

Advances of scanning probe microscopy in biomedical applications

I.V. Yaminsky^{1,2}

¹Lomonosov Moscow State University, 119991, Moscow, Russian Federation

²Advanced Technologies Center, 119311, Moscow, Russian Federation

e-mail: yaminsky@nanoscopy.ru

Scanning probe microscopy has proved to be an efficient tool for the visualization of biomacromolecules, bacteria, living cells and tissue in ambient conditions with unprecedented space resolution. Informative scanning probe microscopy atlases of bacterial cells and virus particles are in the stage of permanent successful additions. Scanning probe microscopy is making successful steps in the development of molecular diagnostics methods for personalized medicine - early detection of biological agents and markers of various diseases. Scanning probe microscopy techniques has recently demonstrated the detection of individual bacterium, virus [1], protein and even one atom [2]. An efficient way for the rapid detection of bacterial resistance to antibiotics has been developed and demonstrated in [3]. High-sensitive detection of viral particles at low concentration in liquid solutions is shown in [4].

Modern scanning capillary microscopy plays a crucial role in a variety of biomedical applications. A capillary probe or nanopipette of scanning capillary microscope can act as a drug delivery device, an electrochemical sensor, a pH biosensor, a test system for detecting metal ions, and many others. Capillaries with two or more channels also allow directed mass transfer of substances, biomacromolecules (peptides, proteins, nucleic acids, etc.) to the surface of bioobjects or inside their volume. In our research we use a device built onto an inverted microscope, so that optical and probe microscopy data can be obtained and analyzed simultaneously [5]. In [6], for example, red blood cells were observed with the help of scanning capillary microscope, and analysis of the results has showed that the roughness of their surface was in the range of 20 nm. In the present report we use the term "capillary microscopy", because it unites much more functions and methods of application in comparison with "scanning ion conductance microscopy (SICM)" which was more widely used previously. Scanning capillary microscopy successfully is developing due to the effective application of multichannel capillaries for directional surface modification and 3D printing. It is possible to predict the further widespread use of scanning capillary (ion conductance) microscopy in biomedical applications, testing of drugs using only one cell, rather than their cultures and stereolithography.

The present and future of scanning capillary microscopy for 3D printing and stereolithography is discussed in the report. The artistic printing using fluorescent proteins was initially demonstrated in [7]. This work opens new exciting opportunities for the use of multichannel capillaries for a variety of technological and biomedical applications.

The author is grateful for the financial support of Russian Foundation for Basic Research (project N 17-52-560001).

1. Gupta, D. Akin, R. Bashir, *Appl. Phys. Lett.* **84**, 11, 1976 (2004).
2. K. Jensen, Kwanpyo Kim, A. Zettl, *Nature Nanotechnology* **3**, 533 (2008).
3. G. Longo, L. Alonso-Sarduy, L. Marques Rio, et al., *Nature Nanotechnology* **8**, 522 (2013).
4. P.V. Gorelkin, A.S. Erofeev, G.A. Kiselev, et al., *Analyst* **140**, 6131 (2015).
5. I. Yaminsky, A. Akhmetova, G. Meshkov, et al., *Nanoindustry* **1**, 44 (2018).
6. E. Makarova, D. Bagrov, P. Gorelkin, et al., *Nanoindustry* **2**, 42 (2015).
7. K.T. Rodolfa, A. Bruckbauer, D. Zhou, et al., *Angew. Chem. Int. Ed Engl.* **44**, 6854 (2005).