Supplementary Information (SI) for Digital Discovery.
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Supporting information — In situ synthesis within micron-sized soft chemical reactors created via programmable aerosol chemistry

Luokun Zhang, Hessam Mehr*

Materials and methods

Reagents

All reagents were purchased from Sigma–Aldrich and used without further purification. Sodium alginate stock solution (1%) was prepared by stirring the dry reagent in deionised water overnight and diluted to 0.5% or 0.25% depending on the experiment before use (refer to specific experiments for exact concentration used).

Equipment

Microscopy experiments was carried out on an Olympus SZX7 microscope using a Raspberry Pi HQ Camera for image acquisition. The camera was controlled via a connected Raspberry Pi 4B running Raspberry Pi operating system 11 (based on Debian 11 "Bullseye").

Software

Library used to control piezoelectric driver circuit is *CtrlAer*, available under the Apache 2 licence on github (https://github.com/MehrResearch/pico-ctrlaer). CtrlAer is designed to take advantage of the RP2040's unique programmable input/output (`pio`) subsystem in order to produce time- and frequency-precise activation of the piezoelectric atomisers.

Reagent module

The reagent module consists of a glass vial (Supelco SU860097) and metal screw cap (Supelco SU860102) purchased from Sigma–Aldrich and modified by removing the butyl septum, attaching a piezoelectric actuator (see below) to the cap using cyanoacrylate adhesive, and adding an 8 cm cotton wick. Suitable cellulose cotton wicks are widely available as a consumable for domestic humidifiers. Our testing revealed no dependence on particular brands or vendors.

Piezoelectric actuator and driver circuit

Consumer-grade piezoelectric humidifier actuator with a resonant frequency of ca. 112 kHz were purchased and modified by removing the included silicone brackets and attaching the metal backplate to the reagent module as described above. The driver circuit consists of an N-channel enhancement mode metal-oxide-semiconductor field-effect transistor (MOSFET) in a small outline transistor (SOT) 23-3 package combined with a 10:1 ferrite core transformer used as a voltage multiplier. This combination of actuator and driver circuit can use supply voltages between 5–7.5 V without appreciable depolarisation or thermal degradation of the piezoelectric. The MOSFET gate is capacitively coupled to the microcontroller output pin and grounded via a 100 kΩ resistor. Typical peak-to-peak output voltages are in the 100–150 V range.

Aerosol release control circuit

Aerosol release is orchestrated by programs using our *CtrlAer* library. The software runs entirely on an RP2040 family microcontroller and has been test on the Raspberry Pi Pico as well as the Pimoroni Tiny2040 development boards, the latter used in all experiments. Both boards are readily available for purchase at very low cost. For each atomiser, a general-purpose input/output (GPIO) pin on the board is connected to

an amplifier circuit board using the combination of a MOSFET and autotransformer to increase the amplitude of the applied voltage by a factor of 20. We found it helpful to use an external power supply with adjustable voltage for the amplifier board, using a 7 V supply in all experiments. **Figure 1** shows a possible implementation.

For experiments requiring simultaneous release of two aerosols, we used the control circuit shown in **Figure 2**.

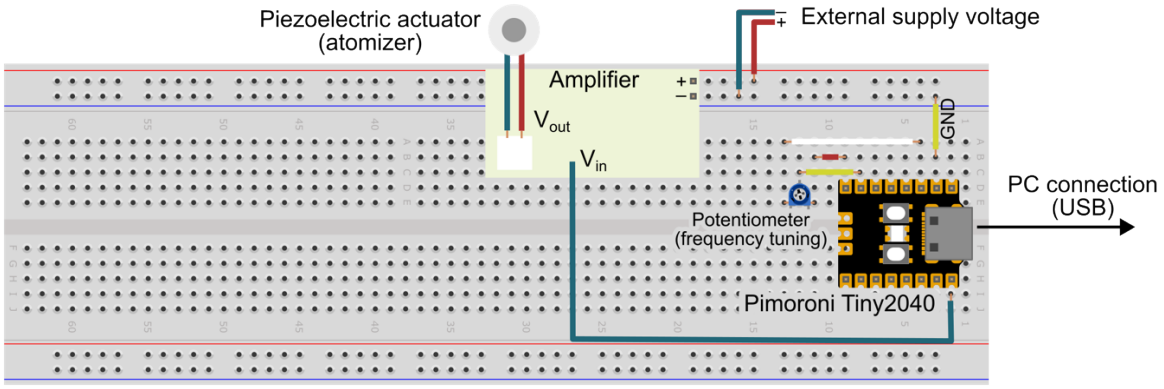

Figure 1. Implementation of the control circuit used in aerosol experiments.

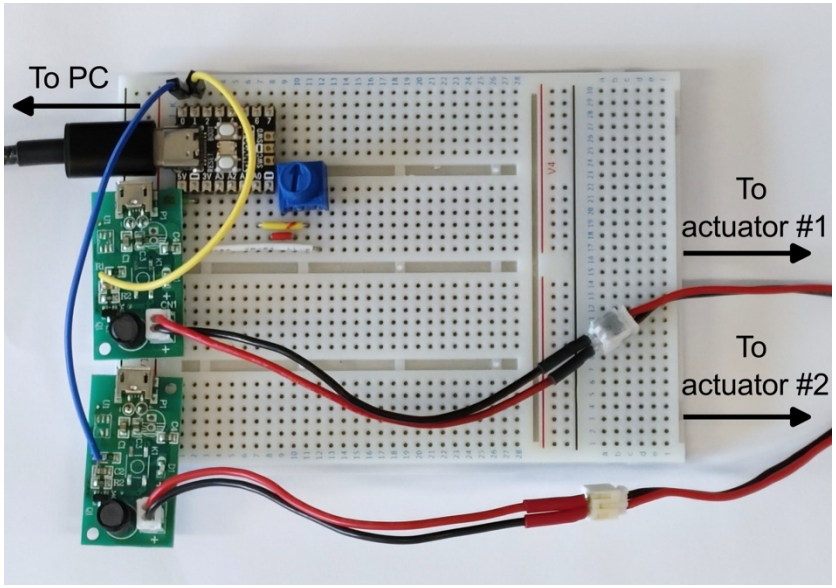

Figure 2. Breadboard layout used in experiments with two actuators (aerosol–aerosol reactivity).

Atomiser element

The aerosol source used in this study is a piezoelectric vibrating mesh atomiser widely available for domestic applications. Liquid droplets are extruded through a metal mesh of laser etched holes, in this case approximately 5 µm in diameter at the narrowest point. The resonance frequency of the actuator is quoted as 110 kHz +/- 5%, with 113 kHz being most common in our experience. Furthermore, this resonance frequency is weakly (+/- 1 kHz) dependent upon the nature of the liquid being atomised. To allow tuning

for optimal resonance, the driver circuit includes a potentiometer used to adjust the frequency of the square wave produced by the microcontroller between 108 and 118 kHz.

Figure 3 shows a microscope image of the back side of the atomiser metal mesh. Laser drilled holes in this type of device are known to have a conical profile, widening significantly from front — where to back

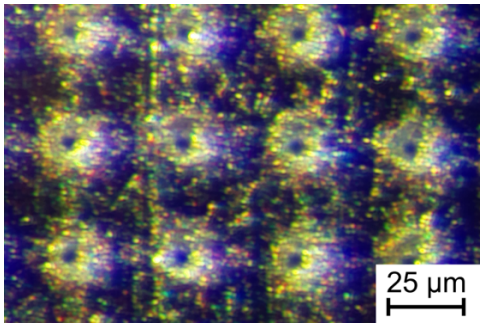

Figure 3. Microscope image of the metal mesh used in the vibrating mesh atomisers used in this study.

Droplet formulation details

Table 1. Composition of reactants used in different experiments.

Experiment no.	Solution A	Solution B	Collected on
1	SA* + NaOH† (1:1)	1% $CaCl_2$‡	Glass slide
2	SA	1% $CaCl_2$	Glass slide
3	SA + PP‡	1% $CaCl_2$	Glass slide
4	SA + methylene blue	1% $CaCl_2$	Beaker
5	SA + RuO_2	1% $CaCl_2$	Beaker
6	SA + black ink	1% $CaCl_2$	Glass slide/beaker
7	SA, 0.025 M $Na_4[Fe(CN)_6]$	1% $CaCl_2$, 0.025 M Fe^{3+}§	Petri dish
8	SA, 0.01 M $Na_4[Fe(CN)_6]$ + PP‡	1% $CaCl_2$, 0.025 M Fe^{3+}	Glass slide
9	SA, 0.01 M $Na_4[Fe(CN)_6]$	1% $CaCl_2$, 0.025 M Fe^{3+}	Glass slide
10	SA solution + water + fluorescent particles (1:1:1)	2% $CaCl_2$ solution	Petri dish
11	0.5% SA, 0.5% dimethylglyoxime	2% $CaCl_2$ + 0.5% $Ni(OCOCH_3)_2 \cdot 4H_2O$	Glass slide
12	1% SA + 0.5% hydroquinone	6% $CaCl_2$ + 1.5% $KMnO_4$	Glass slide/petri dish

*SA: Aqueous sodium alginate (0.25% w/w) †NaOH: 0.1% aqueous sodium hydroxide with trace phenolphthalein
‡ $CaCl_2$: Aqueous calcium chloride § Both $FeCl_3$ and $Fe(NO_3)_3$ were tested.

Optical microscopy results

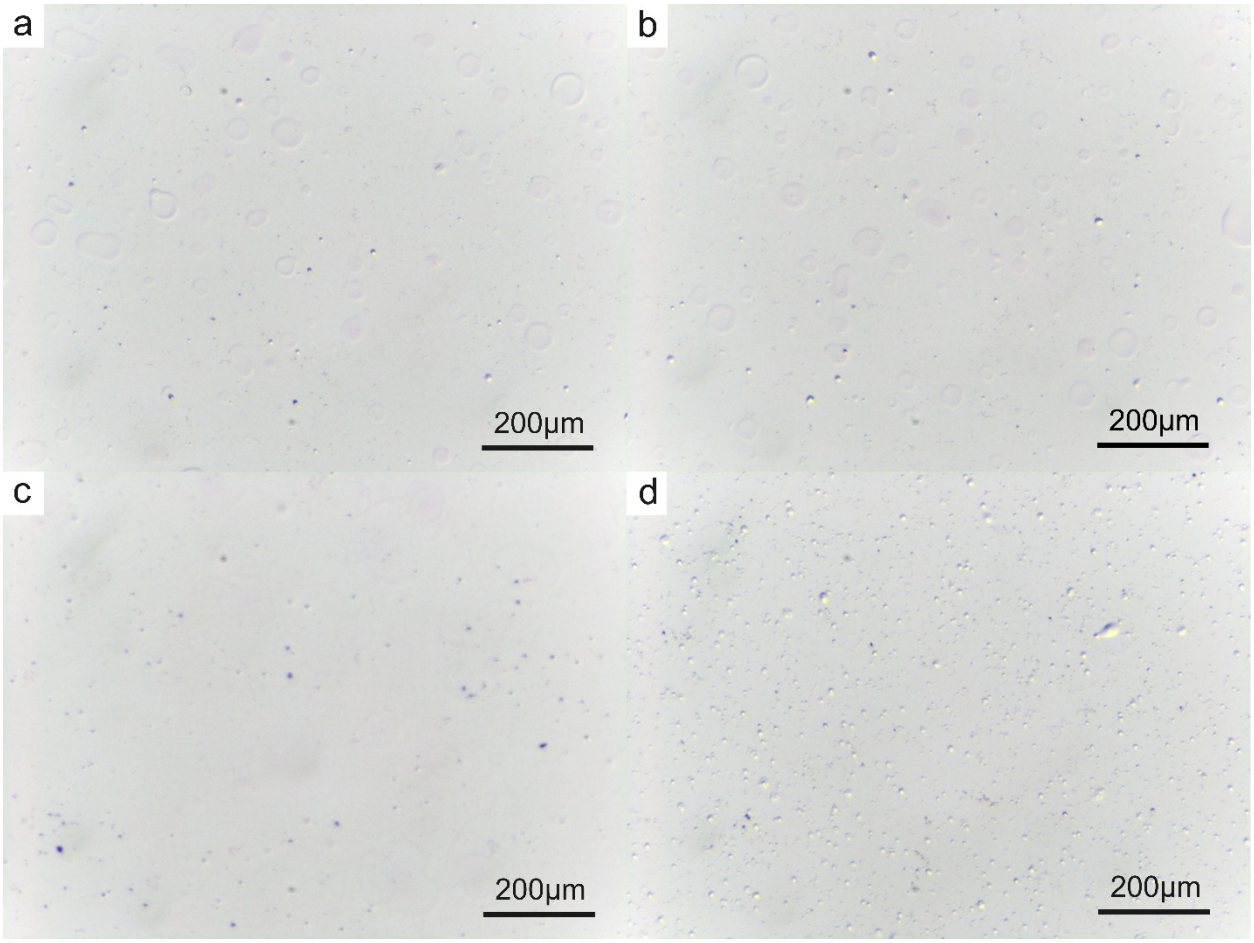

Figure 4. Results of light microscope of experiment 1. This early experiment compares the particles obtained when both alginate and calcium aerosol droplets are present (a and b) with control samples containing only sodium alginate (c) or calcium (d).

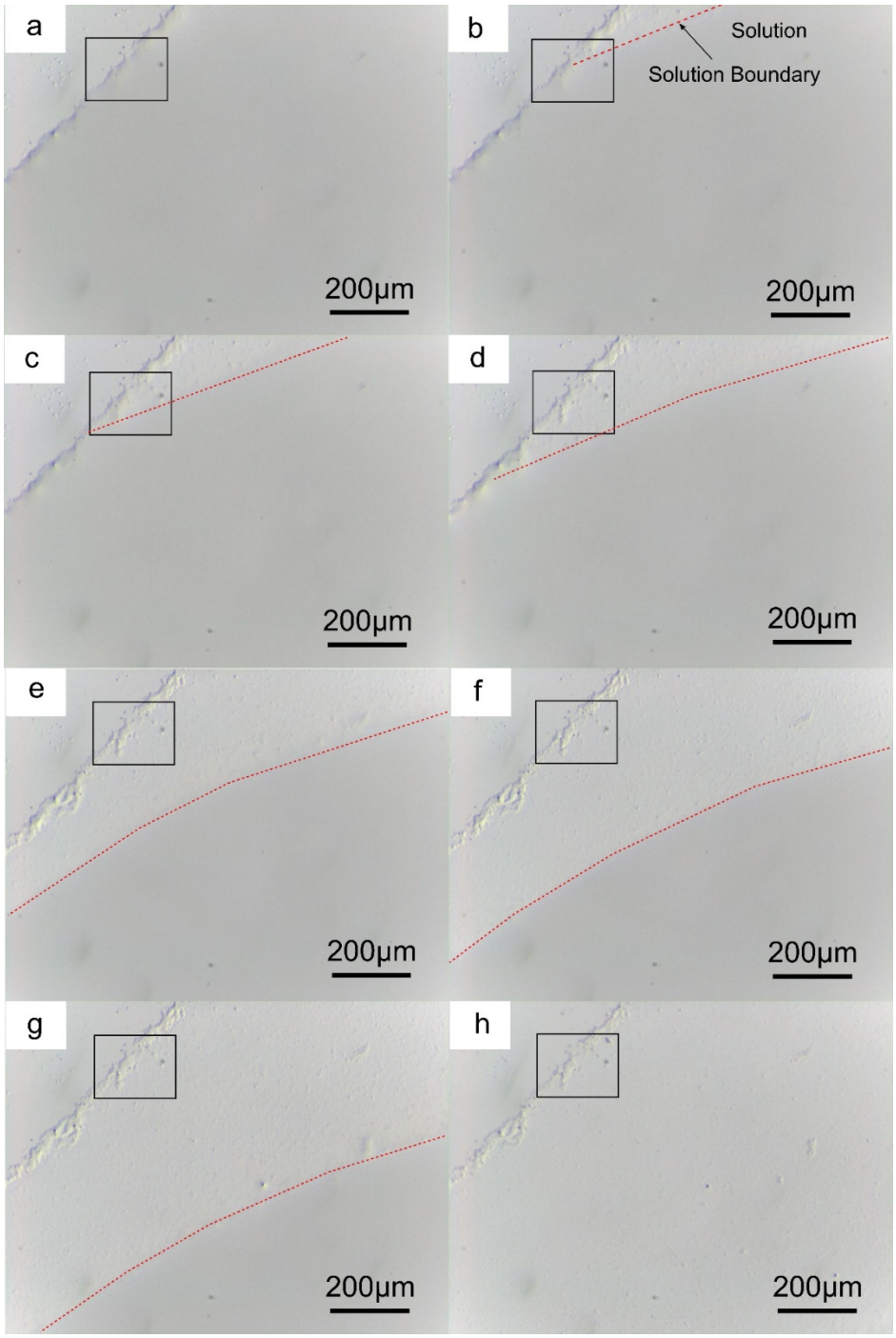

Figure 5. Timelapse photography of experiment 2, showing evaporation of the bulk liquid phase containing calcium chloride. Photos have been taken 17s intervals.

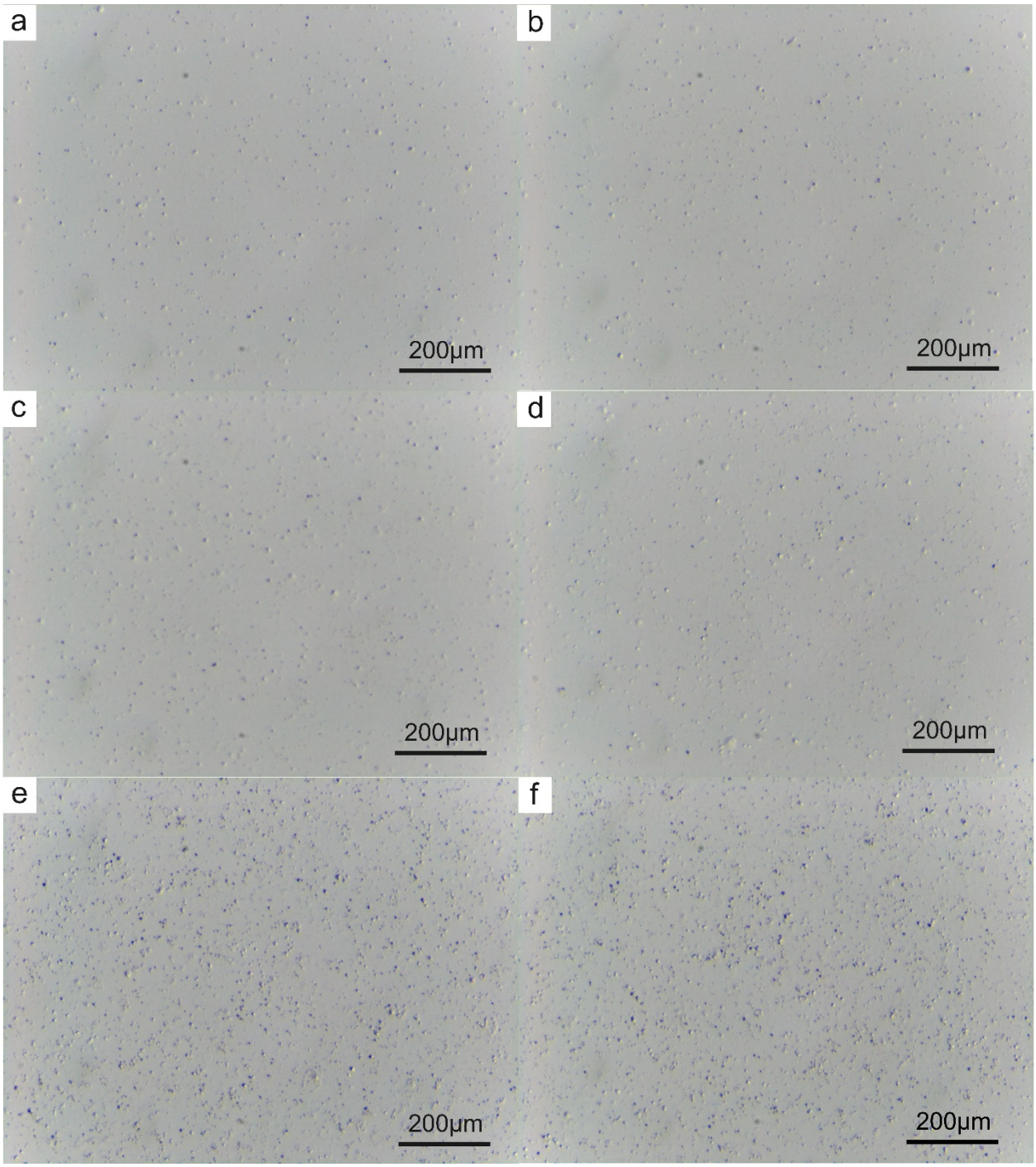

Figure 6. Results of light microscope of experiment 3. a) and b) are 300 synchronised reactant pulses (50 ms each), c) and d) are 450 synchronised reactant pulses (50 ms each), e) and f) are synchronised reactant pulses (50 ms each).

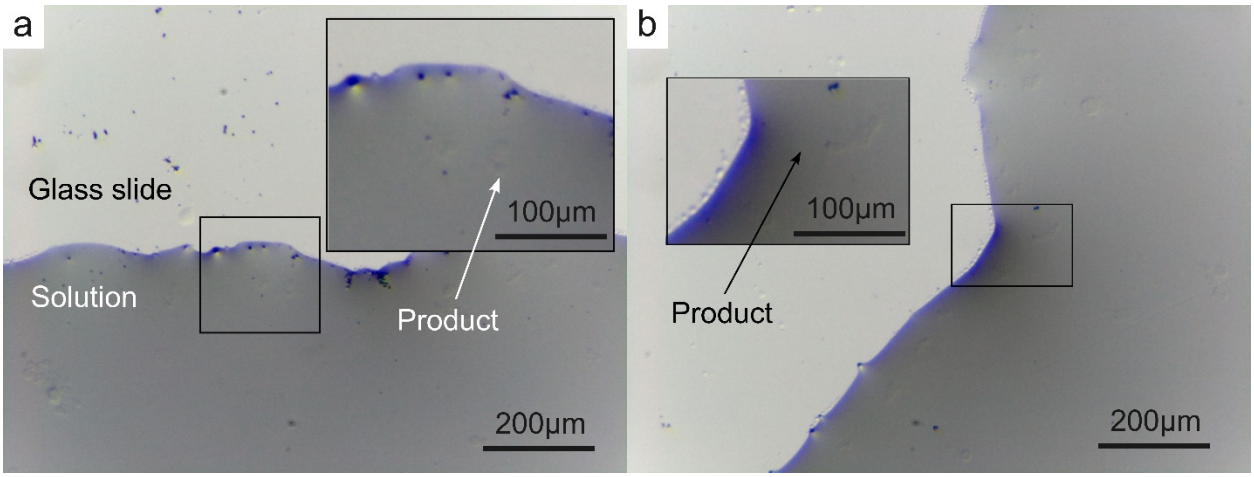

Figure 7. Results of light microscope of experiment 4. The two images were both taken after the reaction. In each figure, the dark region is a liquid drop, and the light region is a glass sheet. In the local magnification diagram, we can observe the blue products, and the products in the four diagrams are mostly distributed in dots or clusters at the solution boundary, and there is no obvious difference in different diagrams.

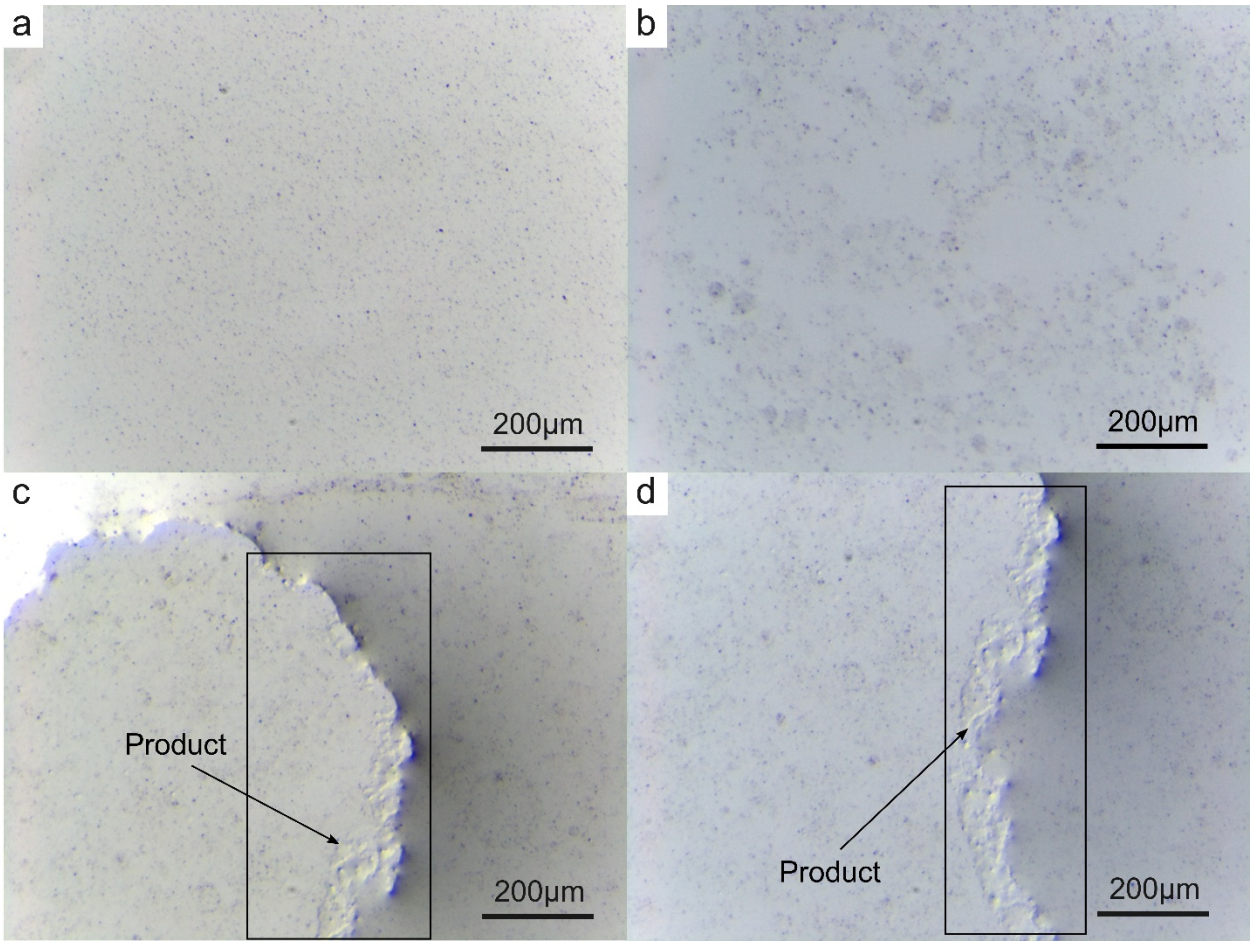

Figure 8. Results of light microscope of experiment 5. a) and c) were taken at the same brightness, and b) and d) were taken at the same brightness, a) and b) are the inside of the solution, and c) and d) are the boundary between the solution and the glass slide.

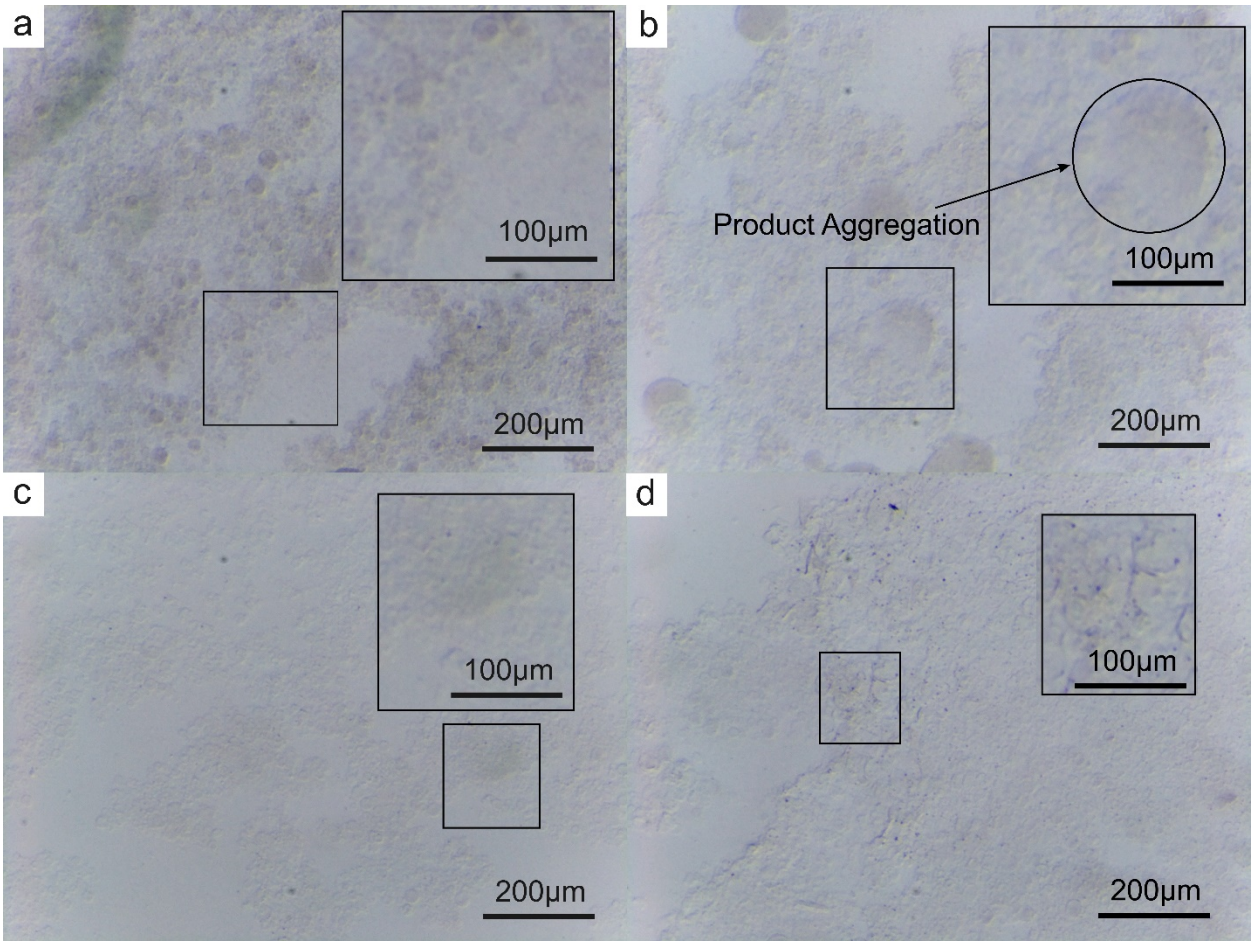

Figure 9. Results of light microscope of experiment 6. The reaction in a) and b) took place on the glass slide, and the reaction in c) and d) took place in the beaker. After the reaction was over, the solution was transferred from the beaker to the glass plate with a dropper for observation and photographing.

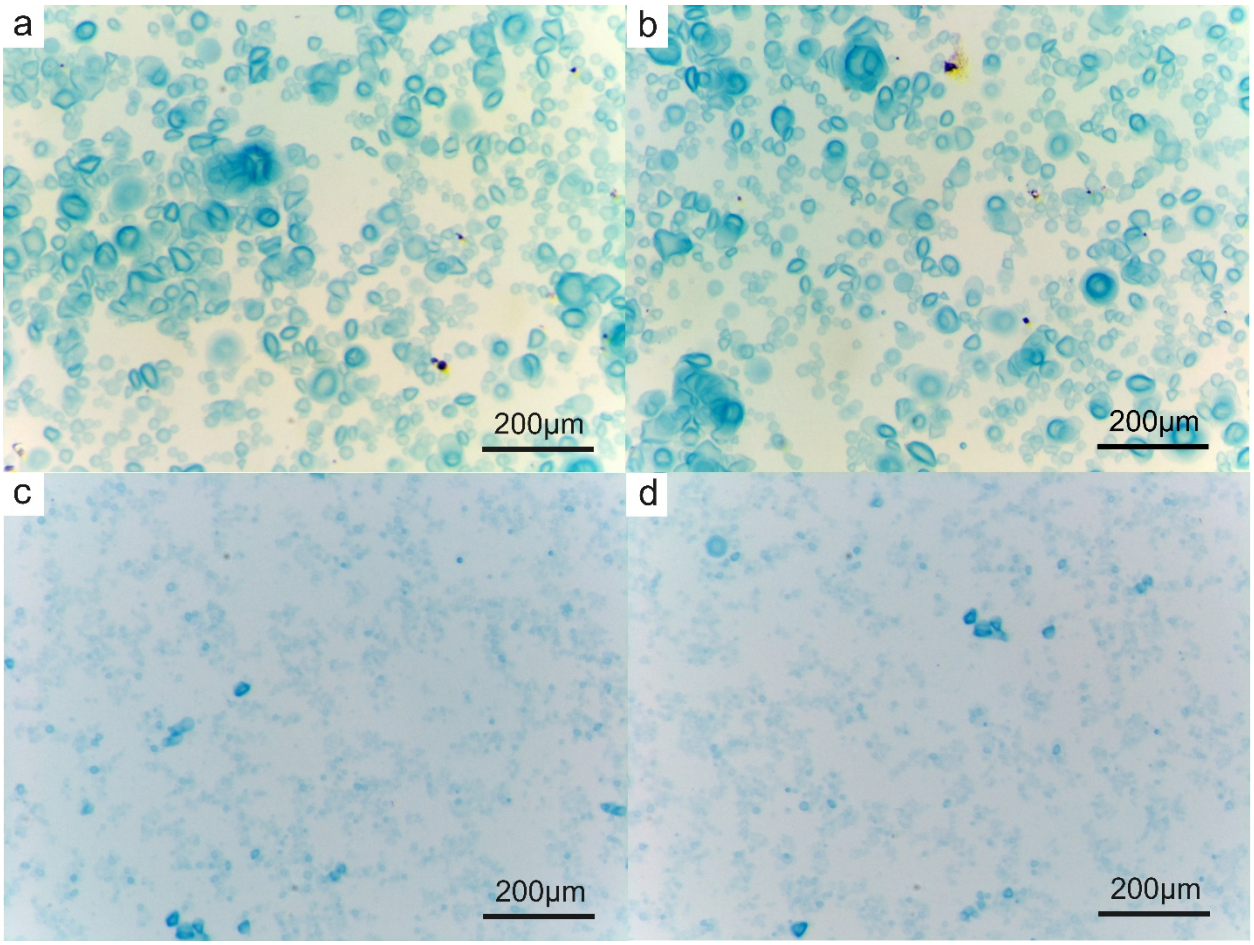

Figure 10. Results of light microscope of experiment 7. a) and b) were produced by the reaction of $Na_4[Fe(CN)_6]$ with $FeCl_3$, and c) and d) were produced by the reaction of $Na_4[Fe(CN)_6]$ with $Fe(NO_3)_3$. The two types of reactions were both in petri dish.

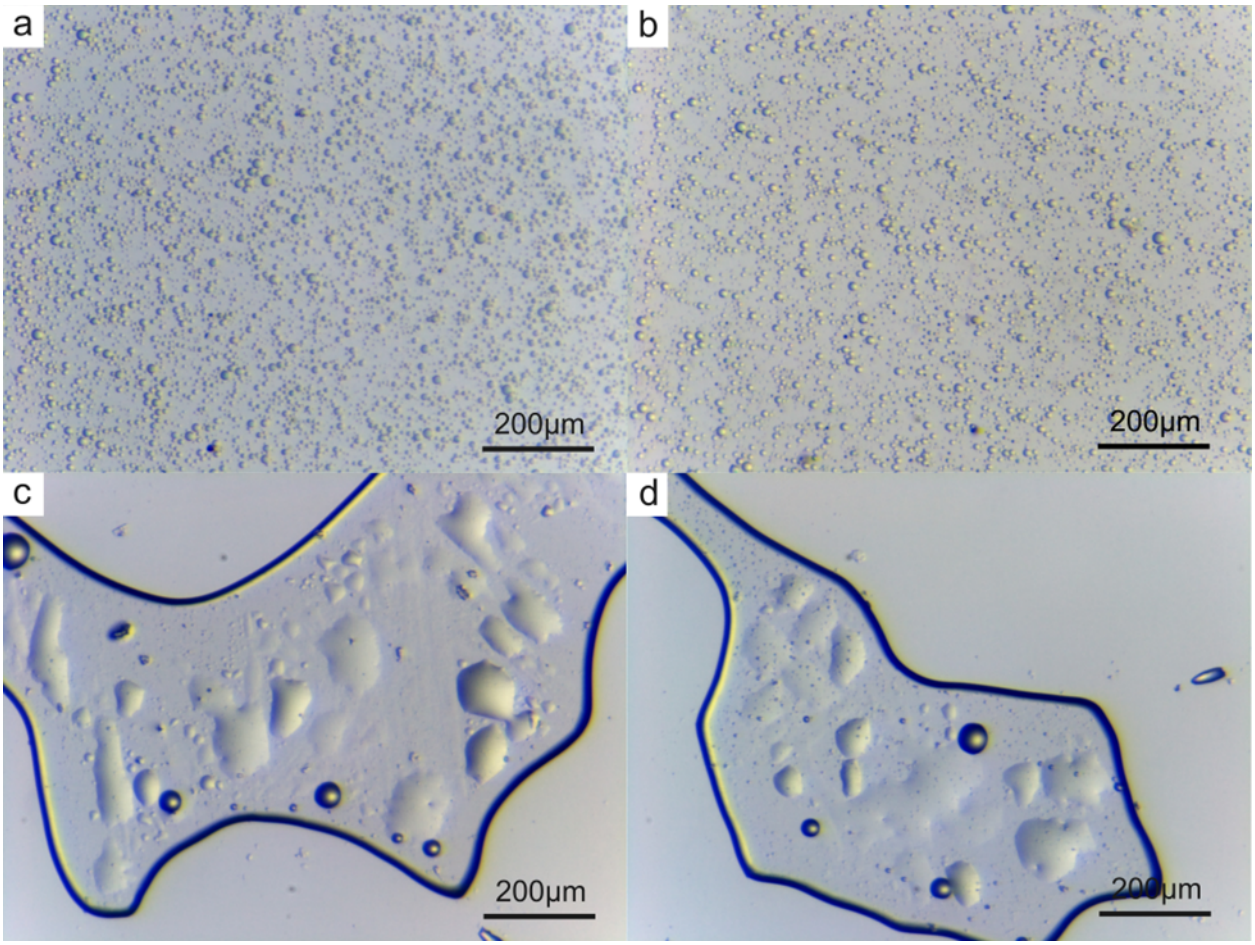

Figure 11. Results of light microscope of experiment 8. The reactants of these four figures were the same, and all the reactions were on the glass slide. The glass slide of a) and b) were covered by oil, and that of c) and d) were covered by water.

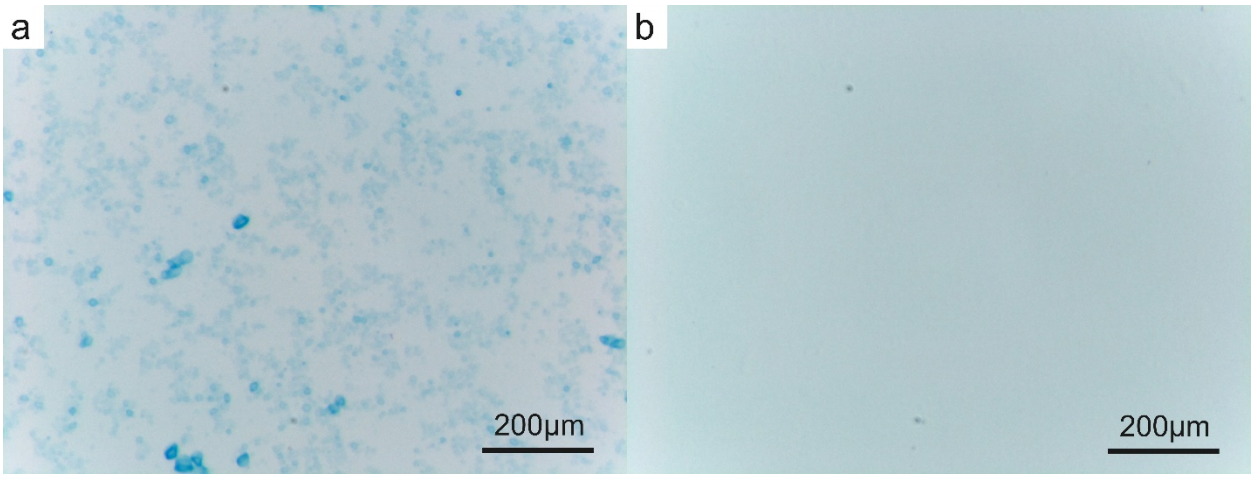

Figure 12. Results of light microscope of experiment 9, which is EDTA-responsive disintegration of soft calcium alginate microspheres. a) Prussian-blue containing microspheres before the addition of EDTA. b) Disintegrated microspheres 1 hour following the addition of 1 mL EDTA.

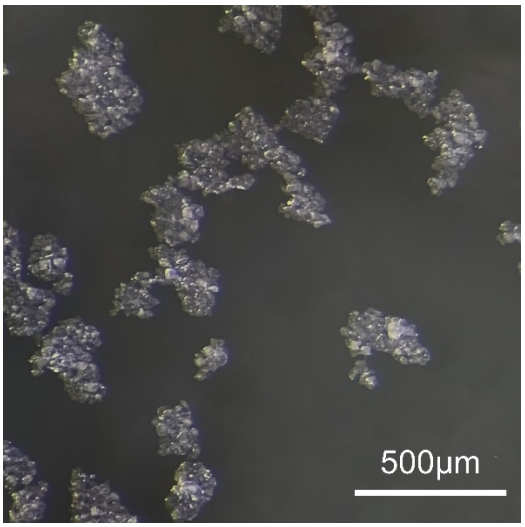

Figure 13. Results of light microscope of experiment 10, which is fluorescent particles of soft calcium alginate microspheres.

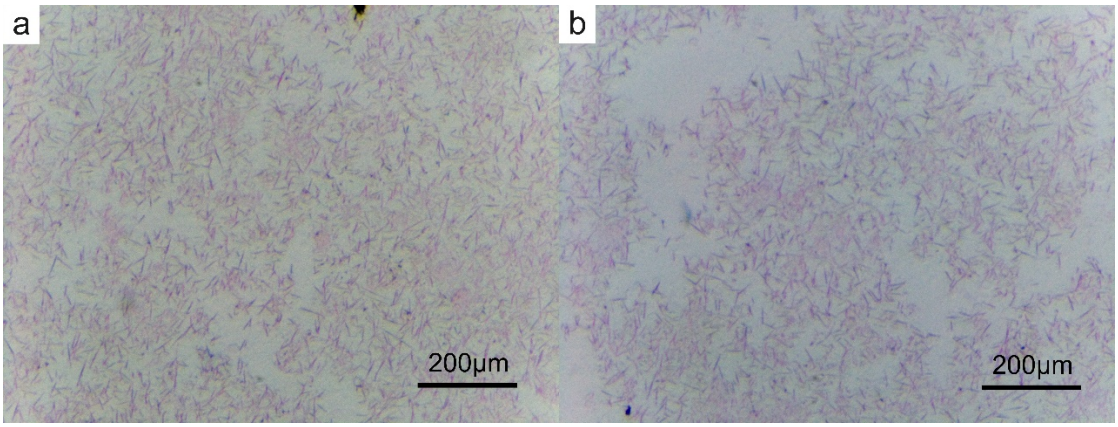

Figure 14. Results of light microscope of experiment 11, showing encapsulation of $[Ni(dmg)_2]$ within calcium alginate microspheres.

Determination of particle diameter

Particle diameters are determined from imaging data following automated segmentation using the Segment Anything Model (SAM). Once a bit mask is assigned to each particle, its diameter in pixels was estimated by assuming that the shape is approximately circular (area = 2 π r).

Aerosol control programs

These programs govern the formation of microdroplets, allowing us to control both their quantity and duration. They can be executed on RP2040-compatible microcontroller boards (see https://github.com/MehrResearch/ureactors for further instructions).

```
from rp2040hw.pio import pios, clkdiv
from pico_ctrlaer import ON, OFF, mux, CtrlAer
from machine import ADC, Pin
```

```
adc = ADC(Pin(26))

def prog1():
    for i in range(600):
        reading = adc.read_u16()
        freq = 106_500 + (reading >> 3)
        ctrlaer.set_freq(freq)
        print(freq)
        yield ON, 250
        yield OFF, 250

# GP0: Alginate solution
progs = [prog1()]

prog = mux(progs)

ctrlaer = CtrlAer(sm_number=0, base_pin=0, n_pins=len(progs))
ctrlaer.run(prog)
```

Listing 1. CtrlAer program used for experiments 1, 2, 3, 4, 5, and 6.

```
from rp2040hw.pio import pios, clkdiv
from pico_ctrlaer import ON, OFF, mux, CtrlAer
from machine import Pin
import time

def prog1():
    yield OFF, 60000
    for i in range(1200):
        print(i)
        yield ON, 50
        yield OFF, 250

# GP0: Alginate solution
progs = [prog1()]

prog = mux(progs)

ctrlaer = CtrlAer(sm_number=0, base_pin=0, n_pins=len(progs))
ctrlaer.run(prog)
```

Listing 2. CtrlAer program used for experiments 7, 8, 9, and 10.

```
from rp2040hw.pio import pios, clkdiv
from pico_ctrlaer import ON, OFF, mux, CtrlAer
from machine import ADC, Pin
import time

adc = ADC(Pin(26))

def prog1():
    for i in range(500):
        reading = adc.read_u16()
        freq = 108_500 + (reading >> 3)
        ctrlaers[0].set_freq(freq)
        print(i, freq)
        yield ON, 100
        yield OFF, 600

# GP0: Alginate solution
progs = mux([prog1()])
ctrlaers = [
    CtrlAer(sm_number=0, base_pin=0, n_pins=1, freq=114_500),
]

while True:
    for i, (ctrlaer, prog) in enumerate(zip(ctrlaers, progs)):
        ctrlaer.run(prog, block=False)
```

Listing 3. CtrlAer program used for experiments 11.

```
from pico_ctrlaer import ON, OFF, mux, CtrlAer
from machine import Pin, ADC

adc = ADC(Pin(26))

def prog1():
    for i in range(200):
        reading = adc.read_u16()
        freq = 108_500 + (reading >> 3)
        ctrlaer.set_freq(freq)
        print(i, freq)
        yield ON, 100
        yield OFF, 600

def prog2():
```

```
    for i in range(200):
       yield OFF, 325
       yield ON, 50
       yield OFF, 325

# GP0 (prog1): Sodium alginate + hydroquinone
# GP1 (prog2): Calcium chloride + potassium permanganate
prog = mux([prog1(), prog2()])

ctrlaer = CtrlAer(sm_number=0, base_pin=0, n_pins=2, freq=110_600)

ctrlaer.run(prog)
```

Listing 4. CtrlAer program used for experiment 12.

Reactor

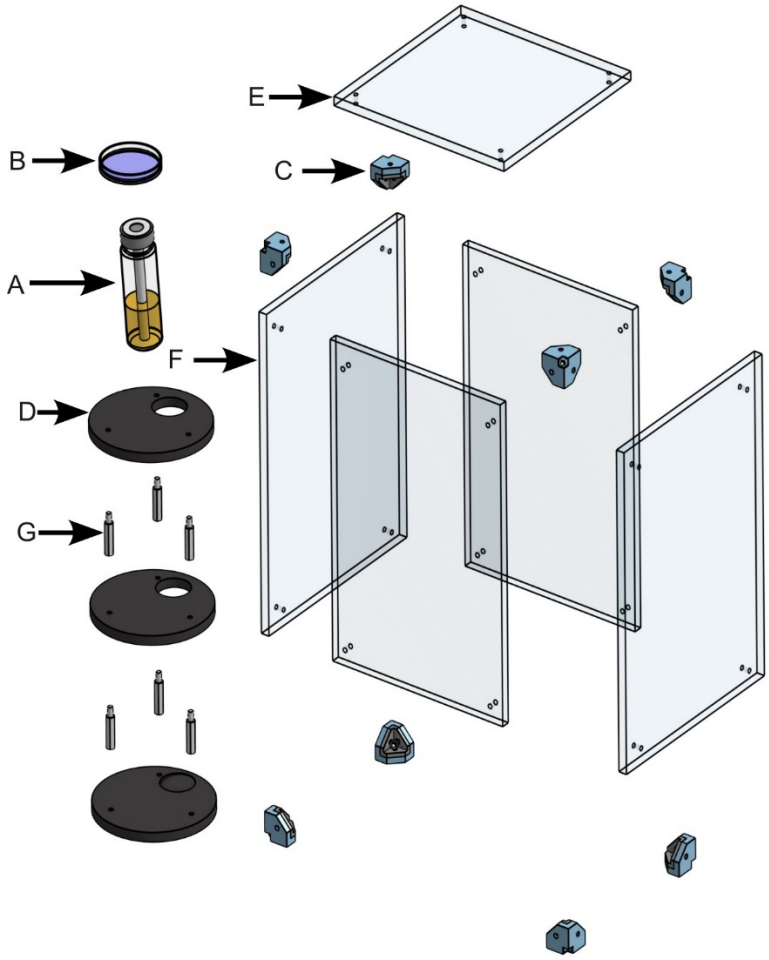

Figure 15. Full mechanical specification of reactor, reagent holder, and reagent module.

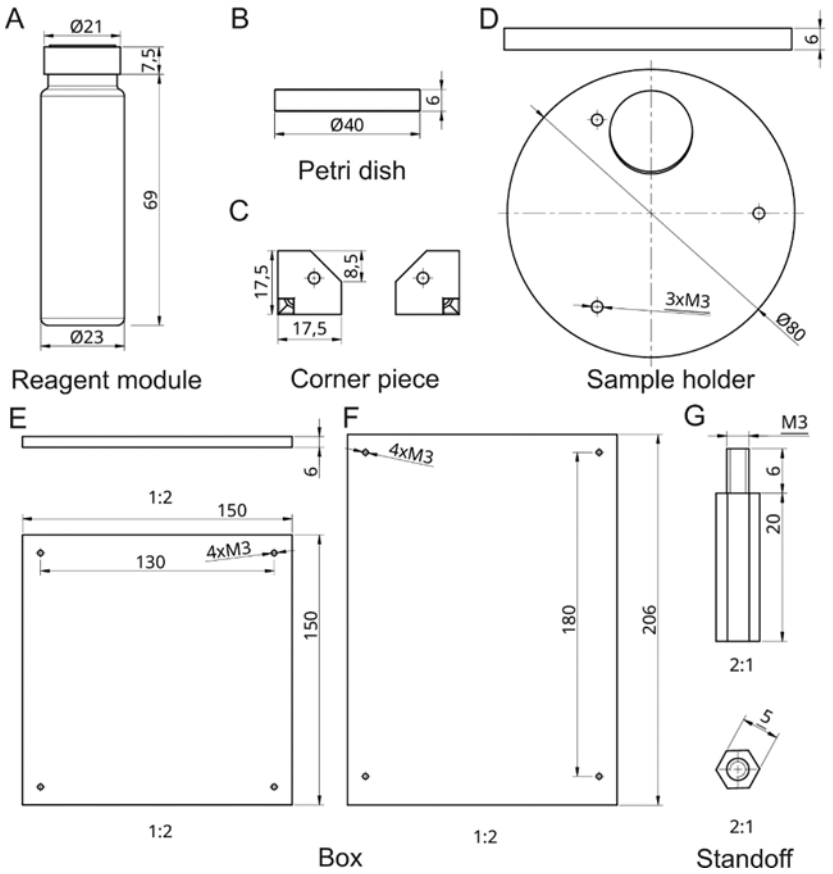

Figure 16. Full mechanical specification of reactor, reagent holder, and reagent module. All dimensions are specified in millimetres.

Microscope image acquisition

The vendor-provided raspi suite of programs, specifically raspistill and raspivid, were used for image acquisition. The specific command used to capture still images is shown in **Listing 5**.

```
#!/usr/bin/env bash

raspistill -n -ss 142000 -ISO 5 -co 90 -o "$1 $(date +%Y-%m-%d_%H-%M-%S).jpg"
```

Listing 5. Command line used for image acquisition on the Raspberry Pi HQ camera.

Particle diameter comparison for different experimental parameters

Alongside the box plots presented in the manuscript, **Table 2** presents a matrix comparing 95% confidence intervals for difference between mean diameters for each pair of experimental conditions obtained via bootstrapping (number of samples: 10,000). To summarise, most intervals include zero, indicating no statistically significant difference between many condition pairs, with a few subtle trends. Longer pulse durations (50 ms) tend to produce slightly larger particles compared to shorter durations (25 ms), and higher pulse counts generally yield marginally larger particles, particularly evident in the 600-pulse experiments. The most substantial differences occur between extreme conditions (e.g., 75 pulses at 25 ms vs 600 pulses

at 50 ms). Despite these trends, the majority of differences remain small relative to typical particle sizes, with no clear linear trends emerging.

Table 2. 95% confidence intervals for difference in mean particle diameter (column label minus row label) obtained using bootstrap (N=10,000).

	# pulses	75		150		300		600	
	Pulse duration (ms)	25	50	25	50	25	50	25	50
# pulses	Pulse duration (ms)								
75	25	-1.08 – 1.09	0.98 – 3.08	0.25 – 2.42	-1.76 – -0.14	-1.59 – 0.10	-2.01 – -0.44	-0.77 – 0.77	-4.41 – -2.84
	50	-3.06 – -0.99	-1.03 – 0.98	-1.75 – 0.34	-3.78 – -2.22	-3.62 – -1.97	-4.00 – -2.54	-2.76 – -1.30	-6.41 – -4.93
150	25	-2.41 – -0.28	-0.32 – 1.78	-1.10 – 1.09	-3.08 – -1.45	-2.92 – -1.18	-3.35 – -1.75	-2.10 – -0.53	-5.76 – -4.18
	50	0.15 – 1.74	2.21 – 3.78	1.47 – 3.13	-0.44 – 0.43	-0.27 – 0.70	-0.64 – 0.09	0.60 – 1.31	-3.06 – -2.30
300	25	-0.10 – 1.58	2.00 – 3.60	1.23 – 2.93	-0.69 – 0.28	-0.51 – 0.53	-0.89 – -0.07	0.34 – 1.16	-3.33 – -2.46
	50	0.44 – 1.97	2.54 – 4.01	1.75 – 3.33	-0.09 – 0.62	0.07 – 0.88	-0.25 – 0.24	0.97 – 1.48	-2.68 – -2.14
600	25	-0.77 – 0.77	1.30 – 2.77	0.53 – 2.11	-1.32 – -0.60	-1.18 – -0.34	-1.47 – -0.98	-0.25 – 0.25	-3.91 – -3.37
	50	2.86 – 4.41	4.94 – 6.40	4.15 – 5.74	2.30 – 3.04	2.47 – 3.31	2.14 – 2.68	3.37 – 3.91	-0.29 – 0.29

Particle diameter comparison between aerosol–aerosol and aerosol–bulk modalities

Shows a histogram of particle sizes for microreactors formed via the two methods shown in the paper. Full analysis code is included in the Jupyter notebook located in the accompanying GitHub code repository.

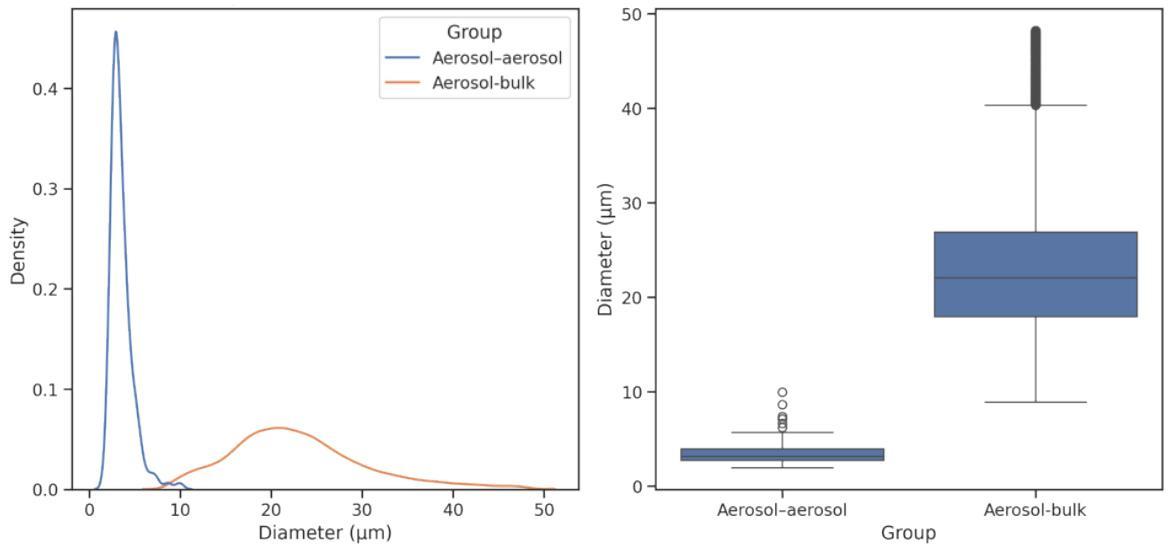

Figure 16. Diameter comparison between particles formed via the