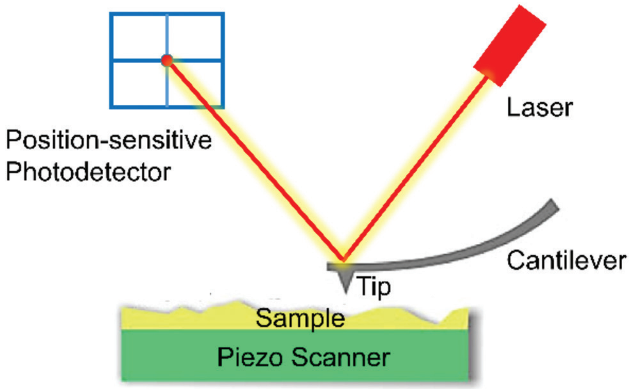
Highlights from Microscopy AND Microanalysis

Biological Applications

Atomic Force Microscopy for Tumor Research at Cell and Molecule Levels by Y Qin, W Yang, H Chu, Y Li, S Cai, H Yu, and L Liu, *Microsc Microanal* | https://doi.org/10.1017/S1431927622000290.

Tumors pose a serious threat to human life and health. Researchers can determine if cells are cancerous, whether the cancer cells are invasive or have metastasized, and the effects of drugs on cancer cells by physical properties such as hardness, adhesion, and Young's modulus. Atomic force microscopy (AFM) has emerged as an important tool for biomechanics research on tumor cells due to its ability to image and collect force spectroscopy information of biological samples with its nano-level spatial resolution under near-physiological conditions. This article reviews results from studies of cancer cells with AFM. The main focus is on the operating principles of AFM and research advances in mechanical property measurement, ultra-microtopography, and molecular recognition of tumor cells. Studies are presented in a systematic way with a summary and discussion of future directions.

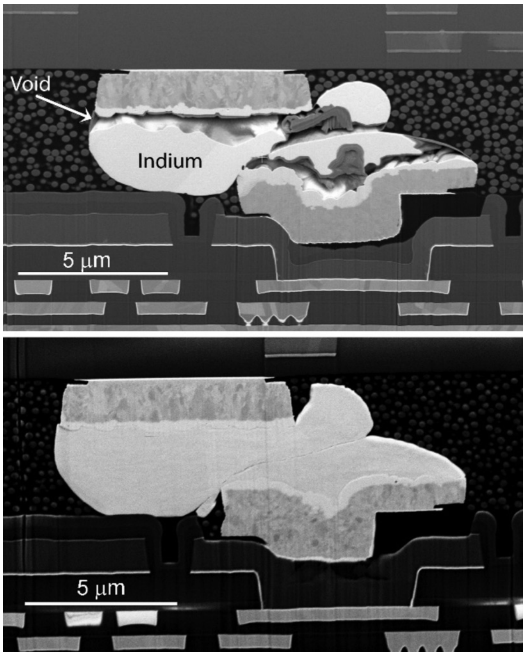


Schematic illustration of how an AFM works. A laser diode emits a beam onto the back of the cantilever at the tip. The magnitude of the beam deflection changes in response to the interactive force between the tip and the sample. The AFM system senses these changes in position and maps surface topography or monitors the interactive force between the tip and the sample.

Materials Applications

Focused Ion Beam Preparation of Low Melting Point Metals: Lessons Learned From Indium by JR Michael, DL Perry, DP Cummings, JA Walraven, and MB Jordan, *Microsc Microanal* | https://doi.org/10.1017/S1431927622000496.

Low melting point metals (like indium and lead) are commonly used to make interconnections in electronic devices. Indium is a low melting point metal that is used in producing modern hybridized circuits. The metallurgy of the indium impacts the reliability of these interconnects. Focused ion beam (FIB), using Ga^+ or Xe^+, has been used to prepare cross sections of these interconnects with limited success due to voiding artifacts that occur in the indium. In this work, it is shown that the artifacts observed are related to the temperature rise caused by the exposure of the indium to the energetic ion beam. The use of modified milling strategies to minimize the increased local sample temperature are shown to produce cross sections that are representative of the indium microstructure in some, but not all, sample configurations. Furthermore, cooling of the sample to cryogenic temperatures is shown to reliably eliminate artifacts in FIB-prepared cross sections of indium allowing the true microstructure to be observed (Figure).



Electroplated indium bump cross sections prepared with Xe^+ FIB. The cross section prepared at room temperature (top) shows the typical void artifact, while the sample cross sectioned at cryogenic temperatures (bottom) is free of the artifact.

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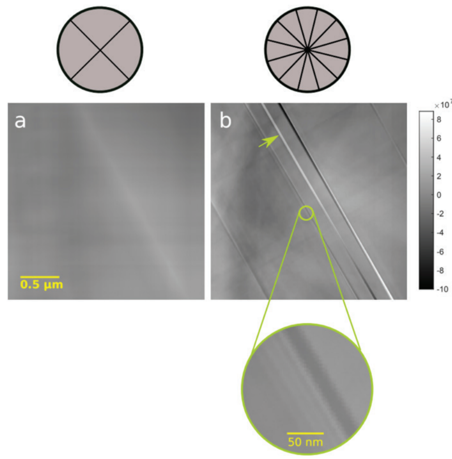
Microscopy AND Microanalysis

Techniques

Integrated Differential Phase Contrast (IDPC)-STEM Utilizing a Multi-Sector Detector for Imaging Thick Samples by Z Li, J Biskupek, U Kaiser, and H Rose, *Microsc Microanal* | https://doi.org/10.1017/S1431927622000289.

The IDPC method is useful for generating a map of a thin sample. We evaluate the potential of IDPC imaging for thick samples from focal-series calculations. We found that the anisotropy of the contrast transfer function (CTF) is enhanced at higher defoci when applying a standard quadrant detector, which is not the case when using a multi-sector detector for IDPC imaging. Sector-number-dependent calculations for both C_c/C_3-corrected and C_3-corrected STEM show that increasing the number of detector sectors results in an almost isotropic contrast transfer and also enhances the image contrast and resolution. We suggest that the enhanced contrast at low spatial frequencies will be extremely helpful for imaging biological samples effectively without applying a large defoci or using a phase plate. For a proof-of-principle IDPC-STEM (uncorrected) experiment, we realize the functionality of a 12-sector detector from a physical quadrant detector and demonstrate the improvement in contrast and resolution on a InGaN/GaN quantum well structure (Figure).



Experimental IDPC-STEM images of InGaN/GaN quantum wells on 1 µm thick GaN prepared in cross section. Images were obtained at an accelerating voltage of 200 kV and the probe focused at a sample slice 20 nm from the top. The IDPC mode employs a) the fixed quadrant detector, and b) a virtual 12-sector detector generated from the fixed quadrant detector.