural and mechanical insights at the nanoscale and potential opportunities from other fields. *Food Bioscience*, *36*, 100654.

Pavliček, N., & Gross, L. (2017). Generation, manipulation and characterization of molecules by atomic force microscopy. *Nature Reviews Chemistry*, *1*, 0005.

Posé, S., Paniagua, C., Matas, A. J., Gunning, A. P., Morris, V. J., Quesada, M. A., & Mercado, J. A. (2019). A nanostructural view of the cell wall disassembly process during fruit ripening and postharvest storage by atomic force microscopy. *Trends in Food Science & Technology*, *87*, 47−58.

Prats-Mateu, B., & Gierlinger, N. (2017). Tip in−light on: Advantages, challenges, and applications of combining AFM and Raman microscopy on biological samples. *Microscopy Research and Technique*, *80*, 30−40.

Sapra, K. T., Spoerri, P. M., Engel, A., Alsteens, D., & Müller, D. J. (2019). Seeing and sensing single G protein-coupled receptors by atomic force microscopy. *Current Opinion in Cell Biology*, *57*, 25−32.

Shi, C., He, Y., Ding, M., Wang, Y., & Zhong, J. (2019a). Nanoimaging of food proteins by atomic force microscopy. Part I: Components, imaging modes, observation ways, and research types. *Trends in Food Science & Technology*, *87*, 3−13.

Shi, C., He, Y., Ding, M., Wang, Y., & Zhong, J. (2019b). Nanoimaging of food proteins by atomic force microscopy. Part II: Application for food proteins from different sources. *Trends in Food Science & Technology*, *87*, 14−25.

Si, H., Zhang, S., Ma, S., Xiong, Z., Kausar, A., Liao, Q., … Zhang, Y. (2020). Emerging conductive atomic force microscopy for metal halide perovskite materials and solar cells. *Advanced Energy Materials*, *10*, 1903922.

Slobodskyy, T., Zozulya, A. V., Tholapi, R., Liefeith, L., Fester, M., Sprung, M., & Hansen, W. (2015). Versatile atomic force microscopy setup combined with micro-focused X-ray beam. *Review of Scientific Instruments*, *86*, 065104.

Sokolov, I., Dokukin, M. E., & Guz, N. V. (2013). Method for quantitative measurements of the elastic modulus of biological cells in AFM indentation experiments. *Methods (San Diego, Calif.)*, *60*, 202−213.

Stylianou, A., Lekka, M., & Stylianopoulos, T. (2018). AFM assessing of nanomechanical fingerprints for cancer early diagnosis and classification: From single cell to tissue level. *Nanoscale*, *10*, 20930−20945.

Takeyasu, K. (2014). *Atomic force microscopy in nanobiology*. CRC Press.

Thiruvallur Eachambadi, R., Boschker, H. T. S., Franquet, A., Spampinato, V., Hidalgo-Martinez, S., Valcke, R., … Manca, J. V. (2021). Enhanced laterally resolved ToF-SIMS and AFM imaging of the electrically conductive structures in cable bacteria. *Analytical Chemistry*, *93*, 7226−7234.

Uchihashi, T., & Scheuring, S. (2018). Applications of high-speed atomic force microscopy to real-time visualization of dynamic biomolecular processes. *Biochimica et Biophysica Acta (BBA) - General Subjects*, *1862*, 229−240.

Wang, J., & Nie, S. (2019). Application of atomic force microscopy in microscopic analysis of polysaccharide. *Trends in Food Science & Technology*, *87*, 35−46.

Wen, Y., Xu, Z., Liu, Y., Corke, H., & Sui, Z. (2020). Investigation of food microstructure and texture using atomic force microscopy: A review. *Comprehensive Reviews in Food Science and Food Safety*, *19*, 2357−2379.

Wilson, L., Matsudaira, P. T., Jena, B. P., & Horber, J. H. (2002). *Atomic force microscopy in cell biology*. Academic Press.
Yadavalli, V. K., & Ehrhardt, C. J. (2021). Atomic force microscopy as a biophysical tool for nanoscale forensic investigations. *Science & Justice*, *61*, 1–12.
Yuan, G., Liang, T., Liang, Y., Pang, X., & Jia, Z. (2021). The controlled growth of conjugated polymer-quantum dot nanocomposites via a unimolecular templating strategy. *Chemical Communications*, *57*, 1250–1253.
Zhao, D., Liu, S., & Gao, Y. (2018). Single-molecule manipulation and detection. *Acta Biochimica et Biophysica Sinica*, *50*, 231–237.
Zhao, L., Kristi, N., & Ye, Z. (2021). Atomic force microscopy in food preservation research: New insights to overcome spoilage issues. *Food Research International*, *140*, 110043.
Zhong, J. (2011). From simple to complex: Investigating the effects of lipid composition and phase on the membrane interactions of biomolecules using in situ atomic force microscopy. *Integrative Biology*, *3*, 632–644.
Zhong, J., Finglas, P., Wang, Y., & Wang, X. (2019). Application of atomic force microscopy in food science. *Trends in Food Science & Technology*, *87*, 1–2.
Zhong, J., & He, D. (2012). Recent progress in the application of atomic force microscopy for supported lipid bilayers. *Chemistry—A European Journal*, *18*, 4148–4155.
Zhong, J., Liu, X., Wei, D., Yan, J., Wang, P., Sun, G., & He, D. (2015). Effect of incubation temperature on the self-assembly of regenerated silk fibroin: A study using AFM. *International Journal of Biological Macromolecules*, *76*, 195–202.
Zhong, J., Ma, M., Li, W., Zhou, J., Yan, Z., Ding, J., & He, D. (2014). Self-assembly of regenerated silk fibroin from random coil nanostructures to antiparallel β-sheet nanostructures. *Biopolymers*, *101*, 1181–1192.
Zhong, J., Ma, M., Zhou, J., Wei, D., Yan, Z., & He, D. (2013). Tip-induced micropatterning of silk fibroin protein using in situ solution atomic force microscopy. *ACS Applied Materials & Interfaces*, *5*, 737–746.
Zhong, J., Sun, G., & He, D. (2014). Classic, liquid, and matrix-assisted dip-pen nanolithography for materials research. *Nanoscale*, *6*, 12217–12228.
Zhong, J., & Yan, J. (2016). Seeing is believing: Atomic force microscopy imaging for nanomaterial research. *RSC Advances*, *6*, 1103–1121.
Zhong, J., Yang, C., Zheng, W., Huang, L., Hong, Y., Wang, L., & Sha, Y. (2009). Effects of lipid composition and phase on the membrane interaction of the prion peptide 106–126 amide. *Biophysical Journal*, *96*, 4610–4621.
Zhong, J., Yang, C., Zheng, W., Huang, L., Hong, Y., Wang, L., & Sha, Y. (2010). The role of calcium ions in the interactions of PrP106–126 amide with model membranes. *Colloids and Surfaces B: Biointerfaces*, 77, 40–46.
Zhong, J., Zheng, W., Huang, L., Hong, Y., Wang, L., Qiu, Y., & Sha, Y. (2007). PrP106–126 amide causes the semi-penetrated poration in the supported lipid bilayers. *BBA - Biomembranes*, *1768*, 1420–1429.
Zhou, G., Zhang, B., Tang, G., Yu, X.-F., & Galluzzi, M. (2021). Cells nanomechanics by atomic force microscopy: Focus on interactions at nanoscale. *Advances in Physics: X*, *6*, 1866668.