

AN AUTOTOMATED GRID HANDLING SYSTEM FOR TEM

C.S. Potter*, C. Suloway*, B. Carragher* and P. Smith**

* Dept. of Cell Biology, The Scripps Research Institute, La Jolla, CA 92037

** SSI Robotics, 3002 Dow Ave., Tustin, CA 92780

Automatic sample handling methods have been a critical component in the rapid development of high throughput methods for protein crystallography. Recently, robotic sample handling has started to be widely used in the X-ray crystallography community to automatically mount sample pins to the goniostat [1]. Our goal is to develop similar high throughput methods for molecular electron microscopy. To this end, we have designed and demonstrated a grid handling system for automatically loading TEM grids into the specimen holder. It is our objective to integrate this system with our automated data collection software [2] in order to screen approximately 50 grids in a 24 hour period. We hope that automated screening methods will broaden the range and resolution of combinatorial experiments for screening conditions for protein crystallization and viral assembly.

The automated grid loading system is designed to load a grid into a specimen holder from a customized tray that has a capacity of 96 grids. In order to demonstrate the feasibility of the design, we built a prototype using an XYZ micro positioning stage with a precision actuator, as shown in figure 1. The grids are handled by the edges, as shown in figure 2, and the grid can be picked up many hundreds of times by the system without showing any signs of handling. A standard single tilt specimen holder (from an FEI TEM) was slightly modified to work with the system. A small slot (0.22"x 0.050") was machined out on either side of the recessed depression in which the grid sits in order to accommodate the gripper during grid placement. The system takes less than 5 seconds to load a grid into the holder and the loading operation was successfully repeated more than a 100 times with no failures.

Based on the successful performance of the prototype, a complete grid loading system is now under construction. The final system will include the ability to open and close the clamp on the specimen holder that holds the grid in place. The loading system will be integrated with a robotic arm that will transfer the holder into the goniometer of the microscope (Fig. 3). We expect that the grid loader will be completed and integrated with the Leginon system by late spring 2003.

References:

[1] B. Rupp et al., *Acta Cryst. D* 58 (2002) 1514-1518.

[2] B. Carragher et al, *J. Struct. Bio.* 132 (2000) 33-45.

[3] This research was conducted at the National Resource for Automated Molecular Microscopy which is supported by the National Institutes of Health through the National Center for Research Resources' P41 program (RR17573).

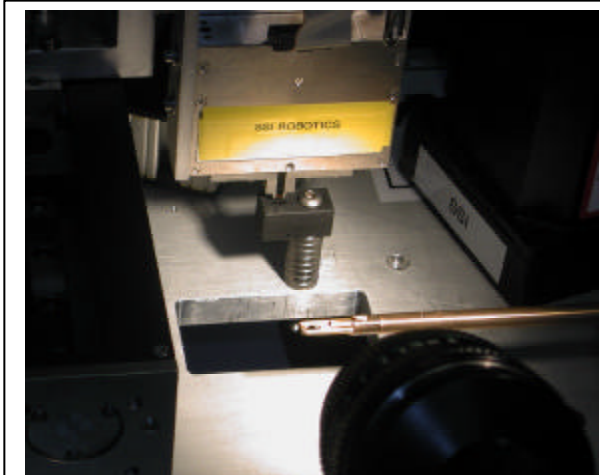


Fig. 1: Grid loading system prototype showing moving coil actuator gripper picking up a grid. The specimen holder is in the foreground.

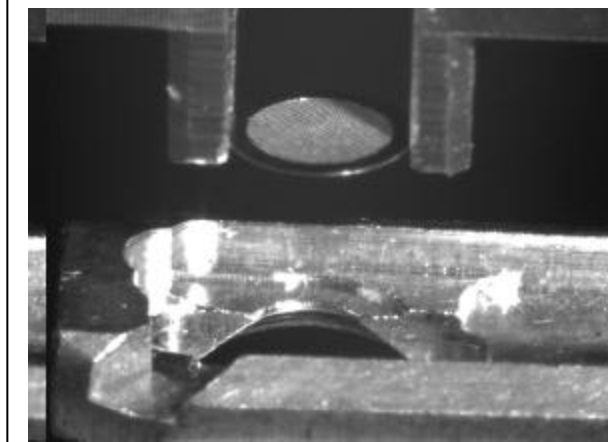


Fig. 2 Moving coil actuator gripper holding a standard 400 mesh copper grid.

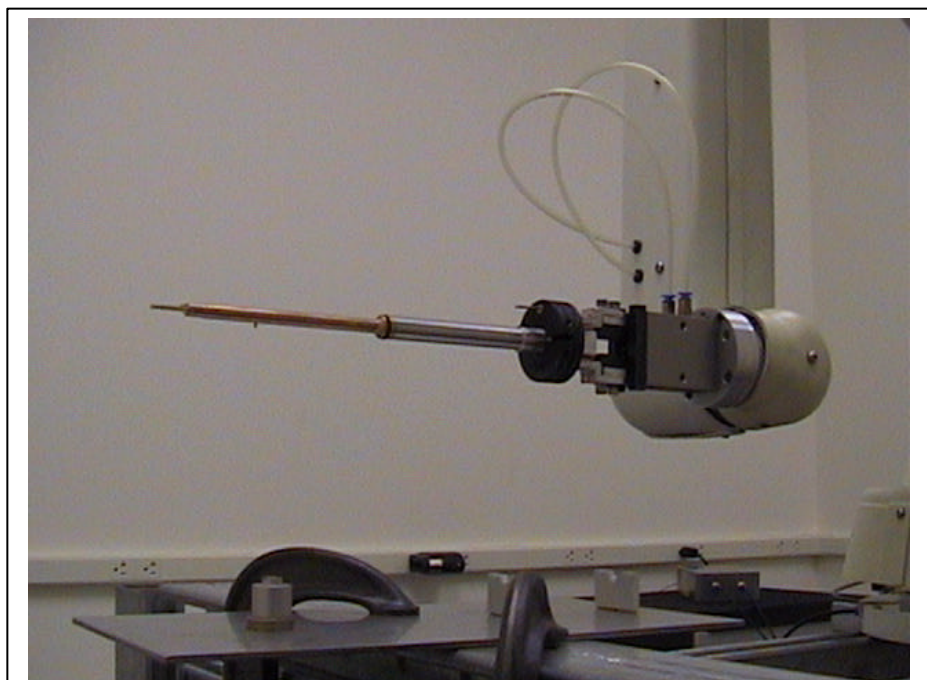


Fig 3. Robotic arm picking up specimen holder.