The Clockwork Crystallographer

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Motivation:

or: When The Only Tool You Have is a Robot, Every Problem Looks Like a Toyota Chassis

- **Reduce "Labor Content"**
- **Protect Workers from Danger**
- **Increase Throughput**
- **<u>Improve Yield</u>**

Background:

Suggested by Dr. Bernhard Rupp-

- **Minimize Late Stage Damage**
- **<u>Lower Crystal Size Threshold</u>**
- **Refine Crystal Conditioning**
- **Speed-Up the Process**

Funded by the NIH via an STTR Grant

Basic Project Goal:

Develop a Robotic System Capable of Harvesting Protein Crystals

Automatically

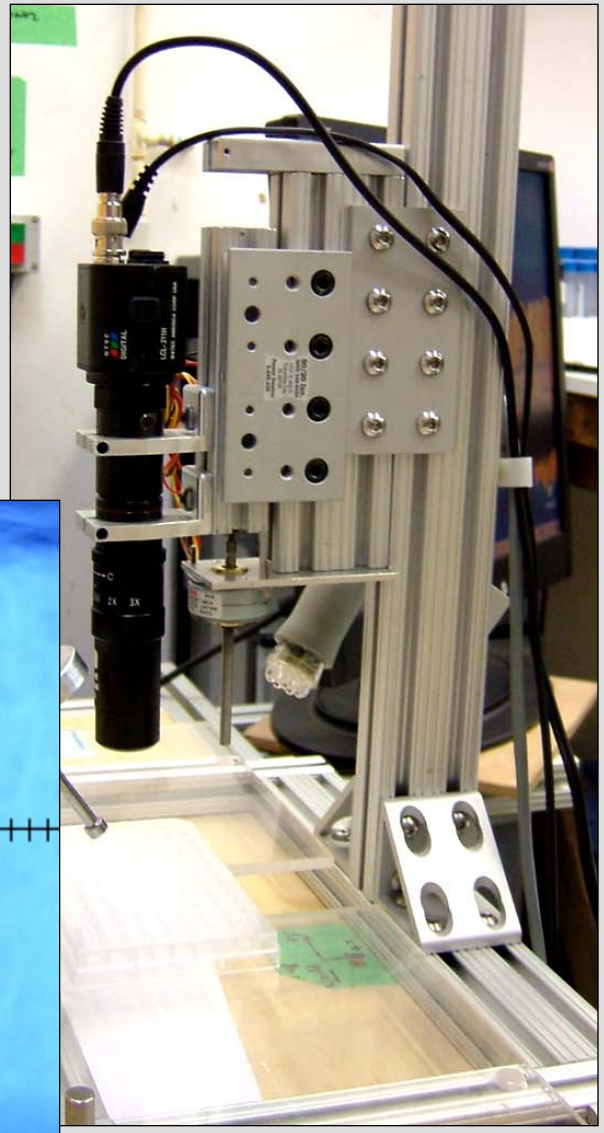
Constraints:

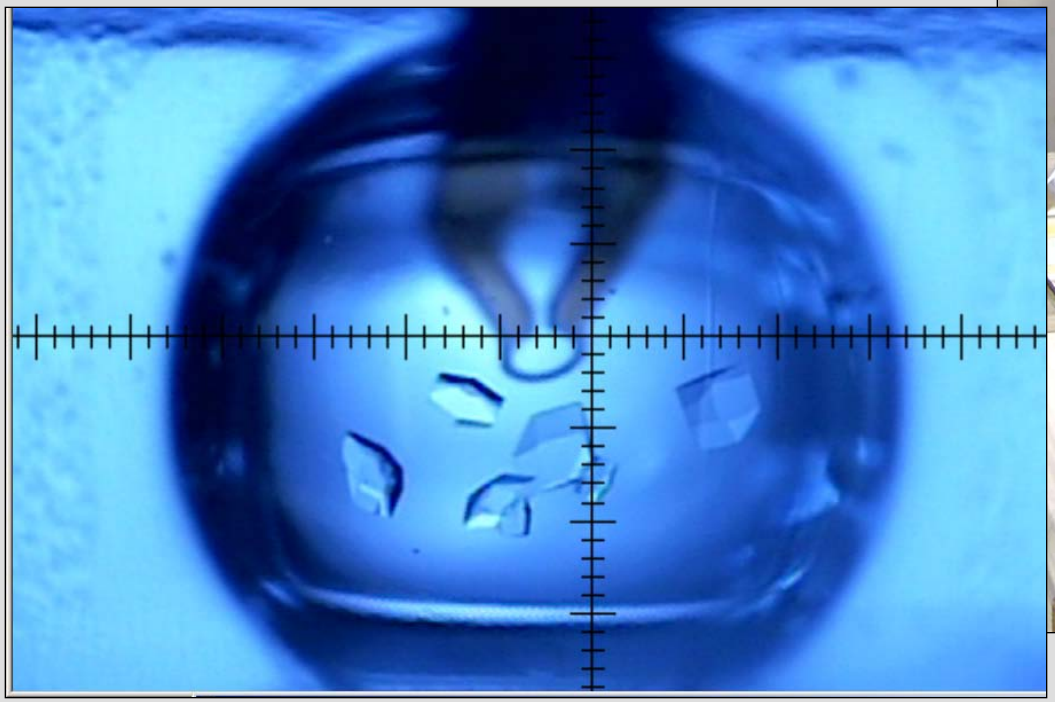
- **Compatible with Existing Hardware**
- **As Fast or Faster**
- **As Small or <u>Smaller</u>**
- **Affordable**

Design Foundations:

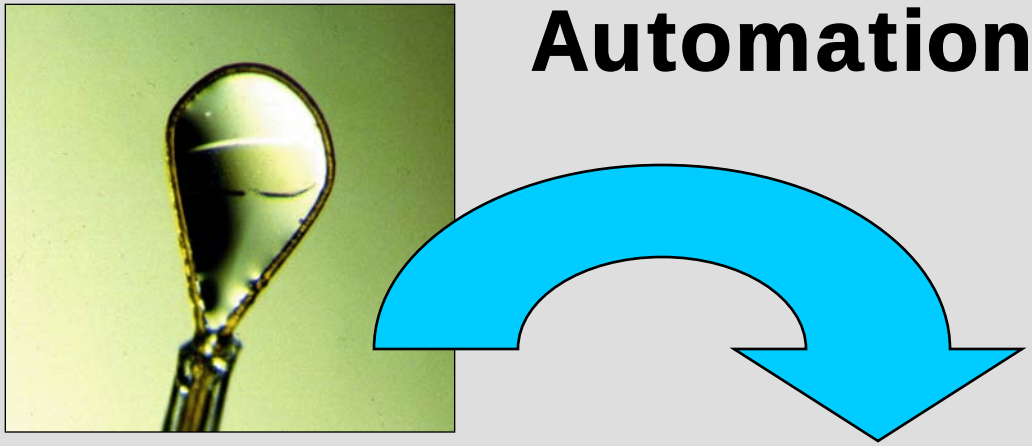
- **High-Resolution Six Axis Robot**

- **Imaging System Link With Machine Vision**

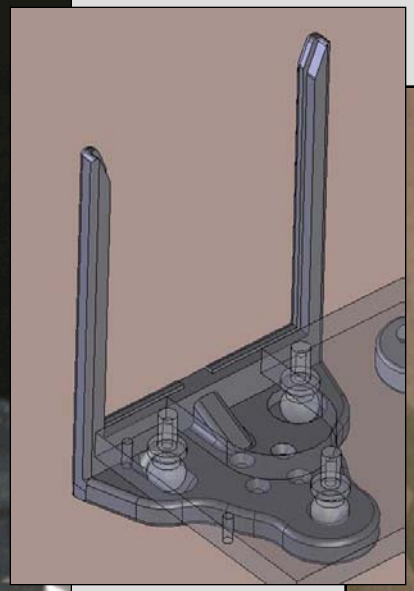


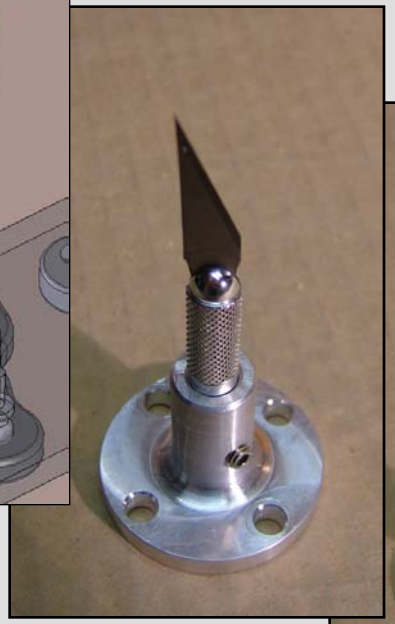


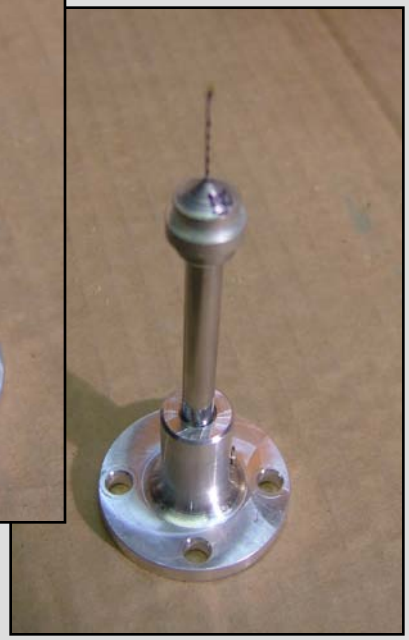
Automation-Friendly Loops



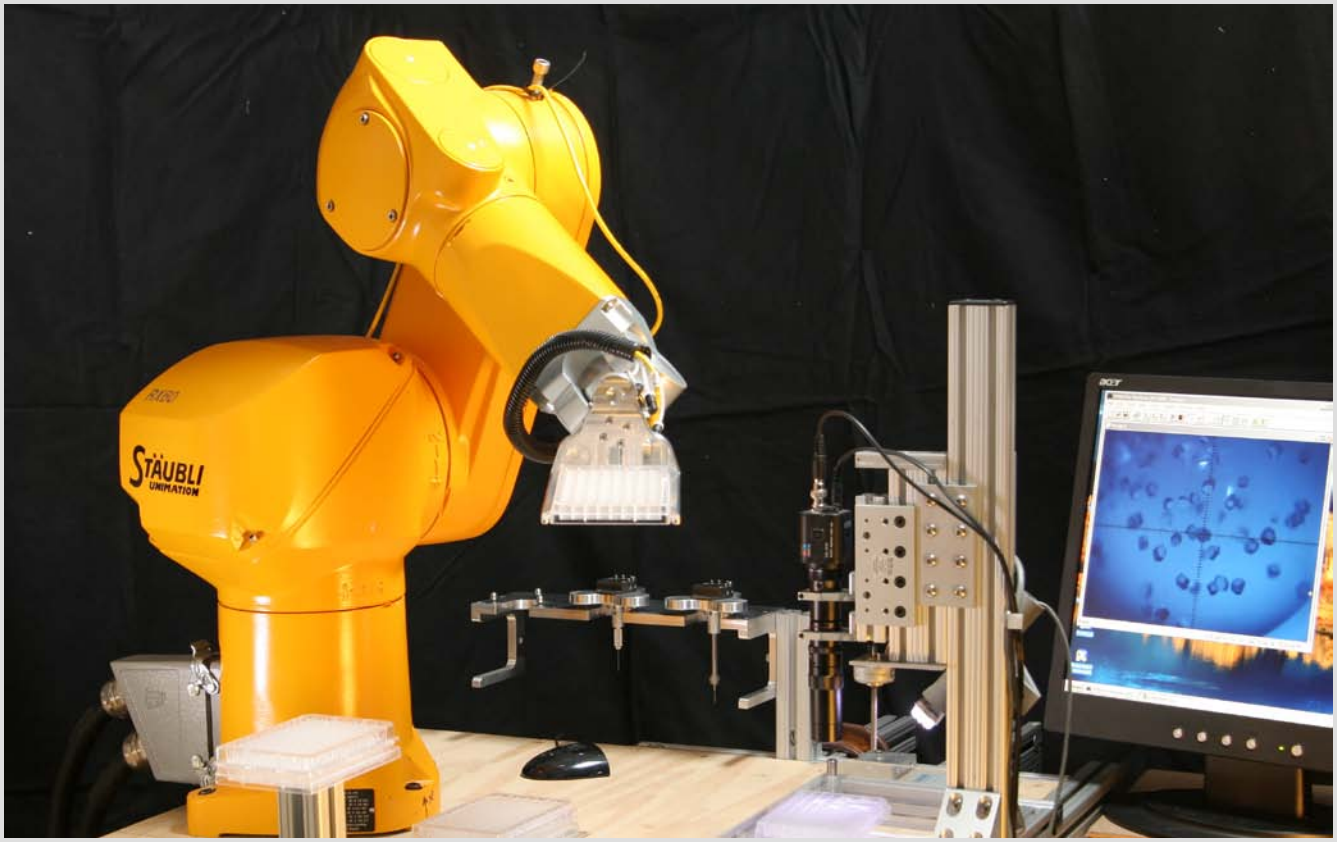
Automated Tool Exchange





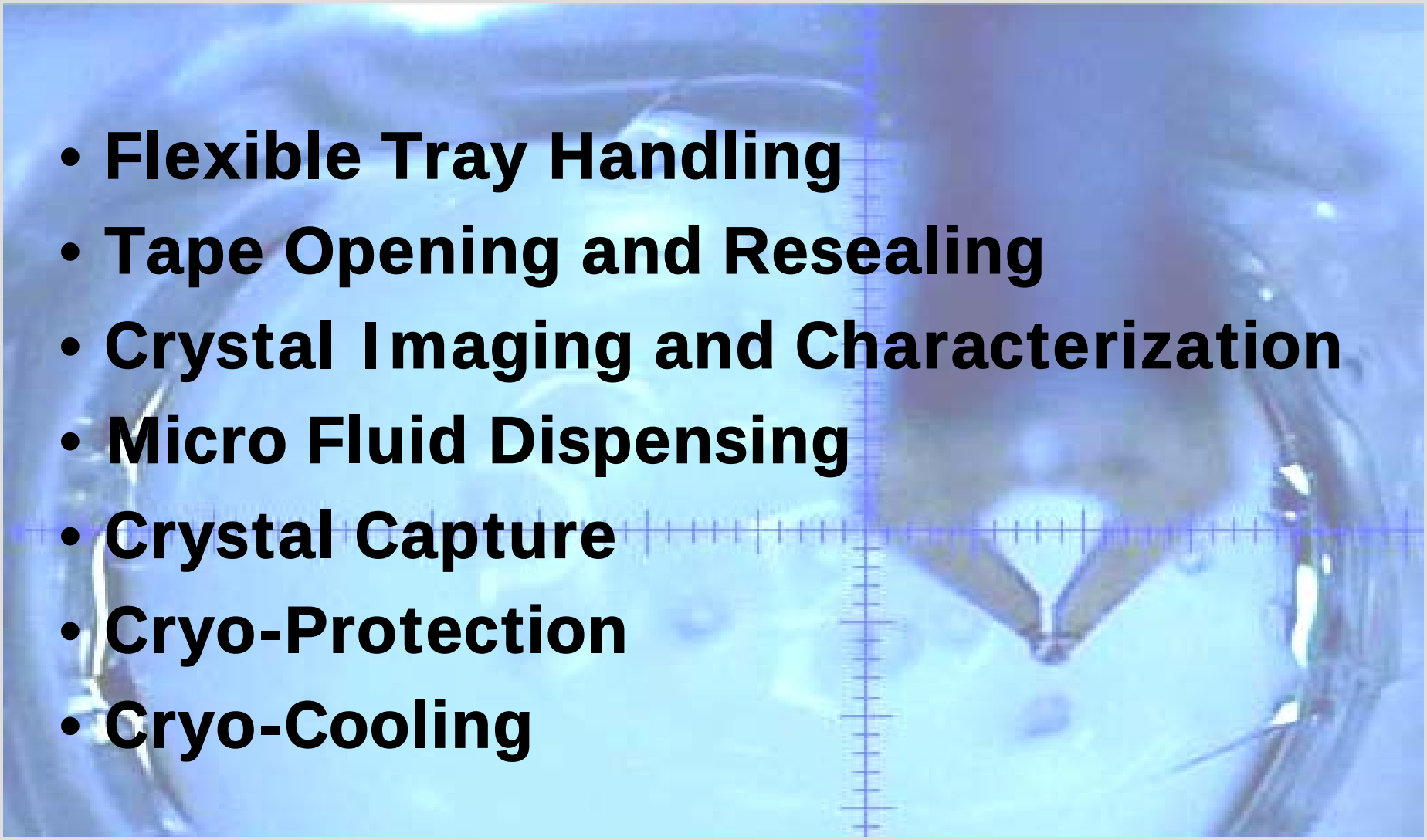


Putting it All Together:



The Universal Micromanipulation Robot

Realized Automated Capabilities:



- **Flexible Tray Handling**
- **Tape Opening and Resealing**
- **Crystal Imaging and Characterization**
- **Micro Fluid Dispensing**
- **Crystal Capture**
- **Cryo-Protection**
- **Cryo-Cooling**

Next Step… a Commercially Viable System

How Can We Keep

<u>Cost</u> And <u>Complexity</u>

At a Reasonable Level?

The 90-10 Rule….

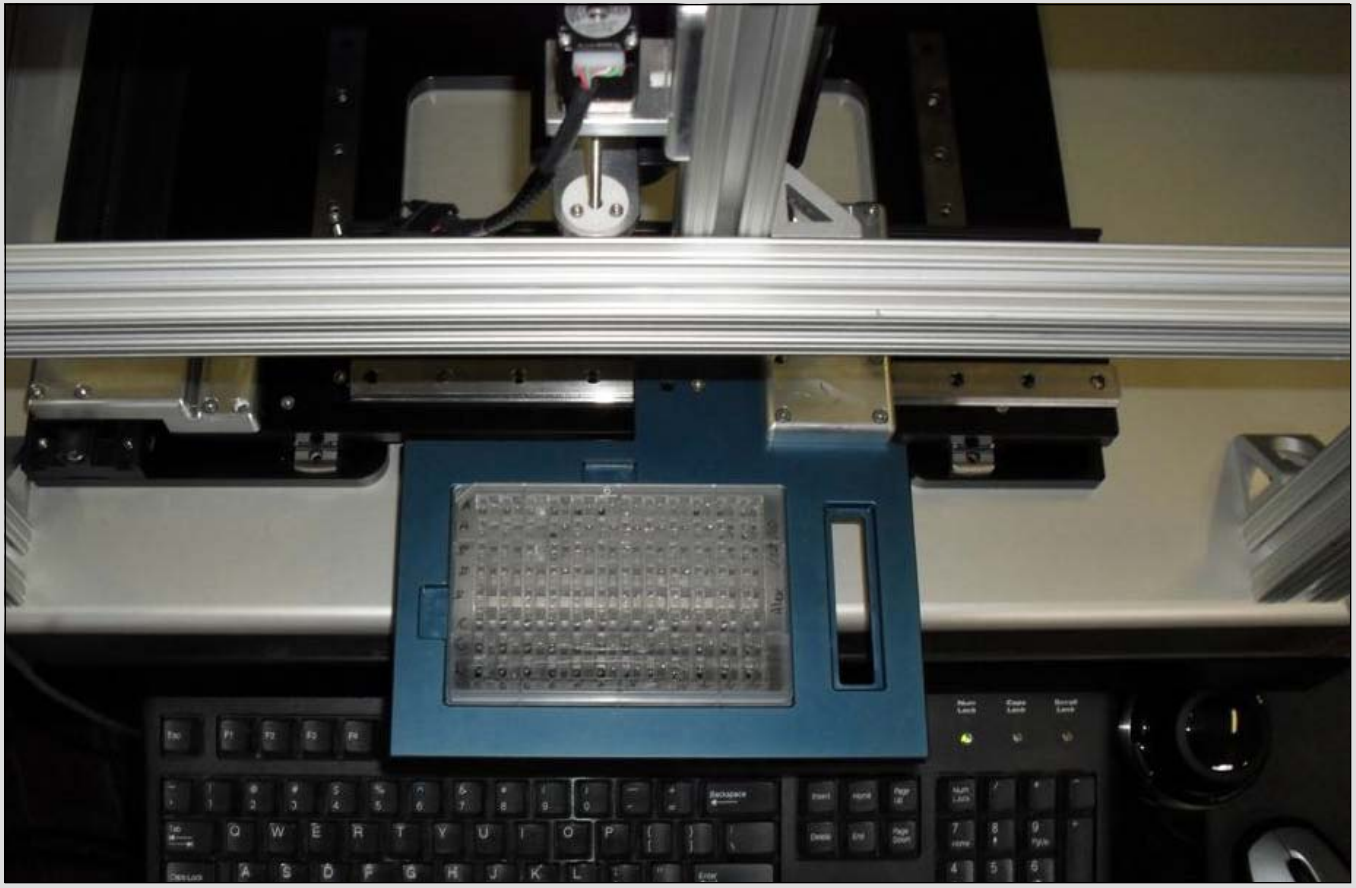
When Buying a Bicycle, One Gets 90% of the Performance for the First $1000…

And the Remaining 10% for the *Next* $1000…

The Commercial UMR

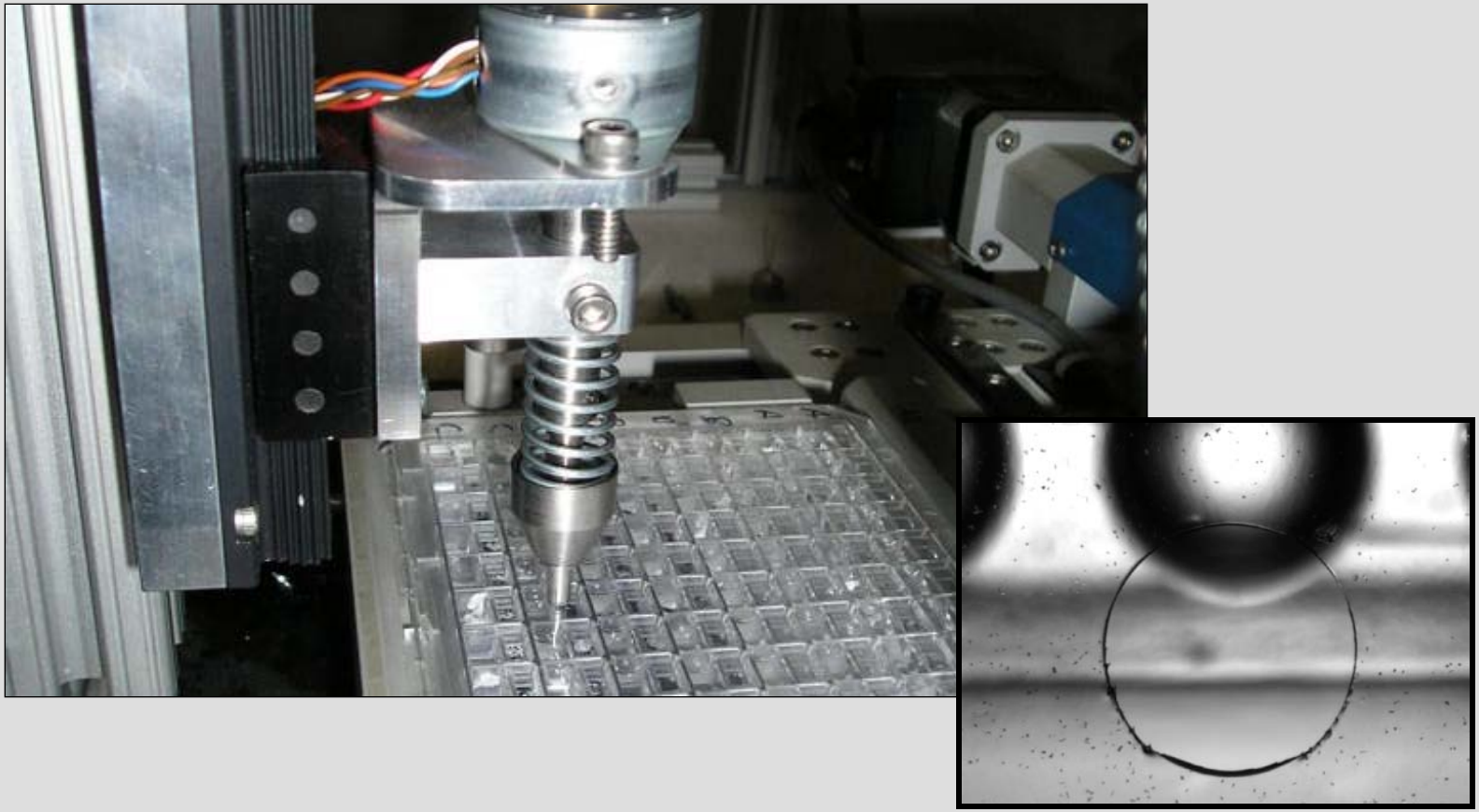
Predicated on the New Stäubli TX60 Robot

Trays Are Manually Loaded/Unloaded...



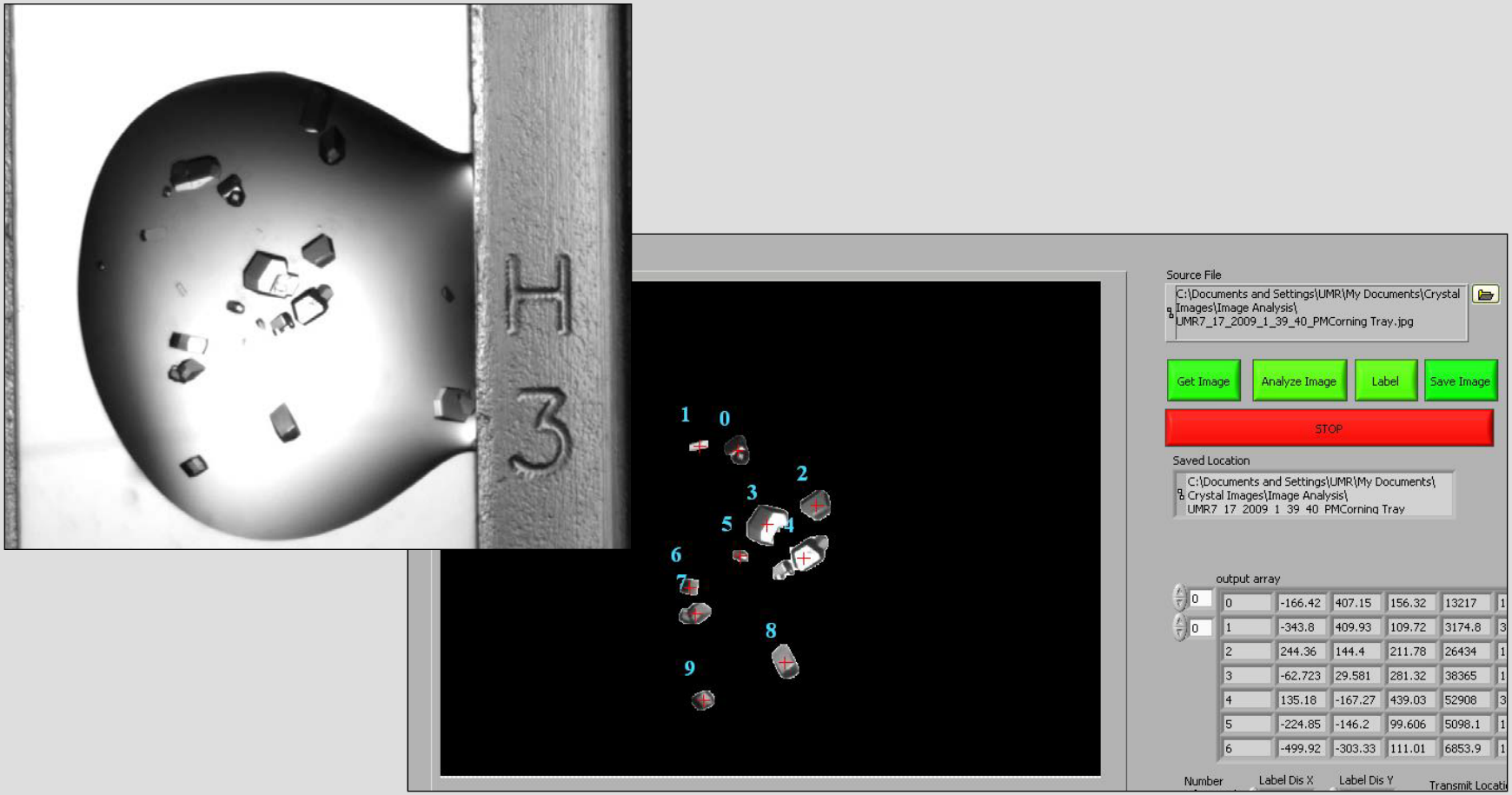
...But Automatically Positioned

Wells Are Automatically Opened…



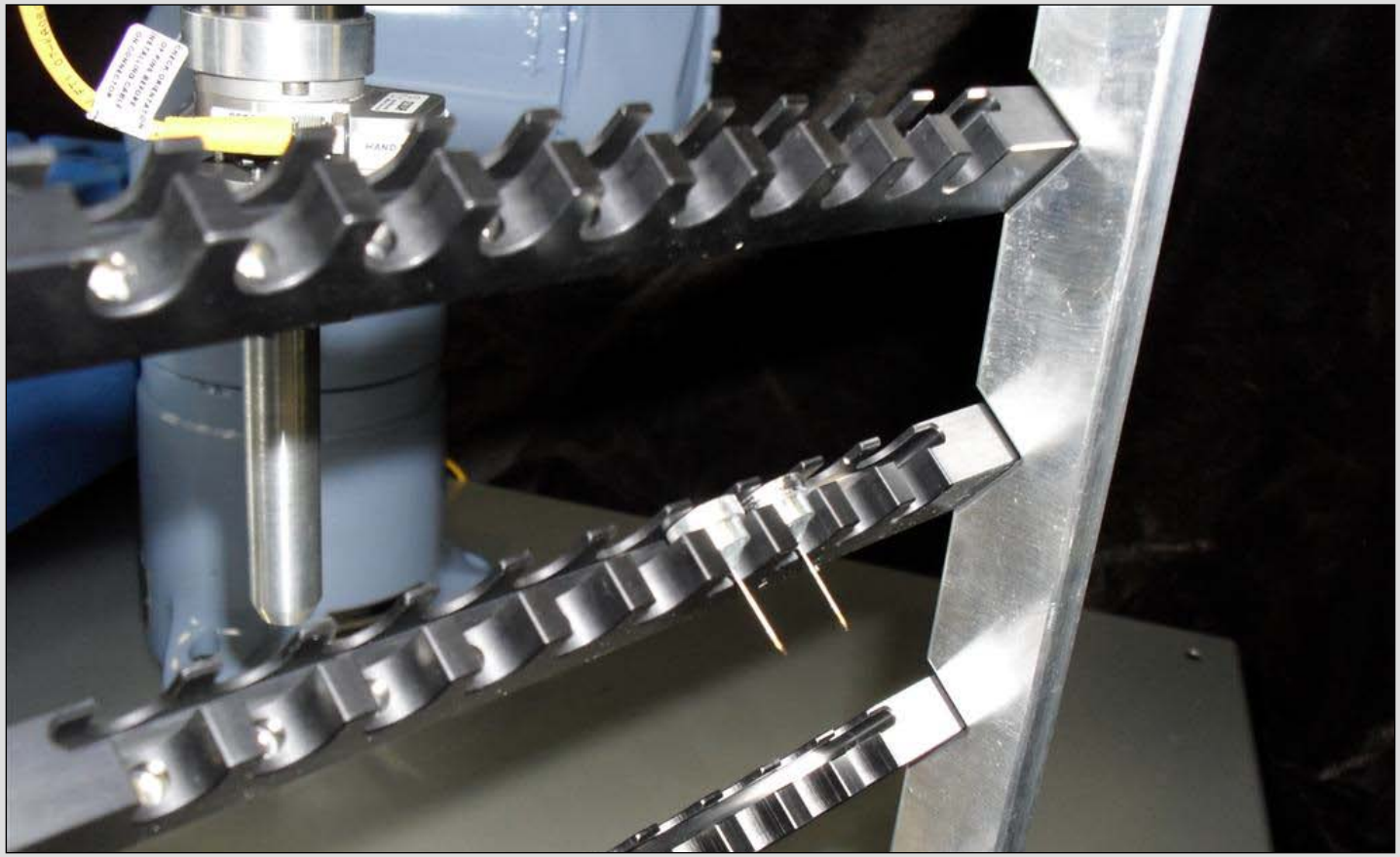
…But Manually Sealed

Crystals Are Automatically Measured…

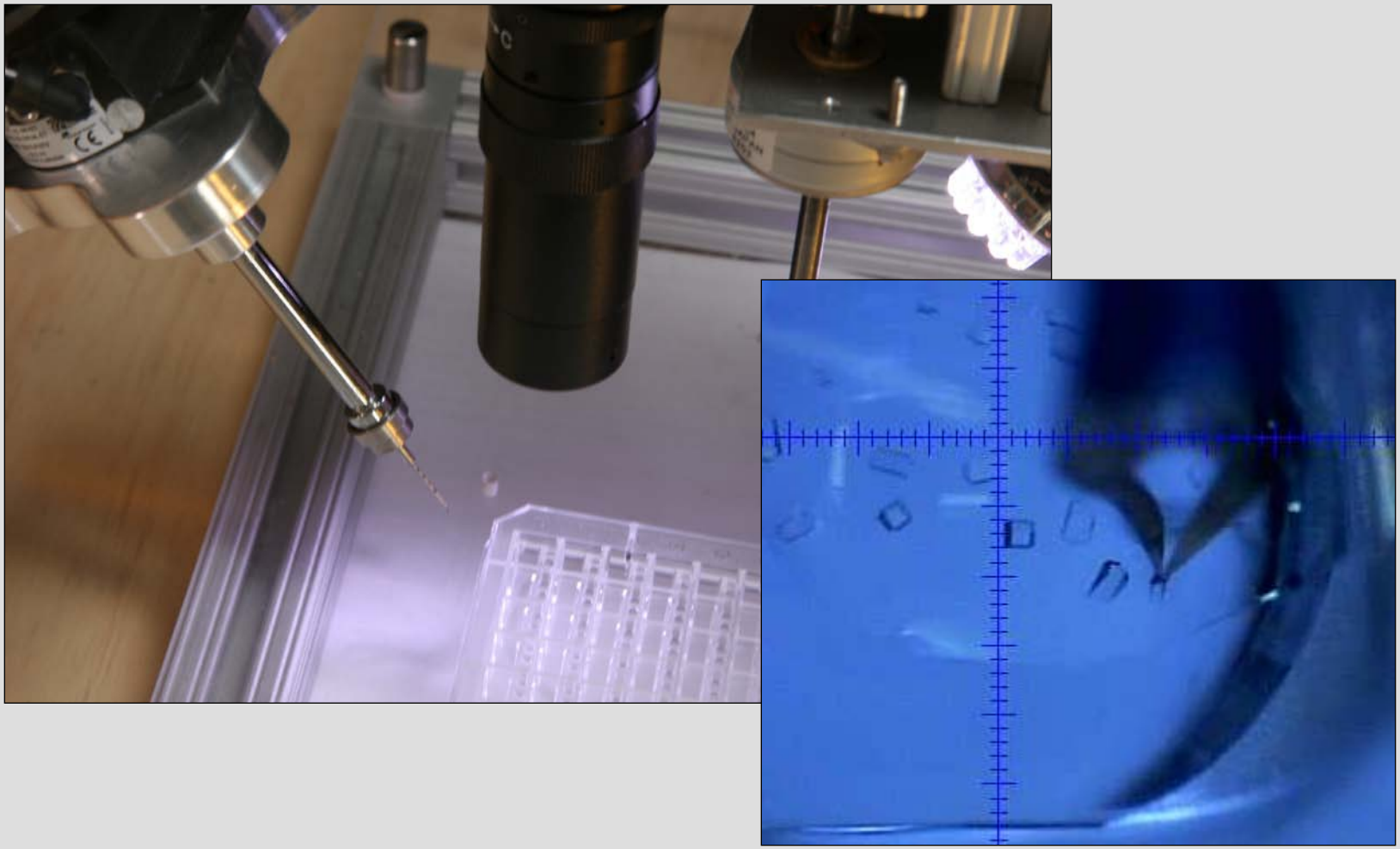


…But Targets Are Operator Selected

Harvesting Tips Are Automatically Chosen to Match the Size of the Target Crystal……



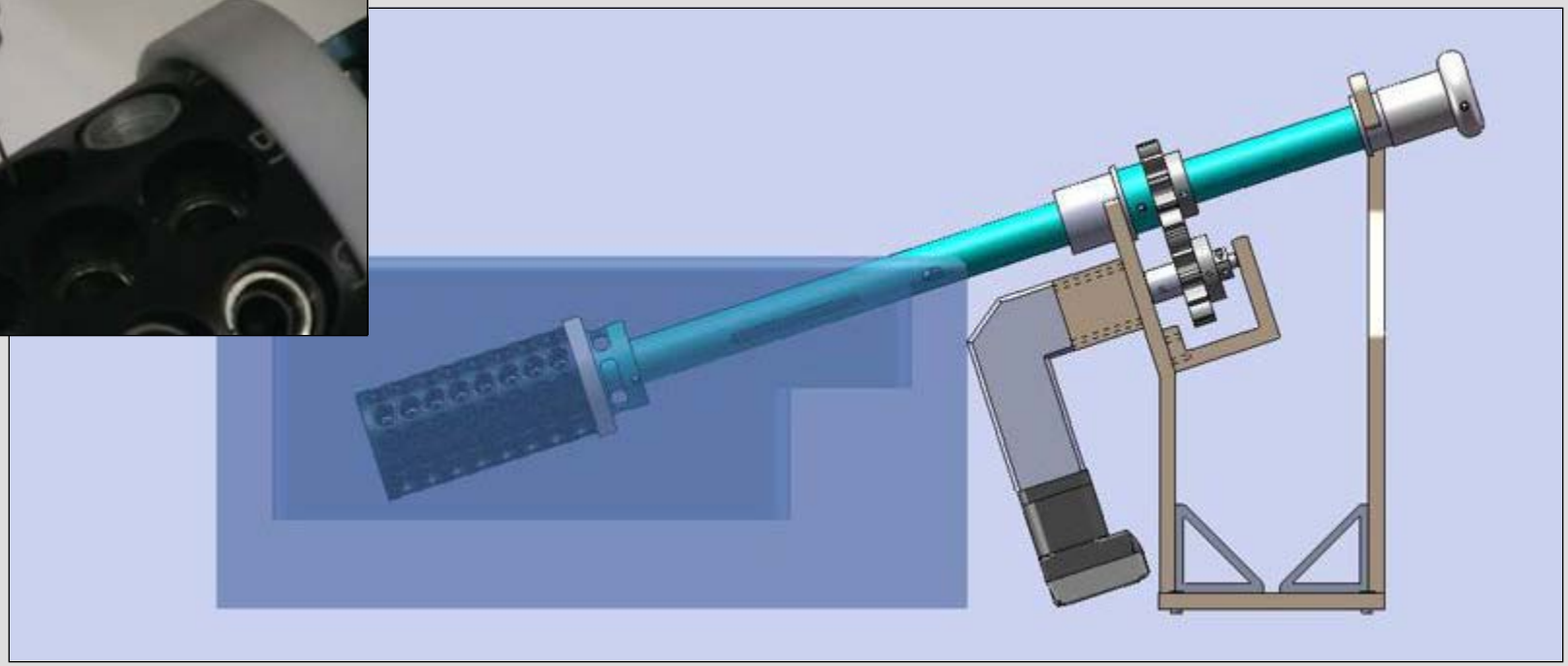
Harvesting is Performed by the Robot…



…But Directed by the Operator

Cryo-Protecting May be Automated Drip *or* Conventional “Dip and Swish

Cryo-Cooling is Fully Automated



Current Status

First System Goes Operational This Week

(Should Be) Capable of Harvesting Crystals Smaller Than 5 Microns

Beta Testing at Scripps This Summer

The Path Forward

Refine the System Based on Feedback from Scripps

Enhanced Imaging (with JH-APL)

Automated Target Selection

Advanced Cryo-Cooling Protocols

Robot Directed Ligand Application

Seamless Integration with Upstream Process Automation

The Ultimate Goal (Remains)…

Endow the Robot with Complete Autonomy

A fully-automated UMR capable of anchoring a "lights out" crystallography production line

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Thank You

Square One Systems Design

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