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Advances in High-resolution Imaging Using Atomic Force Microscopy: From Biology to Nanomaterials

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Introduction

Atomic Force Microscopy (AFM) has evolved into one of the most powerful tools for high-resolution imaging and characterization at the nanoscale. Originally developed for surface topology analysis, modern AFM techniques have expanded into dynamic imaging, molecular force measurements, and real-time visualization of biological processes. This article reviews recent advances in AFM technologies, including high-speed AFM, peak force tapping, and functionalized probes, and highlights their transformative applications in biology, materials science, and nanotechnology. We discuss current limitations and future directions, emphasizing the role of AFM in bridging structural gaps across diverse scientific domains. Atomic Force Microscopy (AFM), introduced by Binnig, Quate, and Gerber in 1986, has become indispensable for nanoscale imaging and manipulation. Unlike electron microscopy, AFM operates in ambient or physiological environments, making it uniquely suited for studying biological samples and soft materials without extensive sample preparation. The evolution of AFM from a topographical imaging tool to a multifunctional platform marks a significant milestone in nanoscience, with implications across cell biology, polymer science, semiconductors, and 2D materials.

Description

Recent innovations in High-Speed AFM (HS-AFM) have dramatically increased imaging rates, allowing real-time visualization of dynamic biological processes. These systems employ smaller cantilevers with higher resonance frequencies and optimized feedback control systems, achieving frame rates of several frames per second. Applications include observing conformational changes in proteins, tracking motor protein activity, and mapping dynamic membrane fluctuations. Peak Force Tapping, developed by Bruker, provides superior force control compared to traditional tapping or contact modes. This approach captures force-distance curves at every pixel, enabling simultaneous mapping of mechanical properties such as modulus, adhesion, and deformation. This capability is particularly useful in studying heterogeneous materials, polymer blends, and biological tissues. Functionalized AFM tips with specific chemical groups, antibodies, or ligands allow targeted interactions with sample surfaces. Chemical Force Microscopy (CFM) leverages these interactions to map surface chemistry at molecular resolution. These probes have been essential in receptor-ligand binding studies, membrane protein localization, and selective detection of nanomaterial surface functionalities.

AFM has enabled unprecedented insights into biological structures and functions. In cell biology, it provides nanomechanical profiles of live cells, offering biomarkers for disease states such as cancer. AFM has also been used to study DNA-protein interactions, virus morphology, and protein aggregation in neurodegenerative diseases. With HS-AFM, dynamic events like actin polymerization and enzyme activity can be observed in real-time under near-physiological conditions. AFM plays a pivotal role in characterizing nanomaterials, especially low-dimensional systems such as graphene, MoS_2, and nanowires. Its ability to measure layer thicknesses, mechanical stiffness, and surface potential complements electron microscopy and spectroscopy techniques. In nanofabrication, AFM has also been used for lithography and nanoscale manipulation. In polymer science, AFM facilitates phase imaging, compositional mapping, and mechanical analysis of blends and block copolymers. The ability to perform these measurements under varied environmental conditions, such as temperature and humidity, makes AFM a key tool for understanding soft material behavior in realistic settings.

Despite its advantages, AFM faces several challenges. Imaging speed remains a limitation for observing fast processes in live systems. Tip convolution effects can reduce lateral resolution, and functionalized probes may suffer from variability and drift. To address these, developments are underway in machine learning-enhanced image reconstruction, integration with other techniques like super-resolution microscopy, and the creation of more robust, reproducible probes. The future of AFM lies in hybrid techniques-such as AFM-Raman, AFM-IR, and correlative light-electron-AFM microscopy-that offer multi-modal imaging and chemical characterization. Furthermore, automation and AI-driven analysis are expected to enhance throughput and reproducibility, expanding AFM's utility in high-content biological and materials screening [1-5].

Conclusion

Atomic Force Microscopy continues to evolve as a central tool in nanoscience, enabling high-resolution, real-time, and multifunctional imaging across diverse fields. From unveiling the mechanics of living cells to analyzing the surface chemistry of advanced nanomaterials, AFM has expanded the frontier of what is possible at the nanoscale. Continued innovation in instrumentation, probe design, and data integration will further cement its role in next-generation research and development.

Acknowledgment

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Conflict of Interest

None.

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