Final Report, CRADA No. BNL-C-93-10

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1. Period of the CRADA: August 13, 1993 through August 12, 1994

2. CRADA partners
   • BNL Biology Department, Paul Hough, Ph.D., Sr. Biophysicist
   • Digital Instruments, Inc., Virgil Elings, Ph.D., President

3. Significant accomplishments

The most significant accomplishment was the training of the Brookhaven partner in methods of Atomic Force Microscopy applicable in principle to biological samples. However, it became clear in the course of this work that instruments available at that time were excessively damaging to biological molecules.

With the collaboration of Professor Seth Darst of Rockefeller University and Dr. Andrew Ku of Stanford University, methods were developed for routine preparation of two-dimensional crystals of the protein streptavidin. We expected that the properties of i.) flatness on an atomic scale and ii.) structure known at the atomic level would make these crystals ideal test specimens for biological AFM.

4. Significant problems

The two-dimensional crystals described under 3. were necessarily prepared on the surface of a Langmuir trough, and it proved impossible to move them to the stage of the AFM without destroying the crystal structure. Attempts in Europe and in the Hansma Laboratory at the University of California, Santa Barbara, confirmed this result. After the CRADA, our attention shifted to the surfaces of 3-dimensional protein crystals, which have proved successful.

5. Industry benefits realized

None in the short term. However, the result 2–3 years after the termination of this CRADA was the creation of a new species of Atomic Force Microscopy which markedly reduces the damage to biological materials.

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6. Laboratory benefits realized

Just before the CRADA began, and incorporated in the CRADA, a NanoScope II AFM was contributed by Digital Instruments, permitting initial study of the damage problem. This work continued using a NanoScope III instrument purchased by the Materials Science Division at Brookhaven, and a MultiMode AFM purchased jointly by the Biology Department and Materials Science Division, leading in August 1995 to the conception of a novel instrument based on new logic called Sensing Mode.

7. Recommended follow-on work

See under 6.

8. Potential benefits from pursuing follow-on work

Follow-on work at Brookhaven led to the new method for carrying out Atomic Force Microscopy called Sensing Mode AFM.
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