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Automation in Everyday Laboratory Routine

Laboratory Manual

MSc Chemistry
University of Vienna

WS 25/26

Contents

Safety Notice

General Safety

This course involves the use of hazardous chemicals, pressurized systems, and UV radiation. Standard laboratory safety rules (goggles, lab coats) apply at all times. Consult the Material Safety Data Sheets (MSDS) for all chemicals before use.

Specific Hazards in Flow Systems

- **Pressurization:** Flow systems can build pressure rapidly if a blockage occurs (e.g., precipitation). Always monitor the system visually and via pump feedback. Never disconnect a pressurized line pointing towards yourself.
- **Leaks:** Capillary connections are prone to leaking. Always perform a "solvent-only" leak test before introducing reactive chemicals.
- **Solvent Compatibility:** Ensure all wetted parts (syringes, tubing, fittings) are compatible with the solvents used. We primarily use PFA, PTFE, and glass, which are highly resistant.

Good Automated Laboratory Practice (GALP)

- **Verification:** Do not trust the display. Verify flow rates gravimetrically (Exp 7) before critical runs.
- **Logging:** Record the actual parameters (e.g., measured room temperature), not just the setpoints.
- **Steady State:** A flow reactor takes time to equilibrate. Data collected before 3τ (three residence times) has passed is invalid due to dispersion.

Topoi of the Imminent: Futures Visions of Advancement

In the lexicon of classical rhetoric, *topoi* are the "places" where arguments reside. In the context of the contemporary chemical sciences, they are the loci of inevitable transformation—the conceptual territories where the future of matter is currently being negotiated.

We stand at the precipice of a paradigm shift that transcends mere instrumentation. The transition from batch to flow, and from manual to automated, is not simply an upgrade in efficiency; it is a fundamental restructuring of the chemist's relationship with the material world. The traditional laboratory, defined by the stochasticity of the round-bottom flask and the artisanal "golden hands" of the operator, is yielding to a new topology: one defined by deterministic fluidics, algorithmic reproducibility, and the digitization of chemical space.

This manual serves as a navigational chart for this imminent terrain. It posits that the chemist of the future is not merely a manipulator of reagents, but an architect of autonomous systems. By integrating the precision of engineering, the logic of code, and the creativity of synthesis, we move toward a horizon where the laboratory becomes a programmable entity—a "Self-Driving" engine of discovery capable of navigating the vastness of chemical possibility with a speed and fidelity previously unimaginable.

These experiments are the first steps into that future. They are invitations to perceive the laboratory not as it is, but as it is becoming.

Vienna, 2025

Chapter 1

Introduction: The Digital Laboratory

General Information

For further information and detailed instructions, please consult the course repository:

`https://github.com/cosmopax/Automation_in_Everyday_Lab_Routine`

In the event of intractable technical difficulties that cannot be resolved through the provided documentation, inquiries may be directed to patrick.schimpl@univie.ac.at.

Requirement: It is strongly recommended to bring a laptop to all sessions.

1.1 Purpose and Scope

Welcome to "Automation in Everyday Lab Routine." This course is designed to bridge the gap between classical synthetic chemistry and modern process engineering. The traditional image of a chemist standing over a fume hood, manually adding reagents dropwise, is evolving. The laboratory of the future often termed "Lab 4.0" integrates digital tools, automated actuators, and continuous data streams to enhance scientific productivity [1]. This is not a course on industrial robotics. Instead, it focuses on democratizing automation: using accessible, modular, and often open-source tools [2] to automate standard unit operations such as dosing, mixing, heating, and sensing. You will move from being the manual operator of an experiment to the architect of an automated process.

1.2 The Pillars of Laboratory Automation

Why automate? Beyond the obvious benefit of labor reduction, automation introduces three critical advantages to chemical research:

1.2.1 Reproducibility

Manual synthesis is fraught with operator-dependent variables: the rate of addition from a dropping funnel, the consistency of magnetic stirring, or the precise timing of a quench. Automated actuators (such as syringe pumps) remove this human variability. A script

executed in Vienna will yield the exact same physical conditions as one executed in Boston, addressing the reproducibility crisis in science.

1.2.2 Safety by Design

Automation separates the operator from the hazard. By automating the handling of toxic reagents or energetic intermediates (e.g., diazonium salts), the risk of exposure or accident is minimized. In flow chemistry, the active inventory of hazardous material is often microliters, making thermal runaways physically impossible.

1.2.3 Data Density

A human observer might record temperature or pressure every 15 minutes. An automated sensor logs this data at 1 Hz (once per second). This high-density data reveals kinetic insights, transient spikes, and process deviations that are invisible to the manual operator.

1.3 Flow Chemistry as the Platform

To teach automation, we utilize Continuous Flow Chemistry. Unlike a batch flask, which is a static vessel defined by time, a flow reactor is a dynamic system defined by space and velocity [3].

1.3.1 The Concept of Residence Time

In a flow reactor, reaction time is replaced by Residence Time (τ). It is a deterministic value defined by the reactor geometry and the pump settings:

$$\tau = \frac{V_R}{Q} \tag{1.1}$$

Where:

- V_R is the internal fluidic volume of the tubing (mL).
- Q is the volumetric flow rate (mL/min).

By controlling Q via software, you control the reaction time with extreme precision. This turns the reaction coordinate into a programmable variable.

1.3.2 Process Intensification

Micro- and mesofluidic reactors possess massive Surface-to-Volume Ratios (S/V).

$$\frac{S}{V} \propto \frac{1}{r} \tag{1.2}$$

As the radius r decreases, the ability to transfer heat and light increases effectively. This allows for:

- **Isothermal Chemistry:** Highly exothermic reactions (e.g., nitrations, oxidations) can be run without heat accumulation.

- **Efficient Photochemistry:** Light penetrates the entire depth of the reactor (path length < 1 mm), accelerating reactions from hours to minutes.

1.4 Course Overview

You will progress through a series of modules designed to build your competency in automation:

- **Exp 1-2 (Kinetics):** You will use flow rates to rapidly screen reaction times and determine kinetic constants for a model reaction (DDM).
- **Exp 3 (Process Intensification):** You will use ultrasound and flow to accelerate the synthesis of a drug (Phenytoin) and manage solids.
- **Exp 4 (Multistep Synthesis):** You will "telescope" two dangerous reactions (Diazotization + Coupling) into a safe, continuous stream to make a dye.
- **Exp 5 (Multiphase Flow):** You will exploit the hydrodynamics of segmented flow to perform efficient biphasic oxidations.
- **Exp 6 (Hardware):** You will use 3D printing to create custom reactor geometries for droplet generation.
- **Exp 7 (Metrology):** You will learn to calibrate and verify your robots (Pumps).
- **Module 8 (Capstone Project):** An individual project where you choose a track—Code, System Design, or Theoretical Research—to apply automation principles to a specific challenge.

1.5 Assessment Structure

Evaluation is predicated upon the quality of group protocols and practical laboratory performance. Furthermore, proactive engagement and demonstrated initiative will be positively recognized.

1.5.1 Group Protocols

Experiments 1–7 are assessed as group work.

- **Submission Format:** Protocols must be submitted as a single, collective PDF per group.
- **Folder Naming:** This PDF must be placed in a single folder named according to the following schema:

  `25WS_Protocol_LastName_FirstName_of_all_members`

- **Upload Location:** Submit this folder to the course repository at:

  `https://github.com/cosmopax/Automation_in_Everyday_Lab_Routine/tree/students_deliverables/25WS/group_protocols`

Documentation of Collaboration: In the event that a student has performed experiments in a group other than their primary team, this must be explicitly documented on the first page of **both** relevant protocols (the primary group's and the host group's). It must be clear which student participated in or missed which experiment. Additionally, a `README.md` file must be included in the protocol folder, clearly illustrating the constellation of collaboration for each session.

1.5.2 Individual Achievement (Capstone)

Module 8 is an individual effort.

- **Folder Naming:** Your work must be submitted in a single folder labeled:

  `25WS_LastName_FirstName_LetterOfChosenTrack_TitleOfProject`

- **Documentation:** Include a `README.md` file briefly summarizing your effort and the project scope.

- **Upload Location:** Submit to:

  `https://github.com/cosmopax/Automation_in_Everyday_Lab_Routine/tree/students_deliverables/25WS/individual_achievement`

1.6 Comments on the Course

This course provides a foundational introduction to automation in chemical research, with a specific emphasis on flow chemistry. This methodology was selected due to its burgeoning relevance in both academic research and industrial application—driven largely by its intrinsic suitability for automated systems—and its relative underrepresentation in the current chemical curriculum.

The course aims to equip the novice with essential tools and novel skill sets applicable to a rapidly expanding and ubiquitous field—one that permeates not only scientific and industrial chemistry but spans domains from manufacturing and logistics to sociotechnical organization. Consequently, the course seeks to foster an understanding of imminent technological developments, sharpen the eye for workflow optimization opportunities in the workplace, and ignite a lasting interest in the subject matter.

Given the relatively recent inception of this practical course in its current format, alongside constraints regarding budget and dedicated laboratory space, the scope and sophistication of the experiments are constrained by available resources. They serve primarily as conceptual anchors for the fundamental principles of automation and flow chemistry, providing a stable foundation upon which more complex projects and advanced concepts can be illustrated.

It is our sincere hope that this course proves both enjoyable and ignite enthusiasm to delve deeper into the propitious field of automation.

Chapter 2

Experiment 1: Photochemical Pinacol Coupling

2.1 Adapting Batch Photochemistry to Continuous Flow

2.1.1 Educational Objectives

- Compare photon efficiency in batch vs. flow reactors.
- Calculate reactor dimensions and flow rates to achieve specific residence times.
- Understand the Beer-Lambert law constraints in photochemical scale-up.

2.2 Theoretical Background

Photochemistry allows access to unique reactivity landscapes under mild conditions. However, scaling photochemistry in a traditional batch flask is notoriously difficult due to the Beer-Lambert Law:

$$A = \varepsilon \cdot l \cdot c \tag{2.1}$$

As path length (l) increases in a large flask, light penetration drops exponentially. This leaves the bulk of the solution in the dark and leads to long reaction times and surface over-irradiation [4].

2.2.1 Reaction Scheme

Benzophenone undergoes reductive coupling in the presence of 2-propanol (which acts as both solvent and Hydrogen-atom donor) and UV light ($h\nu$) to form benzopinacol.

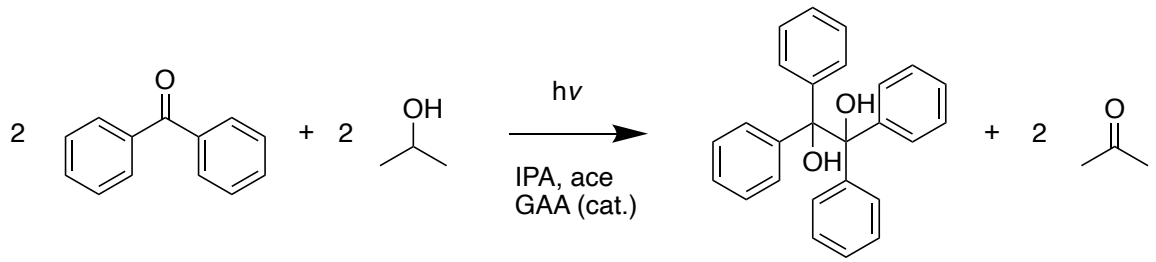

Figure 2.1: Photochemical pinacol coupling of benzophenone. Adapted from Volpe and Podlesny [5].

In a narrow bore tubing reactor (micro-reactor), the path length (l) is sub-millimeter. This ensures uniform irradiation of the entire reaction volume, accelerating the reaction from hours (in batch) to minutes (in flow).

2.3 Materials and Chemicals

2.3.1 Chemicals

Chemical	CAS	Role / Hazard
Benzophenone	119-61-9	Reactant / Irritant, aquatic tox.
2-Propanol	67-63-0	Reagent & Solvent / Flammable.
Acetone	67-64-1	Co-solvent / Flammable.
Acetic Acid (Glacial)	64-19-7	Catalyst (trace) / Corrosive.
Benzopinacol	464-72-2	Product / Low hazard.

2.3.2 Equipment

Item	Specifications	Function
Syringe Pump	1x Poseidon (Single)	Flow control
Syringe	10 mL All-Plastic	Reagent delivery
Light Source	26 W UVB Bulb	365 nm source
Tubing	PFA, ID 0.8 mm	UV-transparent reactor

2.4 Reactor Volume and Calculations

Constraint: You must construct a reactor with a volume of 0.5 mL using the available 0.8 mm ID tubing.

2.4.1 Volume-Length Calculation

Using the cylinder formula $V = \pi r^2 L$, with target $V = 500\,\mu\text{L} = 500\,\text{mm}^3$ and radius $r = 0.4\,\text{mm}$:

$$L = \frac{500}{\pi \cdot (0.4)^2} \approx 994.7\,\text{mm} \approx 1.0\,\text{m} \tag{2.2}$$

2.4.2 Flow Rate Calculation

Target Residence Time (τ) = 10 minutes.

$$Q = \frac{V}{\tau} = \frac{0.5\,\text{mL}}{10\,\text{min}} = \mathbf{0.050\ mL/min}\ (50\,\mu\text{L/min}) \tag{2.3}$$

2.5 Experimental Procedure

2.5.1 Part A: Reactor Assembly

1. Cut approx. 120 cm of PFA tubing. Measure exactly 100 cm for the irradiated zone.
2. Coil this 100 cm tightly around a 400 mL beaker. Secure with transparent tape. Ensure coils do not overlap.
3. Wrap the outside of the beaker/tubing with aluminum foil (shiny side facing inwards) to create a reflector.
4. Place the UVB lamp inside the beaker.

2.5.2 Part B: Solution Preparation

1. **Solvent:** Mix Acetone and 2-Propanol (1:1 v/v).
2. Weigh 0.364 g of Benzophenone (2.0 mmol) into a 10 mL volumetric flask.
3. Add 1 drop of glacial acetic acid.
4. Fill to the mark with the solvent mixture. Sonicate to dissolve. (Concentration = 0.2 M).

2.5.3 Part C: Continuous Flow Execution

1. **Priming:** Flush the system with pure solvent at 0.5 mL/min to remove air. Check for leaks.
2. **Startup:** Switch inlet syringe to the Benzophenone solution. Set flow rate to 50 μL/min.
3. **Reaction:** Turn on the lamp. Allow the system to run for **25 minutes** ($2.5 \times \tau$) to equilibrate. Discard this output.
4. **Collection:** Place a tared vial at the outlet. Collect product for **60 minutes**.
5. **Clean-up:** Flush reactor with 5 mL pure solvent. Turn off lamp and pump.

2.5.4 Part D: Batch Control

1. Pipette 0.5 mL of the Benzophenone solution into a glass vial.
2. Place the vial directly next to the UVB bulb (distance approx. 1 cm).
3. Irradiate for exactly **10 minutes** (matching the flow residence time).

4. Retain sample for analysis.

2.5.5 Part E: Work-up and Analysis

1. Evaporate solvent from both Flow and Batch samples (using air stream or N_2).
2. **Purification:** Triturate the solid residue with 0.5 mL cold 2-propanol. Filter the white solid (Benzopinacol), wash with cold 2-propanol, and dry. Determine isolated yield.
3. **NMR Analysis:** Dissolve crude residue from both Batch and Flow in $CDCl_3$. Acquire ^{1}H-NMR spectra.

2.6 Data Analysis

Calculate Percent Conversion using ^{1}H-NMR integrals:

$$\text{Conversion } (\%) = \left[\frac{I_{\text{Product}}/12}{(I_{\text{SM}}/4) + (I_{\text{Product}}/12)} \right] \times 100 \tag{2.4}$$

- **Starting Material (SM):** Benzophenone doublet at $\delta \approx 7.82$ ppm (4H).
- **Product:** Benzopinacol multiplet at $\delta \approx 7.18$ ppm (12H).

2.7 Questions for Reflection

1. **S/V Ratio:** Calculate the Surface-to-Volume ratio (S/V) for the flow reactor tubing ($r = 0.4$ mm) versus the batch vial ($r \approx 7.5$ mm). How does this explain the difference in conversion?
2. **Scaling:** You want to scale this reaction to produce 10 g of product. Would you choose a larger diameter tube (e.g., 5 cm) or run multiple micro-reactors in parallel ("numbering up")? Explain based on the Beer-Lambert law.
3. **Steady State:** Why is a "stabilization period" of 25 minutes required before collecting the product? What phenomenon occurs during the startup phase?
4. **Advanced Automation Design:** Design an autonomous, open-source flow platform to execute this workflow (priming to characterization) without human intervention. Propose a concrete hardware stack incorporating programmable fluidics (microcontrollers, solenoid valves) and inline analytics, prioritizing DIY solutions. Critically assess the engineering challenges of the unit operations and identify specific open-source tools that facilitate this degree of automation.
5. **Process Intensification:** Benzopinacol undergoes the acid-catalyzed Pinacol rearrangement to yield benzopinacolone. Design a telescoped flow process to effect this transformation immediately downstream of the photochemical step. Detail the requisite reagents, reactor modality, and thermal parameters, specifically addressing the engineering challenge of bridging the photochemical and acidic reaction environments.

Chapter 3

Experiment II: Kinetic Study of Diphenyldiazomethane

3.1 Automated Data Acquisition and Reaction Kinetics in Flow

3.1.1 Introduction and Automation Context

Determining reaction kinetics (rate constants, activation energy) in a traditional batch setting is labor-intensive. It requires manually drawing aliquots at precise time intervals, quenching them, and analyzing them offline. This manual sampling introduces significant timing errors and limits data density.

Relevance to Automation and Flow: This experiment illustrates how flow chemistry transforms kinetic profiling into a steady-state operation. By converting "reaction time" into "residence time" (a function of flow rate), we can obtain kinetic data points without a stopwatch. From an automation perspective, this setup represents the transition from discrete to continuous data acquisition. When coupled with an inline sensor (UV-Vis spectrophotometer), the system becomes a data generator that can rapidly sweep through temperatures and stoichiometry to map the reaction landscape in a fraction of the time required for batch methods.

3.2 Theoretical Background

The reaction under investigation is the protonation of diphenyldiazomethane (DDM) by *p*-nitrobenzoic acid (*p*-NBA) in ethanol. This is a classic model reaction for physical organic chemistry because DDM is intensely colored (purple, $\lambda_{max} \approx 525$ nm), while the reagents and products are colorless.

3.2.1 Reaction Scheme

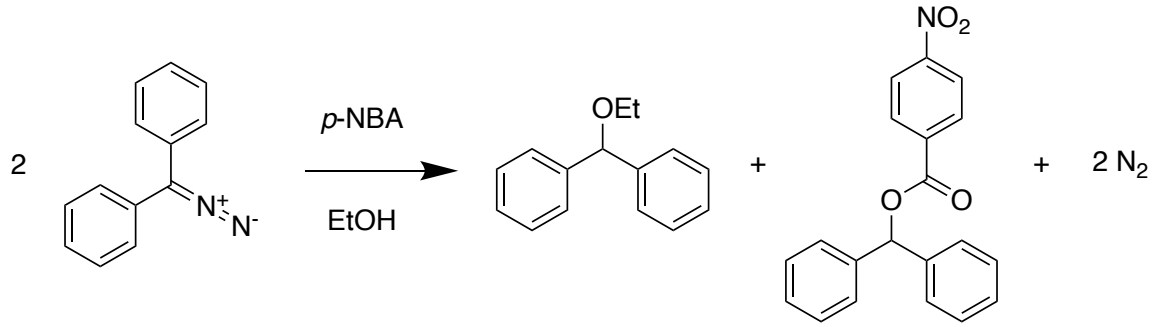

Figure 3.1: Reaction scheme for DDM protonation. Based on the work of Zhang et al. [6].

3.2.2 Kinetics

The rate-limiting step is the proton transfer to the DDM carbon. The rate law is second-order overall:

$$Rate = k \cdot [DDM] \cdot [Acid] \tag{3.1}$$

To simplify analysis, we employ Pseudo-First-Order conditions by using a large excess of acid ($[Acid]_0 \gg [DDM]_0$, typically 10:1). Under these conditions, $[Acid]$ remains effectively constant.

$$Rate = k_{obs} \cdot [DDM] \quad \text{where} \quad k_{obs} = k \cdot [Acid]_0 \tag{3.2}$$

Integrating the rate law gives the linear relationship used to determine k_{obs}:

$$\ln\left(\frac{A_0}{A_t}\right) = k_{obs} \cdot \tau \tag{3.3}$$

Where A is absorbance (proportional to concentration via Beer-Lambert Law). By plotting $\ln(A_0/A_t)$ vs. Residence Time (τ), the slope yields k_{obs}.

3.3 Reactor Design and Calculations

To replicate the literature conditions, we require a reactor volume of 4.4 mL. We will construct this using the available laboratory tubing stock (PTFE, Inner Diameter = 0.8 mm).

3.3.1 Volume-Length Calculation

Using the cylinder volume formula $V = \pi r^2 L$:

- Target Volume $V = 4.4$ mL
- Tubing ID $d = 0.8$ mm ($r = 0.04$ cm)

Target Volume	Tubing ID	Required Length
4.4 mL	0.8 mm	**875 cm** (8.75 m)

3.4 Materials and Chemicals

3.4.1 Chemicals

Chemical	Role	Notes
Diphenyldiazomethane (DDM)	Reactant	Intensely Purple
p-Nitrobenzoic Acid (*p*-NBA)	Reactant	Excess Reagent
Ethanol	Solvent	Anhydrous

3.4.2 Equipment

Item	Specifications	Function
Syringe Pumps	2x Single-channel (Poseidon)	Control stoichiometry & flow rate.
Syringes	2x 10 mL or 20 mL (Luer Lock)	Reagent reservoirs.
Tubing	PTFE, ID 0.8 mm	Reactor coil (Length: 8.75 m).
Mixer	T-piece (PEEK, 1/4"-28 threads)	Combining reagent streams.
Detector	Vernier SpectroVis Plus	Measuring absorbance at 525 nm.
Cuvette	Flow cell (or standard + pipettes)	Interface for detector.

Safety Note: DDM is a diazo compound. While stable in dilute solution, solids can be explosive. Store stock solutions in the dark at -20°C.

3.5 Experimental Procedure

3.5.1 Part A: Batch Control (Baseline)

1. Prepare a blank: Fill a cuvette with pure Ethanol. Calibrate the SpectroVis (Abs = 0).
2. Prepare the kinetic run: In a vial, mix 2.0 mL of 0.1 M *p*-NBA and 2.0 mL of 0.01 M DDM. Quickly transfer to a cuvette.
3. Measure: Record Absorbance at 525 nm every 30 seconds for 10 minutes.
4. Save data: This will serve as your comparison for the flow efficiency.

3.5.2 Part B: Flow Reactor Setup

1. **Assembly:** Connect two approx. 30 cm lengths of tubing to the inputs of the T-mixer. Connect the 8.75 m reactor coil to the output of the T-mixer.

2. **Priming:** Fill two syringes with pure Ethanol. Mount them on the pumps. Pump at 2.0 mL/min until the entire coil is filled and no bubbles remain.
3. **Zeroing:** While Ethanol is flowing, check the Absorbance at the outlet (using a flow cell or collection vial). It should be zero.

3.5.3 Part C: Automated Kinetic Sweep

Note: Total Flow Rate $Q_{total} = Q_A + Q_B$. We keep the ratio 1:1.

1. **Load Reagents:** Load Syringe A with 0.1 M *p*-NBA and Syringe B with 0.01 M DDM. Mount on pumps.
2. **Run 1 (Slow - Long Residence Time):**
   - Set Pump A = 0.5 mL/min; Pump B = 0.5 mL/min ($Q_{total} = 1.0$ mL/min).
   - Calculated Residence Time $\tau = 4.4$ mL/1.0 mL/min = 4.4 min.
   - Start flow. Wait for 15 minutes ($> 3\tau$) to reach steady state.
   - Collect sample/read inline Absorbance. Record value.
3. **Run 2 (Medium):**
   - Set Pump A = 1.0 mL/min; Pump B = 1.0 mL/min ($Q_{total} = 2.0$ mL/min).
   - Calculated $\tau = 2.2$ min.
   - Wait 8 minutes. Record Absorbance.
4. **Run 3 (Fast - Short Residence Time):**
   - Set Pump A = 2.0 mL/min; Pump B = 2.0 mL/min ($Q_{total} = 4.0$ mL/min).
   - Calculated $\tau = 1.1$ min.
   - Wait 4 minutes. Record Absorbance.

3.5.4 Part D: Clean-up

Cleaning/Flushing Protocol:

- Flush the system with pure Ethanol for 10 minutes.
- DDM residues can stain tubing; ensure the effluent runs clear.
- If staining persists, flush with a small amount of Acetone, followed by Ethanol.

3.6 Data Analysis and Questions

3.6.1 Characterization & Calculation

1. **Determine Conversion:** For each flow rate, calculate conversion $X = (A_0 - A_t)/A_0$. Note that A_0 is the absorbance of the initial DDM solution diluted 1:1 (0.005 M).

2. **Kinetic Plot:** Construct a plot of $\ln(A_0/A_t)$ on the y-axis versus Residence Time (τ) on the x-axis.

3. **Rate Constant:** Perform a linear regression. The slope of the line is k_{obs} (min^{-1}). Calculate the true second-order rate constant $k = k_{obs}/[Acid]_0$.

3.6.2 Questions for Reflection

- **The Damkohler Number:** Calculate the Damkohler number ($Da = k\tau C_0^{n-1}$) for your slowest flow rate. Does $Da \gg 1$ or $Da \ll 1$? What does this tell you about the completeness of the reaction within the tube?
- **Steady State Logic:** Why did we wait different amounts of time before sampling for Run 1 vs. Run 3? What physical phenomenon causes the "invalid" data at the start of a flow run (Hint: Taylor Dispersion)?
- **Gas Management:** This reaction produces N_2 gas. In a microreactor, this forms bubbles (slug flow). How might these bubbles interfere with an inline optical sensor, and how could you engineer a solution to filter this noise in the data stream?
- **Vision of Total Automation:** This experiment represents "Level 2" Automation (automated execution of a manual design). How would you upgrade this to a "Self-Driving Laboratory"? Describe how a closed-loop Python script could use Bayesian Optimization to autonomously vary flow rates until 90% conversion is achieved, and how automated temperature profiling could be integrated to extract the Activation Energy (E_a) via the Arrhenius equation without human intervention.

Chapter 4

Experiment 3: Ultrasound-Assisted Synthesis of Phenytoin

4.1 Process Intensification and Solids Handling in Flow

4.1.1 Theoretical Background

Many pharmaceutically relevant reactions, such as the synthesis of heterocycles, often require harsh thermal conditions (reflux) and long reaction times in batch. Process Intensification (PI) is the strategy of using novel technologies to drastically reduce process size, energy consumption, or time. In this experiment, we utilize Power Ultrasound (sonochemistry) combined with flow chemistry. Unlike a heating mantle, which has high thermal inertia, ultrasonic energy is an "instant-on/instant-off" energy source.

4.1.2 Reaction Scheme

Phenytoin (5,5-diphenylhydantoin) is synthesized via the Biltz synthesis, a base-catalyzed condensation of benzil and urea followed by a 1,2-phenyl shift.

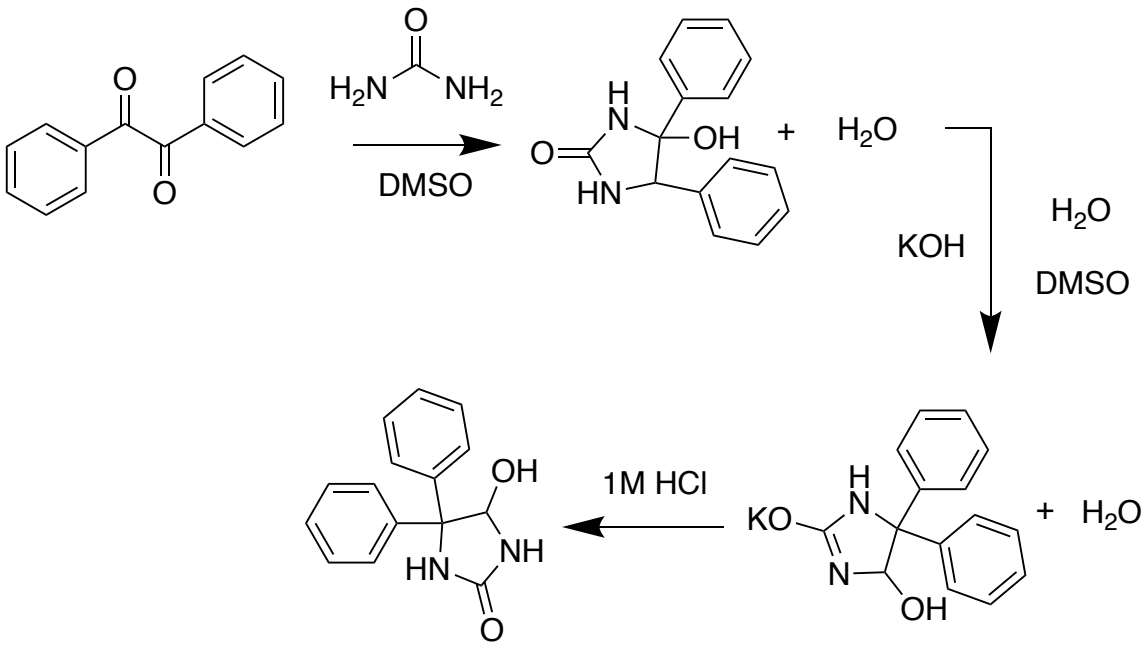

Figure 4.1: Synthesis of Phenytoin via Biltz synthesis. Adapted from Siopa et al. [7].

Acoustic Cavitation: The ultrasonic bath (40 kHz) creates microscopic bubbles that collapse violently. This generates localized "hotspots" with extreme temperatures and pressures, accelerating the reaction kinetics from ≈ 60 minutes (thermal batch) to ≈ 12 minutes (flow). Crucially, the cavitation continuously agitates the mixture, preventing the precipitating product from clogging the tubing.

4.2 Materials and Chemicals

4.2.1 Chemicals

Chemical	Hazards	Role
Benzil	Irritant	Reactant
Urea	Low hazard	Reactant
Potassium Hydroxide (KOH)	Corrosive	Catalyst/Base
DMSO / Ethanol	Permeable / Flammable	Solvent system
Hydrochloric Acid (1 M)	Corrosive	Quenching agent

4.2.2 Equipment

Item	Specifications	Function
Syringe Pump	1x Single-channel (Poseidon)	Flow control
Syringe	20 mL or 60 mL (Luer Lock)	Reagent delivery
Tubing	PVC, ID 3.0 mm	Reactor (Solids handling)
Energy Source	Ultrasonic Bath (40 kHz)	Cavitation source
Collection	Erlenmeyer flask	Product precipitation

4.3 Reactor Volume and Calculations

Constraint: To replicate literature conditions, we require a residence time of 12 minutes at a flow rate of 1.0 mL/min.

$$V_R = \tau \times Q = 12 \text{ min} \times 1.0 \text{ mL/min} = 12.0 \text{ mL} \tag{4.1}$$

4.3.1 Length Calculation

Using PVC tubing with ID = 3.0 mm ($r = 1.5$ mm):

Target Volume	Tubing ID	Required Length
12.0 mL	3.0 mm	**170 cm** (1.70 m)

4.4 Experimental Procedure

4.4.1 Part A: Reactor Assembly

1. Cut a 1.8 m length of PVC tubing. Measure a 1.70 m section for the active zone.
2. Coil this section loosely (to fit inside the ultrasonic bath). Ensure no kinks form.
3. Submerge the coil in the ultrasonic bath filled with water.

4.4.2 Part B: Solution Preparation

Prepare fresh.

1. Dissolve 0.84 g Benzil (4.0 mmol) and 0.43 g Urea (7.2 mmol) in a beaker.
2. Add 24 mL DMSO. Stir until dissolved.
3. Add 4 mL of 1.8 M aqueous KOH. (The solution may turn dark; this is normal).
4. Load 20 mL of this mixture into the syringe. Eliminate bubbles.

4.4.3 Part C: Continuous Flow Execution

1. Connect the syringe to the reactor inlet.
2. Place the outlet tube into a flask containing 30 mL of 1 M HCl on ice.
3. Set the pump flow rate to 1.0 mL/min.
4. Turn on the ultrasonic bath.
5. Allow the reaction to proceed. Residence time is 12 minutes. Watch for turbidity/crystals in the line (ultrasound should keep them moving).
6. Once the syringe is empty, flush with 10 mL Ethanol or air.

4.4.4 Part D: Work-up

1. The product precipitates immediately upon hitting the acidic ice bath.
2. Check that pH < 3.
3. Filter the white solid (Phenytoin).
4. Wash thoroughly with cold water (to remove DMSO/Urea) and a small amount of cold Ethanol.
5. Dry the solid and determine the melting point (Lit: 295–298 °C).

4.5 Questions for Reflection

- **Mechanism:** Draw the arrow-pushing mechanism for the benzylic acid rearrangement step. Why is base required?
- **Process Intensification:** Explain how acoustic cavitation accelerates the reaction. Is it a thermal or mechanical effect?
- **Automation Engineering:** If running this process for 24 hours, the bath water would heat up. How would you automate temperature control?
- **Solids:** Why are solids generally avoided in microfluidics (ID < 1 mm) but manageable here (ID 3.0 mm)?

4.6 Cleaning/Flushing Protocol

- Flush the reactor immediately with 20 mL of Ethanol to remove any remaining organic solids.
- Follow with 20 mL of water to remove salts.
- Dry with air.
- **Note:** PVC tubing can degrade with long-term exposure to DMSO. Inspect tubing for stiffness or discoloration before reuse.

Chapter 5

Experiment 4: Synthesis of Solvent Yellow 7

5.1 Telescoped Multistep Synthesis

We telescope two hazardous reactions (Diazotization and Azo Coupling) into a continuous stream, demonstrating the safety benefits of flow chemistry for handling unstable intermediates.

5.1.1 Theoretical Background

One of the most powerful applications of flow chemistry is telescoping: linking multiple reaction steps into a single continuous stream without isolating intermediates [8]. This is particularly valuable when an intermediate is hazardous, unstable, or toxic, often referred to as "Forbidden Chemistries" [9].

In this experiment, based on the work of Kuijpers et al. [10], we synthesize the diazo dye 4-phenylazoaniline (Solvent Yellow 7). The synthesis consists of two steps:

1. **Diazotization:** Aniline reacts with nitrous acid (generated in situ from sodium nitrite and HCl) to form the unstable phenyldiazonium chloride.
2. **Azo Coupling:** The diazonium salt is captured by an electron-rich aromatic nucleophile (phenol) under basic conditions to form the stable azo dye.

5.1.2 Reaction Scheme

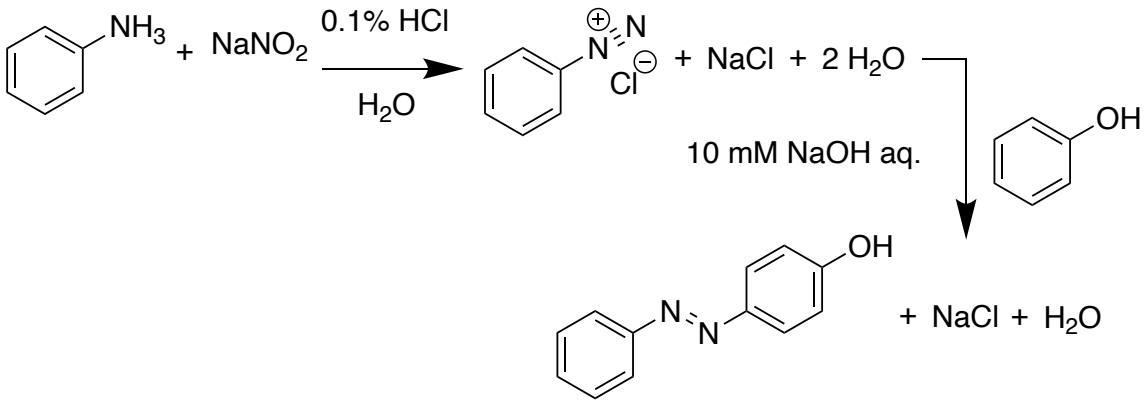

Figure 5.1: Telescoped synthesis of Solvent Yellow 7. Step 1: Diazotization (Acidic). Step 2: Coupling (Basic). Adapted from Kuijpers et al. [10].

5.2 Reactor Design and Calculations

The literature procedure specifies two reactors, each with a volume of $V_R = 1.0$ mL [10]. We will fabricate these using standard PFA tubing ($ID = 0.8$ mm).

5.2.1 Length Calculation

- Target Volume per Reactor: 1.0 mL
- Tubing ID: 0.8 mm ($r = 0.04$ cm)
- Cross-sectional Area: $A = \pi \cdot (0.04)^2 \approx 0.00503$ cm^2

$$L = \frac{V}{A} = \frac{1.0 \text{ cm}^3}{0.00503 \text{ cm}^2} \approx 199 \text{ cm} \tag{5.1}$$

Component	Specs	Required Length
Reactor Coil 1 (Diazotization)	ID 0.8 mm	**200 cm** (2.0 m)
Reactor Coil 2 (Coupling)	ID 0.8 mm	**200 cm** (2.0 m)

5.3 Materials and Chemicals

5.3.1 Chemicals

Solution	Composition	Conc.	Solvent
Feed A	Aniline (1.0 eq)	0.010 M	0.1 M HCl
Feed B	Sodium Nitrite (1.1 eq)	0.011 M	0.1 M HCl
Feed C	Phenol (1.0 eq) + NaOH	0.010 M	Water

Note: Feed C must be sufficiently basic (NaOH) to neutralize the acidic stream from Reactor 1 and maintain pH > 10 for the coupling step.

5.3.2 Equipment

Item	Specifications	Function
Pumps	3x Syringe Pumps	Feeds A, B, and C
Mixers	2x T-mixers (PEEK)	Mixing points
Tubing	PFA, ID 0.8 mm	Reactor coils
Spectrometer	UV-Vis (Cuvette)	Analysis ($\lambda = 400$ nm)

5.4 Experimental Procedure

5.4.1 Part A: Setup Assembly

1. **Mixer 1:** Connect Pump A (Aniline) and Pump B (Nitrite) to the inlets of T-Mixer 1.
2. **Reactor 1:** Connect 2.0 m of tubing to the outlet of T-Mixer 1.
3. **Mixer 2:** Connect the output of Reactor 1 and Pump C (Phenol) to the inlets of T-Mixer 2.
4. **Reactor 2:** Connect 2.0 m of tubing to the outlet of T-Mixer 2. Direct the final output to a waste beaker.

5.4.2 Part B: Execution

Flow Rate Settings: To achieve stoichiometry, we use the ratio $Q_A : Q_B : Q_C = 1 : 1 : 2$.

- Set Pump A: 0.25 mL/min
- Set Pump B: 0.25 mL/min
- Set Pump C: 0.50 mL/min
- **Total Flow Rate:** 1.0 mL/min

1. Start all pumps simultaneously.
2. Allow the system to equilibrate for at least 3 residence times (≈ 15 minutes).
3. Observe the color change. Reactor 1 should remain clear/pale; Reactor 2 should turn bright yellow/orange immediately upon mixing.
4. Collect 1 mL of product from the outlet.

5.4.3 Part C: Analysis

1. Dilute 100 μL of the product sample into 10 mL of Ethanol (1:100 dilution).
2. Measure the absorbance at $\lambda = 400$ nm using the UV-Vis spectrophotometer.

3. Compare against a calibration curve to determine conversion.

5.5 Questions for Reflection

5.5.1 Question 1: The Combinatorial Library

Azo chemistry is highly modular. **Task:** Identify 8 commercially available precursors (4 Anilines and 2 Phenols/Naphthols) that could be used in this setup to generate a library of 8 unique dyes. List the structures, name the resulting products, and predict the color shift (bathochromic/hypsochromic) for each.

5.5.2 Question 2: Advanced Derivatization

To increase product value, a third flow step can be added. **Task:** Propose a specific transformation (e.g., Reduction, Metal Complexation) downstream of the coupling step. Draw the modified setup and name 3 commercially relevant derivatives (e.g., Mordant dyes) that require this step.

5.5.3 Question 3: The Historical Nexus

Diazo chemistry catalyzed the modern chemical industry. **Task:** Write a brief essay (300 words) covering the origins (Griess, BASF), the societal impact (textiles, pharma), and the modern relevance of azo compounds (e.g., in liquid crystals or photo-switching).

5.6 Cleaning Protocol

Flush the entire system with Water (10 min) followed by Ethanol (10 min) to prevent azo dye precipitation and staining of the PFA tubing.

Chapter 6

Experiment 5: Dimerization of Octanethiol in Continuous Flow

6.1 Multiphase Chemistry and Segmented Flow Hydrodynamics

6.1.1 Educational Objectives

- Perform a biphasic reaction (Organic/Aqueous) in a continuous flow reactor.
- Understand the hydrodynamics of Segmented Flow (Slug Flow) and how it enhances mass transfer via Taylor vortices.
- Safely manage exothermic quenching steps using off-line or semi-automated work-up.

6.2 Theoretical Background

Many chemical processes involve immiscible phases (e.g., extractions, hydrogenations). In batch reactors, mixing these phases relies on vigorous mechanical stirring, which is chaotic and difficult to scale. In micro-fluidic flow reactors, mixing immiscible fluids generates a highly predictable flow regime known as Segmented Flow. As the fluid "slugs" travel through the tubing, friction at the walls induces internal recirculation currents known as Taylor Vortices. These vortices rapidly refresh the interface between the phases, leading to mass transfer rates that are orders of magnitude higher than in batch vessels.

6.2.1 Reaction Scheme

We synthesize dioctyl disulfide via the oxidative dimerization of 1-octanethiol using hydrogen peroxide as the terminal oxidant and iodine (I_2) as a catalyst.

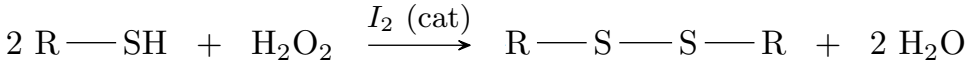

Figure 6.1: Oxidative dimerization of thiol to disulfide. Reference: Kuijpers et al. [10].

The reaction occurs at the liquid-liquid interface. Hydrogen peroxide (aqueous phase) re-oxidizes the iodide/iodine catalyst (partitioned in the organic phase), which in turn oxidizes the thiol to the disulfide.

6.3 Reactor Design and Calculations

Constraint: We require a reactor volume of 2.0 mL (matching literature).

6.3.1 Length Calculation

Using PFA tubing with ID = 0.8 mm ($r = 0.4$ mm):

Target Volume	Tubing ID	Required Length
2.0 mL	0.8 mm	**400 cm** (4.0 m)

6.3.2 Flow Rate Calculation

Target Residence Time (τ) = 5 minutes.

$$Q_{total} = \frac{2.0 \text{ mL}}{5 \text{ min}} = 0.4 \text{ mL/min} \tag{6.1}$$

Since we mix Phase A and Phase B in a 1:1 ratio:

$$Q_A = 0.2 \text{ mL/min}, \quad Q_B = 0.2 \text{ mL/min} \tag{6.2}$$

6.4 Materials and Chemicals

Chemical	Composition	Role
Phase A (Org)	0.1 M 1-Octanethiol + 1 mol% I_2 in EtOAc	Reactant + Catalyst
Phase B (Aq)	10 wt% H_2O_2 (diluted from 30%)	Oxidant
Quench	0.2 M Sodium Thiosulfate (aq)	Neutralizes Iodine
Drying Agent	$MgSO_4$	Removes water

Safety Note: Iodine causes stains. Hydrogen peroxide is an oxidizer. The quench reaction is exothermic.

6.5 Equipment and Setup

- **Pumps:** 2x Single-channel syringe pumps.
- **Syringes:** 2x 20 mL All-Plastic (ensure chemical compatibility with Ethyl Acetate).
- **Tubing:** PFA, ID 0.8 mm (Transparent for viewing slugs).
- **Mixer:** 1x T-mixer (PEEK or ETFE).
- **Work-up:** Separatory funnel.

6.6 Experimental Procedure

6.6.1 Part A: Solution Preparation

1. **Phase A (Organic):** In a 25 mL volumetric flask, dissolve:
   - 0.36 g 1-Octanethiol (2.5 mmol)
   - 6.3 mg Iodine (0.025 mmol, 1 mol%)
   - Fill to mark with Ethyl Acetate.
2. **Phase B (Aqueous):** Prepare 25 mL of 10 wt% H_2O_2 in water.
3. Load two 20 mL syringes with Phase A and Phase B respectively. Eliminate air bubbles.

6.6.2 Part B: Continuous Flow Execution

1. **Assembly:** Connect both syringes to the T-mixer inputs. Connect the 4.0 m PFA coil to the T-mixer outlet.
2. **Start:** Set both pumps to 0.2 mL/min. Start simultaneously.
3. **Observation:** Watch the T-mixer. You should see regular segments (slugs) forming. The organic phase (pink/violet due to Iodine) and aqueous phase (colorless) will alternate.
4. **Taylor Flow:** Observe the slugs traveling through the coil. Note any internal turbidity indicating mixing.
5. **Steady State:** Wait for 15 minutes (3τ) to ensure stable slug generation.
6. **Collection:** Collect the biphasic output for 25 minutes into a flask. (Total collected volume $\approx$ 10 mL).

6.6.3 Part C: Work-up

1. Transfer the collected mixture to a separatory funnel.
2. **Quench:** Add 20 mL of 0.2 M Sodium Thiosulfate. Shake gently. **Caution:** This reaction is exothermic and produces gas/heat. Vent frequently. The violet iodine color should disappear.

3. **Separation:** Separate the layers. Keep the organic (top) layer.
4. **Wash/Dry:** Wash the organic layer twice with water. Dry over $MgSO_4$, filter, and evaporate the solvent.
5. **Yield:** Weigh the resulting oil (Dioctyl disulfide).

6.7 Questions for Reflection

- **Hydrodynamics:** Calculate the Reynolds number (Re) for this flow. Is it laminar or turbulent? If laminar ($Re < 2000$), how does the system achieve such efficient mixing? Explain the role of Taylor Vortices.
- **Throughput:** How much product (in grams) could this specific setup produce in 24 hours of continuous operation?
- **Automation:** In a batch reactor, H_2O_2 is often added dropwise to prevent thermal runaway. Why can we mix them immediately in the T-mixer without explosion risk? (Hint: Surface-to-volume ratio).
- **Phase Ratio:** If you changed the flow ratio to 3:1 (Organic:Aqueous), how would the slug lengths change? How might this impact the interfacial surface area?

6.8 Cleaning/Flushing Protocol

- Flush with Ethanol for 10 minutes to remove organic residues and iodine.
- Flush with water for 5 minutes.
- Dry with air.

Chapter 7

Experiment 6: Continuous-Flow Synthesis of Calcium Alginate Hydrogel Beads

7.1 Rapid Prototyping, Microencapsulation, and Droplet Microfluidics

Recent advances in additive manufacturing have enabled the fabrication of custom microfluidic devices for encapsulation applications [11–18].

7.1.1 Educational Objectives

- Utilize 3D printing (Additive Manufacturing) to create custom microfluidic hardware (droplet generators) that cannot be bought off-the-shelf.
- Understand the hydrodynamics of Segmented Gas-Liquid Flow and how it controls droplet size distribution.
- Perform a continuous encapsulation process relevant to food science ("Fruit Caviar") and drug delivery.

7.2 Theoretical Background

In previous experiments, automation was achieved by controlling the temporal parameters (flow rate) of existing hardware. In this experiment, we introduce the concept of Hardware Automation via Rapid Prototyping.

7.2.1 Chemistry: Ionic Gelation

Alginate is a copolymer of β-D-mannuronic acid (M) and α-L-guluronic acid (G) extracted from brown algae. In the presence of divalent cations like Calcium (Ca^{2+}), the G-blocks align to form a "buckled" structure that chelates the metal ion. This is known as the "Egg-

Box" Model. The gelation is instantaneous upon contact, forming a crosslinked polymer network.

7.2.2 Physics: Droplet Formation

To form uniform beads, the liquid stream must be broken into droplets. We utilize a Segmented Gas-Liquid Flow. By co-injecting air and the alginate solution into a coaxial or T-junction nozzle, the gas phase "chops" the liquid stream into regular segments. When these segments exit the nozzle and hit the calcium bath, surface tension pulls them into spheres which instantly gel.

7.3 Materials and Chemicals

Chemical	Concentration	Note
Sodium Alginate	1.8% (w/v) in Water	Viscous! Dissolve with heat/stirring.
Calcium Chloride	0.25 M in Water	Crosslinking agent.
Food Coloring	Trace	For visualization.

7.4 Equipment and Setup

- **Pumps:** 2x Single-channel syringe pumps.
- **Syringes:** 2x 20 mL (Luer Lock).
- **Reactor:** 3D-Printed Modular Block (Coaxial nozzle design).
- **Tubing:** PFA, ID 0.8 mm (Connecting pumps to block).
- **Collection:** 250 mL Beaker.

7.5 Reactor Design and Calculations

Unlike the kinetic coil reactors, the "reactor" here is the mixing nozzle itself. We use PFA tubing merely to transport fluids to the block. **Connection Tubing:** We use two 50 cm lengths of PFA tubing (ID 0.8 mm) to connect the syringes to the 3D-printed block. **Note:** The reaction (gelation) occurs externally in the collection beaker, so residence time inside the tubing is not the critical control parameter; flow stability is.

7.6 Experimental Procedure

7.6.1 Part A: Solution Preparation

Prepare in advance as Alginate takes time to dissolve.

1. **Alginate Solution:** Dissolve 0.90 g of Sodium Alginate in 50 mL distilled water. Heat to 60°C and stir vigorously until clear and viscous. Add 2–3 drops of food coloring. Let cool to eliminate air bubbles.

2. **Calcium Bath:** Dissolve 1.38 g of $CaCl_2$ in 50 mL distilled water. Pour into the collection beaker.

7.6.2 Part B: System Assembly

1. **Pumps:** Mount two 20 mL syringes.
2. **Syringe 1:** Filled with Alginate Solution.
3. **Syringe 2:** Filled with Air (simply draw air from the room).
4. **Connections:** Connect Syringe 1 and Syringe 2 to the inputs of the 3D-printed block using the PFA tubing.
5. **Mounting:** Clamp the 3D-printed block so the outlet nozzle is positioned approx. 5–10 cm above the surface of the Calcium Chloride bath.

7.6.3 Part C: Automated Synthesis

1. **Prime:** Start the Alginate pump at 2.0 mL/min until liquid appears at the nozzle. Stop.
2. **Segmentation:** Start the Air pump at 2.0 mL/min.
3. **Run:** Start the Alginate pump at 2.0 mL/min.
4. **Observation:** You should see the air stream "chopping" the alginate stream, creating discrete droplets that fall into the bath.
5. **Optimization:** Adjust the Air flow rate (try 1.0 mL/min and 4.0 mL/min) to change the droplet frequency and size.
6. **Collection:** Let the system run for 5 minutes.

7.6.4 Part D: Analysis

1. Filter the beads from the calcium bath. Rinse with water.
2. Observe the shape (spherical vs. tear-drop).
3. Measure the diameter of 10 random beads using a ruler or calipers. Calculate the Coefficient of Variation (CV).

7.7 Questions for Reflection

- **Hydrodynamics:** Why do we use air to segment the flow? What would happen if we simply pumped the alginate slowly without air? Explain the difference between the dripping regime and the jetting regime.
- **Chemistry:** The beads harden from the outside in. How does this diffusion-controlled crosslinking affect the porosity of the bead? (Hint: Shrinking Core Model).

- **Bio-Applications:** In a biotech context, these beads could encapsulate cells. Why is this flow process (room temp, aqueous, low shear) superior to other polymerisation methods for cell viability?
- **Automation Engineering:** Currently, you collect in a batch beaker. Design a continuous collection system that automatically removes the solid beads from the liquid bath and washes them.

7.8 Cleaning/Flushing Protocol

- **IMMEDIATELY** after use, flush the Alginate line with warm water for 10 minutes. Alginate dries into a hard plastic that ruins tubing.
- Flush the Air line with air.
- Disassemble the 3D printed block and rinse with warm water.

Chapter 8

Experiment 7: Performance Verification of Syringe Pumps

Note: This experiment is intended as a substitute for students who have missed one of the core experiments (Exp 1–6).

8.1 Metrology, Calibration, and Closing the Control Loop

8.1.1 Educational Objectives

- Perform a rigorous Gravimetric Analysis to verify the performance of automated actuators.
- Distinguish between Accuracy (Trueness) and Precision (Repeatability) in the context of fluid handling.
- "Close the loop" by calculating and applying a firmware correction factor to calibrate open-source hardware.

8.2 Introduction and Automation Context

In laboratory automation, we often rely on Open-Loop Control: we send a command to a device (e.g., "move plunger 10 mm") and assume it obeys perfectly. However, real-world physical factors—such as syringe friction, tubing compliance, thermal expansion, or variations in motor manufacturing—can lead to discrepancies between the commanded volume and the delivered volume.

Before entrusting a sensitive chemical reaction to a robot, one must establish Trust through Verification. This experiment uses the mass of dispensed water to determine the reliability of your Poseidon pumps [19–21]. This is the foundational step for all subsequent quantitative experiments.

8.3 Theoretical Background

8.3.1 Gravimetric Analysis

The most accurate way to measure liquid volume in the lab is by mass. Using the density of water (ρ) at a specific measured temperature (T), we convert the recorded mass (m) to volume (V):

$$V = \frac{m}{\rho_{water}(T)} \tag{8.1}$$

Note: The density of water changes with temperature (e.g., 0.9982 g/mL at 20°C vs. 0.9970 g/mL at 25°C). For high-precision calibration, this correction is non-negotiable.

8.3.2 Statistical Metrics

- **Accuracy (Systematic Error):** How close the mean dispensed volume ($\bar{V}$) is to the target volume (V_{target}).

$$\%Error = \frac{\bar{V} - V_{target}}{V_{target}} \times 100 \tag{8.2}$$

- **Precision (Random Error):** How reproducible the dispensing is, measured by the Standard Deviation (σ) or Coefficient of Variation (CV).

$$\%CV = \frac{\sigma}{\bar{V}} \times 100 \tag{8.3}$$

8.4 Materials and Chemicals

8.4.1 Equipment

Item	Quantity	Function
Syringe Pump	1 (Poseidon)	Device under test (DUT)
Syringe	10 mL (Plastic)	Reservoir
Tubing	PTFE, ID 0.8 mm	Dispensing nozzle ($\approx$ 20 cm)
Analytical Balance	1 (0.1 mg)	Measurement standard
Vial	1 (Glass)	Collection vessel (with lid)
Thermometer	1	Water temperature monitoring

8.4.2 Chemicals

Chemical	Grade	Note
Deionized Water	Lab Grade	Equilibrated to room temp.

8.5 Experimental Procedure

8.5.1 Part A: Preparation

1. **Equilibration:** Pour approx. 50 mL of DI water into a beaker and let it sit for 15 minutes to thermally equilibrate to the room. Measure and record the temperature T.
2. **Priming:** Fill the 10 mL syringe with water. Invert and push the plunger to remove ALL air bubbles. Air is compressible and will ruin your precision.
3. **Mounting:** Install the syringe on the pump. Attach a short length ($\approx$ 20 cm) of PTFE tubing.
4. **Flushing:** Drive the pump manually until water drips steadily from the tubing tip, ensuring the line is completely filled.

8.5.2 Part B: Data Acquisition

1. Place a clean, dry vial on the analytical balance. Tare the balance (0.0000 g).
2. Position the tubing tip just inside the vial opening, but not touching the walls or the liquid surface (to avoid capillary forces wicking extra fluid).
3. **Command:** Using the control software (Python/Serial), instruct the pump to dispense 1.0 mL at a flow rate of 1.0 mL/min.
4. Wait for the pump to stop. Wait an additional 5 seconds for any hanging drop to fall or stabilize.
5. **Record:** Write down the final mass (m_i).
6. Tare the balance again (or record cumulative mass and subtract later).
7. **Repeat:** Perform $n = 5$ replicates.
8. **Variation (Optional):** If time permits, repeat the protocol for a target of 5.0 mL to check linearity.

8.6 Data Analysis and Calibration

8.6.1 Calculation Steps

1. Look up the density ρ for your measured temperature using standard water density tables.
2. Convert each mass m_i to volume $V_i = m_i/\rho$.
3. Calculate Mean $\bar{V}$ and Standard Deviation σ.
4. Calculate Accuracy Error (%) and Precision CV (%).

8.6.2 Firmware Correction

If your Accuracy Error is $> 2\%$ (e.g., you commanded 1.00 mL but got 0.96 mL consistently), you must calibrate the hardware steps. The firmware uses a variable `steps_per_mm` (or `steps_per_ml`) to translate rotational motor steps into linear distance.

$$New\_Setting = Old\_Setting \times \frac{Target\ Volume}{Measured\ Mean\ Volume} \tag{8.4}$$

Example:

- Old Setting: 1000 steps/mL
- Target: 1.00 mL
- Measured Mean: 0.96 mL
- New Setting: $1000 \times (1.00/0.96) = 1041.7$ steps/mL.

Task: Calculate your new setting and (if instructed) update the pump firmware.

8.7 Questions for Reflection

- **Sources of Error:** If your pump consistently dispenses less than requested (systematic error), what mechanical factors might be to blame? (Hint: Consider backlash in the lead screw or tubing compliance).
- **Viscosity:** You calibrated with water ($\eta \approx 1$ cP). Would this calibration hold true for a viscous reagent like Glycerol ($\eta \approx 1000$ cP) pumped at high speed? Why or why not?
- **Automation Strategy:** In a "Self-Driving Lab," how could you automate this calibration process? Imagine the balance has a USB connection. Sketch a logic flowchart where the robot self-calibrates before every experiment.

Chapter 9

Module 8: Capstone Project

9.1 The "Lab 4.0" Capstone

9.1.1 Individual Project

Unlike the previous experiments, Module 8 is an **individual project**. You must choose **ONE** of the following three tracks. Each track is designed to require approximately 6 hours of dedicated work.

9.2 Track Options

9.2.1 Option A: Code (Software Automation)

Focus: Python/Data Science.

- **Task:** Develop a Python script to automate a specific laboratory task (e.g., data processing, instrument control, inventory management).
- **Deliverable:** A working `.py` script or Jupyter Notebook, well-documented, submitted via GitHub.
- **Examples:** AI Lab Assistant (Voice-to-Text), NMR Data Processor, Green Chemistry Calculator.

9.2.2 Option B: System Design (The Architect)

Focus: Engineering/Planning.

- **Task:** Design a complete automation system for a specific chemical task. It can be DIY, commercial, or hybrid.
- **Deliverable:**
  - **P&ID:** A Piping and Instrumentation Diagram of your system.
  - **BOM:** A Bill of Materials with supplier links and prices.

  - **Operational Logic:** A flowchart or pseudocode explaining how the system operates.
- **Note:** You do not need to physically build the system, but the design must be detailed and realistic.

9.2.3 Option C: Theoretical Research (The Analyst)

Focus: Academic Writing/Critical Analysis.

- **Task:** Write a rigorous theoretical review or a novel research proposal on the future of laboratory automation.
- **Deliverable:** A research paper (IEEE or ACS format) citing at least 15 peer-reviewed sources.
- **Topics:** Open topic within the "Automation/Chemistry" nexus (e.g., Ethics of AI in Lab, Economics of Flow vs. Batch, History of Automation). Quality and depth are the primary metrics.

9.3 Submission via GitHub

This course utilizes industry-standard version control. All projects must be submitted via a Pull Request (PR) to the official course repository:

`https://github.com/cosmopax/Automation_in_Everyday_Lab_Routine`

Submission Protocol:

1. **Consult the README:** The repository contains detailed setup instructions (Forking, Cloning) and additional resources relevant to each track.
2. **Prepare Your Folder:** Organize your work into a single folder named exactly according to this schema:

   `25WS_LastName_FirstName_ChosenOption(LetterA/B/C)_TitleofWork`

   Example: `25WS_Doe_John_OptionA_NMR_Auto_Process`
3. **Commit and Push:** Upload this folder to your branch.
4. **Pull Request:** Open a Pull Request against the `main` branch of the course repository.

9.4 Deliverables Checklist

Regardless of the chosen track, your submission folder must contain:

- **Core Work:** The code (.py/.ipynb), design documents (PDF/CAD), or research paper (PDF).
- **Documentation (README.md):** A text file explaining:
  - **Abstract:** What problem does this project solve?

  - **Usage:** How to run the code or interpret the design.
  - **Dependencies:** Any libraries or hardware required.
- **Visual Proof:** A screenshot, render, or brief screen recording demonstrating the work.

Chapter 10

Appendix

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10.2 List of Chemicals

The following chemicals are used throughout Experiments 1–7.

- 1-Octanethiol (111-88-6)
- 2-Propanol (IPA) (67-63-0)
- Acetic Acid (Glacial) (64-19-7)

- Acetone (67-64-1)
- Aniline (62-53-3)
- Benzil (134-81-6)
- Benzophenone (119-61-9)
- Benzopinacol (464-72-2)
- Calcium Chloride (10043-52-4)
- Dimethyl Sulfoxide (DMSO) (67-68-5)
- Dioctyl Disulfide (1809-61-6)
- Diphenyldiazomethane (DDM) (883-40-9)
- Ethanol (64-17-5)
- Ethyl Acetate (141-78-6)
- Hydrochloric Acid (7647-01-0)
- Hydrogen Peroxide (30% / 10%) (7722-84-1)
- Iodine (7553-56-2)
- Magnesium Sulfate (7487-88-9)
- p-Nitrobenzoic Acid (p-NBA) (62-23-7)
- Phenol (108-95-2)
- Phenytoin (57-41-0)
- Potassium Hydroxide (KOH) (1310-58-3)
- Sodium Alginate (9005-38-3)
- Sodium Hydroxide (NaOH) (1310-73-2)
- Sodium Nitrite (7632-00-0)
- Sodium Thiosulfate (7772-98-7)
- Solvent Yellow 7 (1689-82-3)
- Urea (57-13-6)
- Water (Deionized) (7732-18-5)

10.3 Equipment and Tubing Inventory

10.3.1 Hardware Inventory

- **Syringe Pumps:** Poseidon Open Source Pumps (3D Printed / Arduino control).
- **Spectroscopy:** Vernier SpectroVis Plus (UV-Vis, 400–700 nm).
- **Microfluidics:** 3D Printed Droplet Generators (PLA/PETG, Coaxial & T-Junction).

- **Ultrasound:** Ultrasonic Bath (40 kHz).
- **Photochemistry:** UV LED Lamp ($\approx$ 365 nm, 10W).
- **Balances:** Analytical Balance (0.1 mg precision).
- **Heating:** Magnetic Stirrer Hotplates.

10.3.2 Tubing Specifications

Material	**ID (mm)**	**OD (mm)**	**Volume (μL/cm)**
PFA (Flow Reactors)	0.8	1.6	5.03
PTFE (Connections)	0.8	1.6	5.03
PVC (Solids/Slurries)	3.0	5.0	70.7