SCANNING PROBE RECOGNITION MICROSCOPY FOR NANO BIOMEDICAL APPLICATIONS

Q. Chen, Y. Fan, L. Udpa, M.S. Schindler and V.M. Ayres
Michigan State University, East Lansing, MI 48824, USA

E-mail: ayresv@egr.msu.edu
http://www.egr.msu.edu/ebnl

To reliably return to and directly interact with a specific nanoscale feature of interest is a highly desirable goal. We are developing this capability within a scanning probe miscopy (SPM) system, focusing on nanobiological applications. In our approach, we give the SPM system itself the power to return to a specific nanoscale site by recognizing the way the site feels to the SPM system rather than by the way the site looks, or even feels (haptic), to a human operator. It is a recognition-driven and learning approach, made possible through combining SPM piezoelectric implementation with on-line image processing and dynamically adaptive learning algorithms. Segmentation plus a recognized pattern is implemented within a scan plan and used to guide the tip in a recognition-driven return to a specific site.

We have successfully recognized and classified tubular versus biological objects from experimental AFM images using a method based on normalized central moments [1]. We have also extended this work to include recognition schemes appropriate for more subtle differences between biological objects of similar globular shape by adding the Continuous Wavelet Transform (CWT) with a differential Gaussian mother wavelet [2]. Normalized central moments are translation and scale invariant, and the 2-D continuous wavelet transform allows multi-scale analysis of images. Thus, these two methods together can be applied to analyze biological objects of any scale.

Once a region of interest in the image has been identified for further investigation, the next step is to send appropriate motion control commands to the scanner. Methods have been identified for motion control and site specific scanning, which are geared towards the scanning of globular and tubular landmarks. These are based on augmentation rather than replacement of the current raster scan plan strategy, thus retaining the maximum amount of self-cancellation of hysteresis and creep effects. In the adaptive mode the length of the scan lines can be kept variable until a positive or negative going edge is detected at the left and right sides respectively. The raster scan will change directions as soon as an edge is detected allowing the scanner to track bends within the bio-feature. Also, the system can be used in a motion tracking mode when 'focusing' on a single site with dynamic properties, by tracking its motion through a changing environment. In this mode, the software performs recognition of a target and creates an appropriate template for the object. An algorithm composed of a combination of correlation and registration operations will be used to track the direction and magnitude of target motion.

With the addition of the recognition capability, we can first focus on a particular cell type, defined by its edges and pattern. We can then explore increasingly small scales of features, through investigations as a function of the CWT scale parameter. Establishing a hierarchy of surface features through direct investigation is an ongoing research effort. The recognition and auto-focus capability of our technique provides great flexiblity for handling a wide array of nanobiological investigations which involve conformational changes.

Acknowledgements: The authors gratefully acknowledge support from the National Science Foundation, USA.

References

1. Qian Chen, Virginia Ayres, and Lalita Udpa, "Biological Investigation Using Scanning Probe Recognition Microscopy", Proceedings of the 3rd IEEE Conference on Nanotechnology (IEEE-NANO 2003), Vol. 2, pp. 863-865 (2003)

2. B. Goolsby, Q. Chen, L. Udpa, Y. Fan, R. Samona, B. Bhooravan, F. M. Salam, D. H. Wang, and V. M. Ayres, "Scanning Probe Microscopy with Landmark Referenced Control For Direct Biological Investigations", J. Nanosci. Nanotech., Vol. 3, No. 4, PP.347-350 (2003).

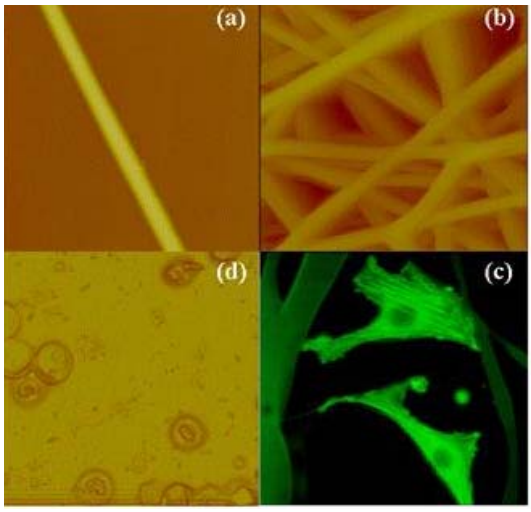

Figure 1. Tubular and globular shapes are common building blocks of biological systems. Variations in shape, such as scaffolding versus cells, and variations in scale, such as cell walls versus cell nuclei, or scaffolding versus actin filaments, can be distinguished and recognized.

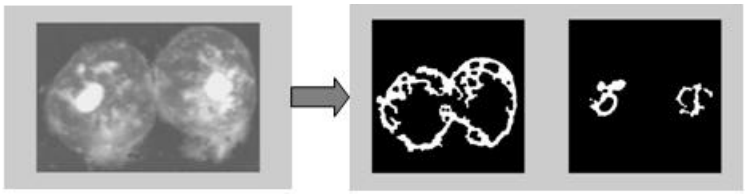

Figure 2. Using continuous wavelet transform and masking, the cell walls have been distinguished from the cell nuclei.

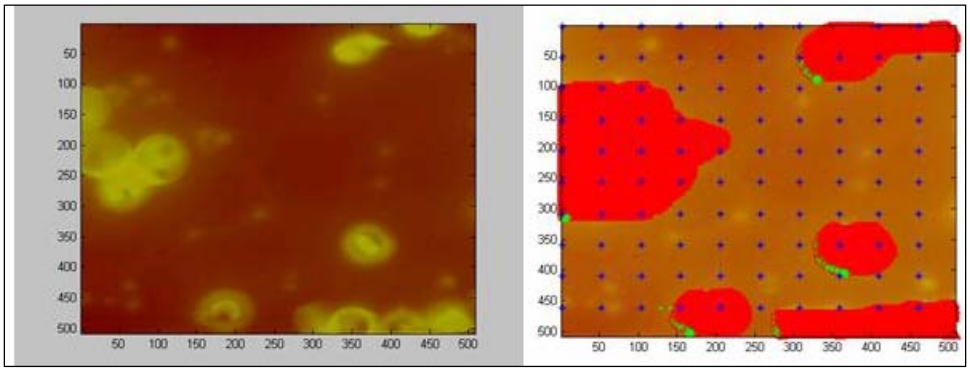

Figure 3. Scan plan implementation begins with large steps until edge recognition along any connected neighbourhood occurs. Backtracking to the start of the feature is then implemented. After the whole feature is fine-scanned, large steps are resumed. The clusters may be further distinguished into individual cells through edge closure or template techniques, but may also be an important themselves if the biological function involves aggregation.