NanoPack for NanoView: Problem Definition and Requirements Review

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***Abstract*—As NanoView expands and offers their services to more customers, they will need to ramp up production of their signature product, which is a specially treated silicon chip that allows their customers to analyze biological samples. The current production process for these chips includes a step where a lab technician must use tweezers to manually move chips from the internal carrier called a *traveler* into their packaging for shipping called *clamshells*. This is both labor-intensive and error-prone. Our proposed solution is an automatic packaging device that is 10 times faster than human-packing and resistant to error when placing chips.**

I. NEED FOR THIS PROJECT

IN the field of bioscience, there is a demand for precise portable cell imaging technologies. Our client, NanoView BioSciences™, has developed a proprietary imaging technology that allows labs to either take in-house samples and then process them with the help of a specialized machine, or send them to NanoView for analysis. This imaging process involves placing the desired biological medium onto a specialized silicon chip, and then inserting the chip into the machine for analysis. The machine is capable of detecting exosomes as small as 50 nanometers. It can also identify up to 5 separate biomarkers on the sample using fluorescent light and dye. This technology allows NanoView to command a competitive advantage in their field. Hence, it is imperative for the company to expand production in the future.

Allowing our client to increase the amount of chips they can manufacture will allow them to service more customers, which in turn helps biosciences research on a whole. Currently one of the most infamous price disparities between cost of production and consumer prices exists in the world of pharmaceuticals. One reason for the high consumer price is the sheer cost that pharmaceutical companies face when developing new drugs. Lowering the cost of development has multiple benefits for the market and society. First, it allows a more competitive drug market so that medium size pharmaceutical companies can be more viable. Additionally, it incentivizes large pharmaceutical companies to lower prices or take more risks when attempting drug development. NanoView's flagship product allows researchers to gain much of the same information that they would from a Scanning Electron Microscope(S.E.M.) for a fraction of the cost and time spent training researchers. They also provide a wider view field of view than a S.E.M., leading to a faster development cycle for researchers.

Currently NanoView is experiencing a manufacturing bottleneck. To get the product to the market more efficiently, NanoView started off doing most of their production by hand. As they have grown, they have attempted to increase throughput at each step in their production line. To decrease bottlenecks, they have decided to have a central tray that carries chips between manufacturing processes. The manufacturing processes are conducive to this model as many of them involve scanning the chips or coating the chips (the chips do not need to be removed from the tray). One of the final processes is packaging these chips to send out to the customer. This step is causing a restriction on output which our project aims to alleviate. Currently chips are pulled from the tray by hand, checked visually against a spreadsheet, and then placed in their corresponding packaging. This process is vulnerable to human error, ties up employees on menial tasks, may damage the chips, and most importantly is slow. We aim to automate the final packing step, thereby increasing the speed at which it is performed. This will allow NanoView to increase throughput of their chips and subsequently grow as an organization. We hope this will make their novel technology accessible to more people and thus help researchers to achieve scientific breakthroughs in the biosciences field.

II. Problem Statement and Deliverables

A. Problem Statement

NanoView has already partially automated many of the manufacturing processes preceding the final packaging of these chips into the clamshells (packaging). Our goal is to automate the process of manually using tweezers to place chips from the traveler into clamshells. We will automate it with a mechanical device that is able to preserve the precise nature of the previous process, seamlessly integrate into the production flow, remove chance of human error, and work at a faster rate.

B. Deliverables

To accomplish our goal it is important for us to do the following:

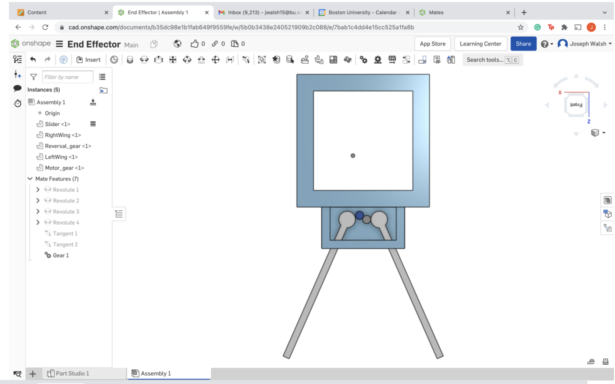
1) Increase the throughput of clamshells from 100 chips placed in eight hours to 1000. This would be a 10x increase compared to current speeds.
2) Create a machine that will package these clamshells with a least the same level of care that a human packer uses.
3) Create a system to check chip number so that the correct chips get placed into the correct clamshell.
4) Ensure that there is no contamination of chips during this process.
5) Make sure that this machine will fit in the client's manufacturing facility.
6) Have an easy method of controlling parts of the packaging process to enable the client to alter elements of their manufacturing process down the line.
7) Integrate the packaging process into the existing manufacturing pipeline.

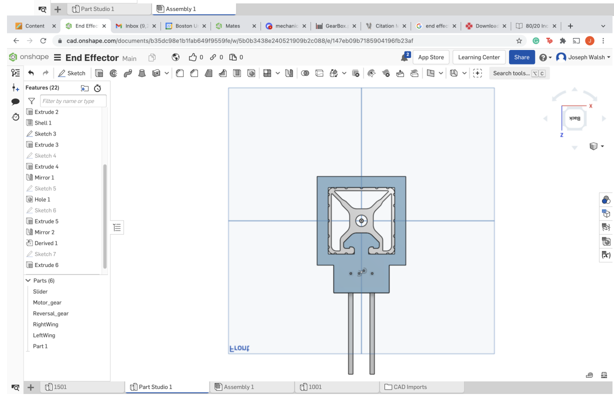
To accomplish these goals we will build a machine that packages chips into clamshells. It will use computer vision (depth and position mapping as well as edge detection) done on a dedicated computer to allow an operator to load it with empty clamshells without a large degree of precision. It will also have an associated software suite that allows the operators to make changes to the packaging process as well as give feedback about the current performance of the machine. This machine and the software package that supports it will be called NanoPack and will be delivered to our client.

III. Visualization

A. Mechanical Visualization

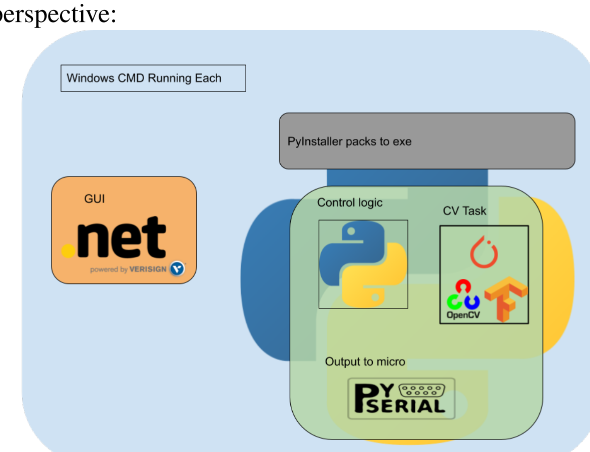
1) End Effector Design: The images below show a preliminary design of the final product we plan to use to transport the chips. It will slide along a 1.5"SQ bar of 80-20 and the "wings" will be swung down to pick up the chips and then back up to release.





B. Software Visualization

1) Software Stack: The below graphics are meant to illustrate the layout of our software stack from a programming perspective:



2) Software Flow Diagrams: The below graphics are meant to illustrate the layout of our software's inputs and outputs as well as serve as a rough diagram for the pipeline of our data-processing:

IV. Competing Technologies

A. Microscopy Competitors

Two major competitors were mentioned by our client:

Fig. 1. Flow diagram for the NanoPack control setup

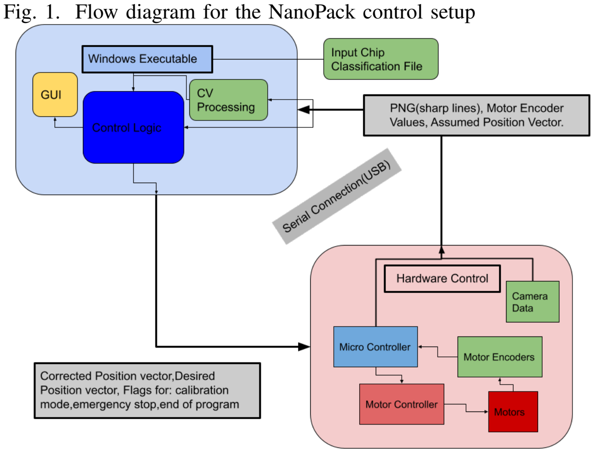
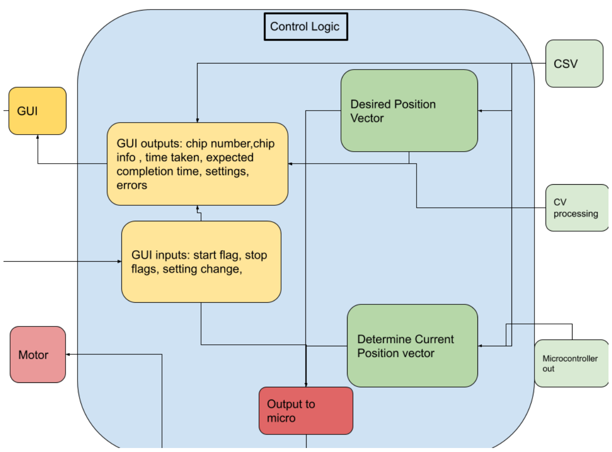


Fig. 2. Flow diagram for the NanoPack control setup zoomed in on the Control logic module



1) Nanoparticle Tracking Analysis(NTA): .
Nanoparticle Tracking Analysis (NTA) microscope utilizes the properties of both light scattering and Brownian motion in order to obtain the nanoparticle size distribution of samples in liquid suspension. These microscopes are manufactured by various companies such as Malvern Panalytical [1] or ZetaView [2]. NanoView is able to measure details with greater accuracy at smaller sizes than NTA microscopes, and is therefore able to detect biomarkers that NTA cannot such as the CD9 gene.

2) Scanning Electron Microscope: .
The scanning electron microscope (SEM) uses a focused beam of high-energy electrons to generate a variety of signals at the surface of solid specimens [3]. These signals can be parsed to reveal a variety of characteristics about the specimens such as chemical composition, external morphology (texture), and crystalline structure. An SEM is capable of measuring an area of 1 cm to 5 um at a spacial resolution of 50 to 100 nm. However, it is only able to measure the characteristics of solid objects. This device is able to measure at a smaller resolution than NanoView's solution. However, the cost of an SEM is exorbitant, ranging from $80,000 to $2,000,000 at its highest, with the average price of an SEM at $294,000 [4]. While specific numbers are proprietary information, NanoView is able to deliver its product to customers at a price point well below the average for an SEM, and therefore holds a competitive advantage in the market.

B. Packing competitors

Our team identified two major competing robotic technologies:

1) KUKA - Custom Robotics Solutions: .
KUKA is a German manufacturer of custom robotic solutions. They tend to design mobile, battery operated robots which are very expensive. They do not list prices on their website, but instead require their customers to reach out to them with their requirements for a robot, and KUKA returns with a price estimate for the product. They have created a wide variety of robots, used across many different industries to increase production, including a custom robotic gripper for handling Si wafers. We believe, however, we will be able to create a more efficient, stationary robot to meet NanoView's needs for a much lower cost than KUKA.

2) isel- Wafer Handler Series: .
isel is another German robotics company, and their wafer-handler series is as close to a direct competitor as we could find for our robot. The isel robot can be purchased in several different sizes with up to 4 degrees of freedom. The robot moves the chips via 1-3 rotating arms attached to a cylinder which can move the arms up or down. The robot also comes with specialized end effectors used to scoop up wafers and move them one by one. We believe our robot will be smarter and faster than the isel robot and will be able to cover a much larger area than their small robots. Coming from above the system will allow for us to move faster and not have to worry so much about dropping/damaging chips with the spatula-like end effector of the isel robots.

V. Engineering Requirements

A. Software Requirements

1) We will need to create a graphical user interface that can be easily be run on any Windows machines. This can be done in C# using the .NET framework. This will create a Windows form application that can be compiled into an executable that can be ran without the need for lab technicians to install specific software onto their computers.
2) For our machine learning components, we will be using Python, as opposed to MATLAB. Although NanoView programs are built in MATLAB, we do not believe that MATLAB is optimal due to the much greater machine vision library support available in Python. Some popular machine vision libraries that may prove helpful to us are PyTorchCV, OpenCV, and PyTesseract. PyTorchCV is simple and easy to use for images. OpenCV has more options and can also be used for realtime video analysis. Finally, PyTesseract will be able to do optical character recognition. This may be useful if we need to read the characters on the chips, however, we are currently undecided if this will be a part of our implementation.

3) We will also use Python for reading and writing to our microcontroller serial ports. The library we will be using to do this is PySerial, and is compatible with an Arduino or any other microcontroller that we decide to use.
4) For our microcontroller firmware, we will be writing in Arduino code. Although we could use C, Arduino code should be able to achieve the same results while being much simpler and easier to write.

B. Hardware Requirements

1) Our product will require programmable microcontrollers which can carry out all the functions in our computer vision code. These microcontrollers will be connected via wiring to servo motors which will be used to move our robotic arm.
2) A circuit device will be needed to connect the microcontrollers to the motors. Our current plan is to use a solderless breadboard for our circuit connection prototype, and we may potentially switch to a solderable one for our final design.
3) Wiring will be necessary to electrically connect all of the components of our product. A connection will have to be made between the computer which a NanoView employee will operate and the microcontrollers which will take in the instructions. Wires will also be required to connect the microcontrollers and the motors which will allow for our robot to move. The gauge of our wires will decided once we determine the torque and speed which our motors will operate.

C. Mechanical Requirements

1) NanoPack: Our product requires a way of moving the chips from the traveler to the clamshells quickly and safely. NanoPack is the name we have given to the robot we will build to accomplish this. The robot will consist of an end effector with two ”wings”, meant to mimic tweezers, attached to gear train driven by a servomotor. These wings will swoop down to pick up a chip, and back up to release the chip into its slot in the clamshells. The effector will slide along a frame build from 80-20 Aluminum to get the chips from point A to point B.
2) A vital part of our product is the computer vision software, which will require cameras to view the workspace. We will build a frame surrounding the NanoPack robot which will hold the camera(s) above the traveler and clamshells at a distance far enough away to see the whole field, but close enough to read the number off of the chips.

VI. Conclusion

NanoPack is a packing machine built specifically for use by NanoView BioSciences for the purposes of automating transfer of chips from lab containers to smaller packages to be sent to consumers. This is necessary because these chips are NanoView’s main product, and packing of them is currently done manually and is extremely slow. Our solution will greatly increase the volume of chips the company is able to put out. NanoPack will consist of a precision robotic arm capable of picking up and transferring the chips as well as a camera-based computer vision system to guide the robotic arm and ensure that all chips are placed properly.

Acknowledgment

The authors would like to thank David S. Freedman for sponsoring this project, providing us with the information needed to make this project possible, and for allowing us to visit the NanoView BioSciences facility to demonstrate the process of removing chips from a traveler and placing them in a clamshell.

We also would like to thank professors Alan Pisano, Michael Hirsch, and Osama Alshaykh for their continued guidance and mentorship throughout this project.

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