A Multi-Channel Microfluidic Flow System for Facilitating and Studying Single-Particle Kinetics

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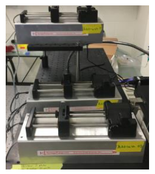
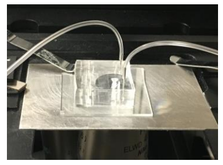
Introduction

A protein's capability to perform specific biological functions depends on whether or not it can properly aggregate/disaggregate with other proteins. This aggregation, however, can be incredibly complex and has become a widely studied field, enabling researchers to obtain a stronger understanding of disorders such as Alzheimer's and Parkinson's.[1] One way in which this aggregation can be considered is through the observation of the macromolecular interactions between individual particles, otherwise known as single-particle kinetics.[2] When taking the measurements associated with this field of study, it is useful to have access to an environment where the rate and direction of fluid flow can be manipulated to simulate various macromolecular interactions.



Microfluidic Flow System (NE-500X2)

Microscope view of the H-Channel in a microfluidic chip



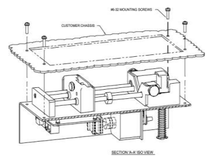
PDMS Microfluidic Chip (Fluid-Flow Testing)

To set up this environment, we have developed a LabVIEW user interface to communicate with a physical system of three OEM syringe pumps. Here, we attempt to observe the stability of the fluid flow facilitated by this system, so we can determine if it can be used for the observation of rapid single-particle kinetics and can thus be applied to the overarching study of protein aggregation.

Microfluidic Flow System Overview

Physical System

To facilitate the fluid flow, three NE-500X2 syringe pumps (New Era Pump Systems) were networked and connected to a computer port. To be able to observe the stability of the fluid flow under a microscope, the syringes were filled with a fluorescent bead solution and were lead into channels in PDMS microfluidic chips.

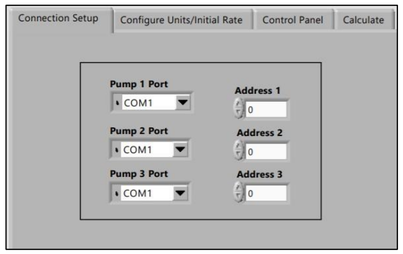


NE-500X2 (OEM Syringe Pump)

User Interface

The computer interface was designed with LabVIEW 2019, a system-design platform used for visual programming. Using LabVIEW allows users to modify the code to integrate triggers for other lab hardware, as well as to couple the code with related software, such as Measurement Studio and modeFRONTIER.

Connection Tab UI



The connection tab serves as the starting point for the interface. Here, users can connect up to three OEM syringe pumps. The addresses of each pump should be set individually using the "Configure Address" VI provided on the National Instruments website.

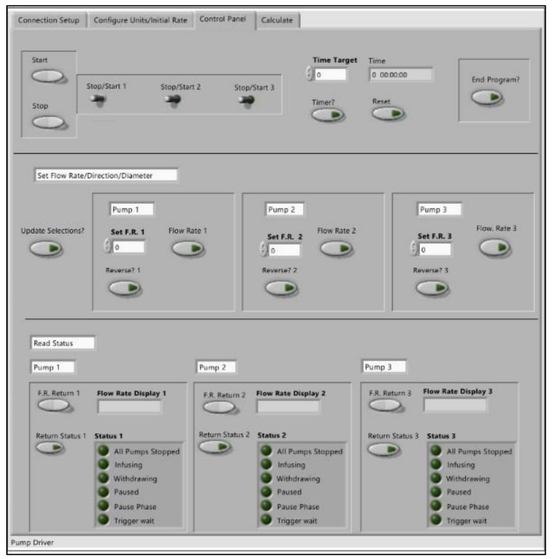
Networked Wiring Arrangement

If the OEM pumps are all wired to each other, users should set each port tab to the COM port to which the first pump has been connected.

Isolated Wiring Arrangement

If the OEM pumps are all wired individually to a computer, users should set each port tab to the COM port to which each pump has been connected.

Control Panel UI

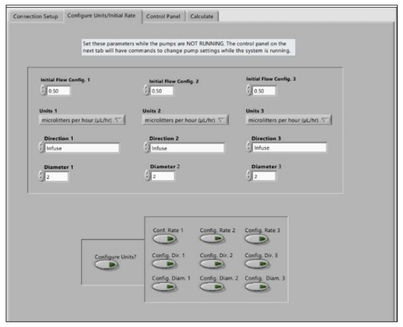


Control Panel Functionality

- Start/Stop Function – Users can update all three pumps at the same time by setting each pump to the desired state and selecting "Start" or "Stop."
- Timer Function – Stops the pumps that have been set to "stop" after the inputted time (in seconds) has passed. Has a reset sub-function.
- Update Flow Rate Function – Updates the magnitude and direction of the flow rate while the pumps are running.
- Read Status Function – Returns the current state of each pump, distinguishing between infusing, withdrawing, and various stopped states.

Configure Units/Initial Rates Tab UI

Before and between each test, users should use the "Configure Units/Initial Rate" tab to configure the initial flow rate, direction, and syringe diameter for each of the pumps. Once all the changes have made, users should select the single update trigger to send all of the configurations at the same time.

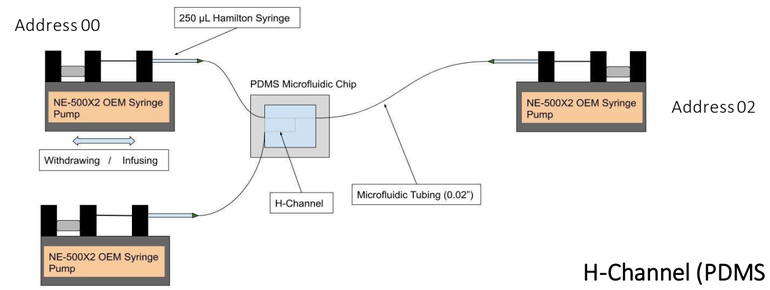


Three-Input Flow Test

Presets

- 00 and 01 Infusion Rate: 0.0005 µL/hr
- 02 Withdrawing Rate: 0.001 µL/hr
- Fluorescent Dye Bead Solution Concentration: 0.10%

Syringe Pump Setup



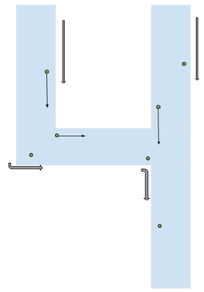
Flow Rates in Microfluidic Chip

250 µL syringes (2.30 mm inner diameter)

Maximum: 250 mL/min
Minimum: 0.001 µL/hr

Flow Stop Time: ~3.5 – 4.5 seconds
Flow Reversal Time: ~5 – 6.5 seconds

H-Channel (PDMS Chip)



Conclusions and Future Directions

The results of the H-Channel test indicate the system can facilitate a minimum flow rate of about 0.001 µL/hr, providing an environment suitable for the observation of rapid single-particle kinetics.

Future work would include altering the code to implement a more robust set of functions, integrating other laboratory equipment to obtain more data, and using other syringe pump models that can support even lower flow rates.

References

[1]: *Morris AM, Watzky MA, and Finke RG. Protein aggregation kinetics, mechanism, and curve-fitting: a review of the literature. Biochimica etBiophysica Acta, 1794:375–397, 2008.*
[2]*: Puchalla, Jason & Krantz, Kelly & Austin, Robert & Rye, Hays. (2008). Burst analysis spectroscopy: A versatile single-particle approach for studying distributions of protein aggregates and fluorescent assemblies. 105. 14400-5. 10.1073/pnas.0805969105.*

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