Crossdisciplinary Applications of Microscopy Techniques, e.g. Physic-Life Science Interfaces

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X-Ray Nano-Imaging of Biomatter and Cells

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Biological systems such as cells and cellular components are governed by processes, which take place on the nanometer to micrometer length scales. X-ray scattering and diffraction techniques are extremely well suited to study such processes as the spatial resolution extends well into the relevant length scales. At the same time, the investigation of such systems, in particular in the field of biophysical research requires well-defined and controllable sample environments. One way to establish such environments is by employing microfluidic devices tailored for the particular experiment. The combination of both microfluidics and X-ray nano-/micro-diffraction provides an innovative tool for biomatter research.

There are two principal approaches to shedding light on the nanometer-scale assemblies found in biological cells. (i) By studying purified *in vitro* systems such as individual proteins “bottom up” and following the assembly kinetics *in situ*, we can access the biophysical principles underlying assembly. In our experiments, the biomolecular assembly of proteins is studied by diffusively mixing in assembly buffer and following the subsequent assembly steps downstream in the flow channel [1,4] (see Figure 2). (ii) In whole cells, structures as assembled *in vivo* can be observed, corresponding to a “top down” approach. Cells are imaged on the nanometer scale by scanning X-ray diffraction using a nanometer-focused beam [2,3] (see Figure 1).

Thus, X-ray imaging provides a complementary tool to electron microscopy, with the advantage of a high penetration depth and the option of dynamic imaging.

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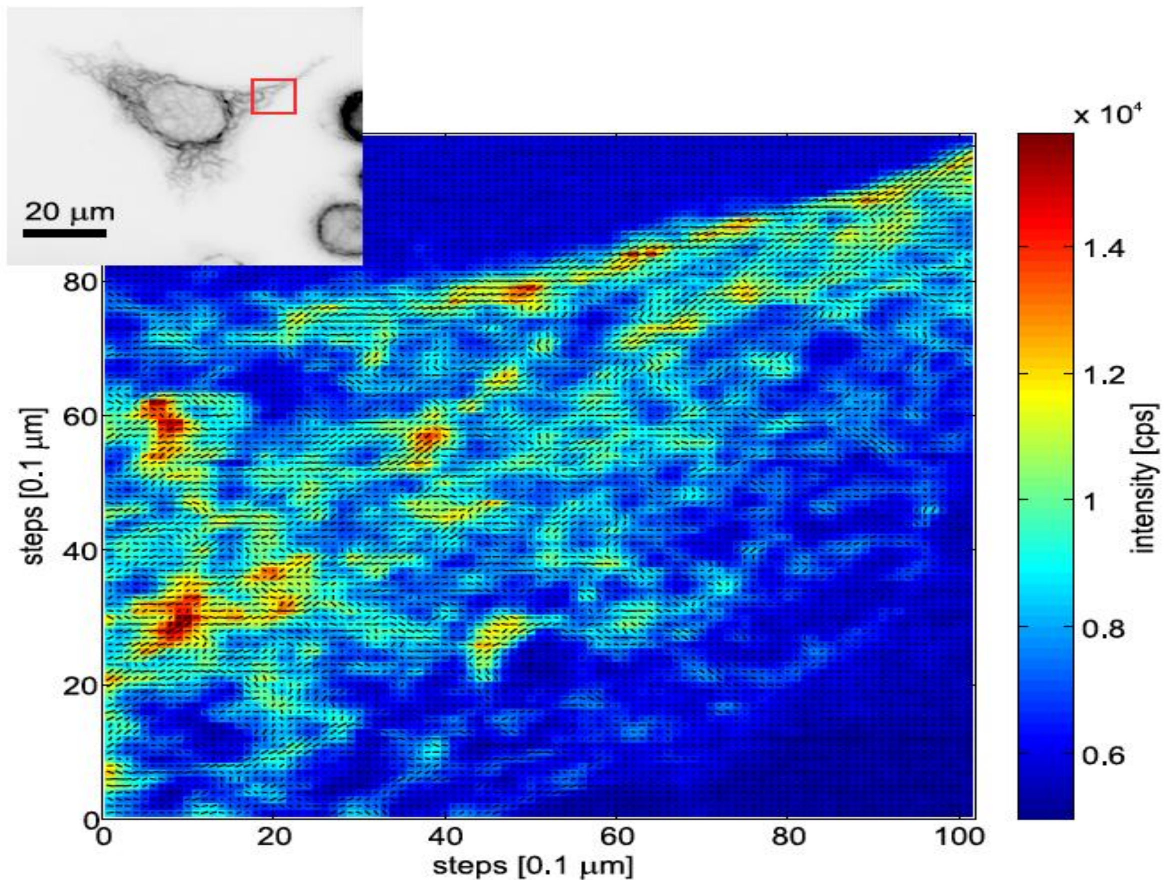

Figure 1. Orientation map and dark-field image of the keratin network in a freeze-dried eukaryotic cell reconstructed from a mesh scan with a step size of 100 nm and 1 s exposure time. The inset shows a fluorescence microscopy image of the keratin network recorded before freeze-drying and the scanned region is marked by a red box (taken from ref. [2]).

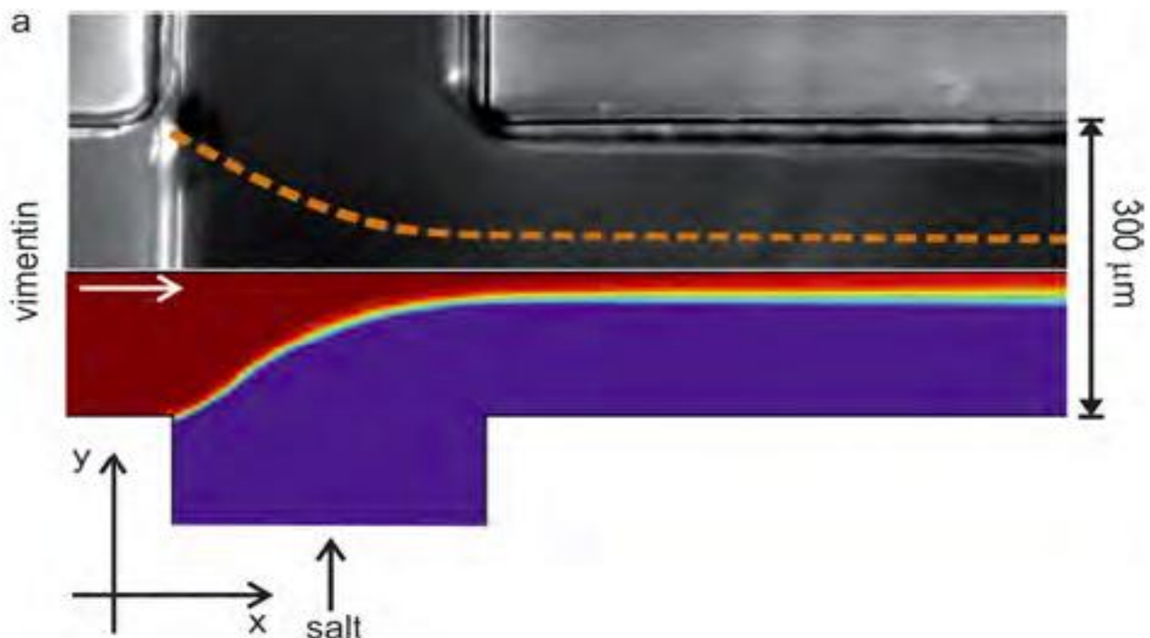

Figure 1. Simulation of protein (vimentin intermediate filaments) and salt concentrations during the assembly process. Shown is the mid-plane of a microfluidic device in the x–y direction. The lower part of the image shows the simulation of the vimentin concentration, the upper part a corresponding DIC image. The dotted line marks the border line in the DIC image (taken from ref. [1]).