Microfluidic dynamic light scattering used for high throughput measurements

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Nanoparticles…

Wide variety: Gold, quantum dots, carbon nanotubes, silica…
polymer latex
liposomes, polymersomes, micelles

Academically important: 11,651 web of science citations
9,677 in the past 5 years

Nanoparticle applications

Targeted drug delivery – stimuli responsive liposomes, polymersomes

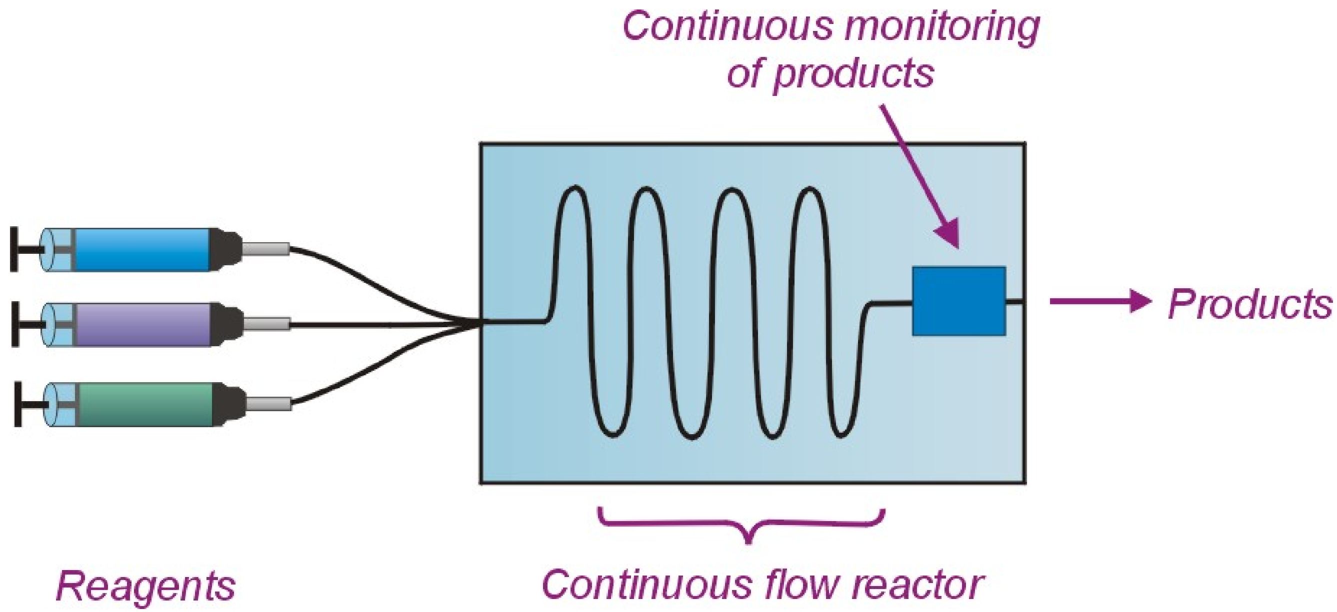
Coatings – self cleaning surfaces, antireflective coatings

Consumer products – clear inorganic sunscreens

“Our ultimate objective”

-- ***Integrate*** the synthesis and characterization of nanoparticles onto a single microfluidic device.

-- Working in the direction of producing particles derived from block copolymers, such as ***micelles*** and ***vesicles***.

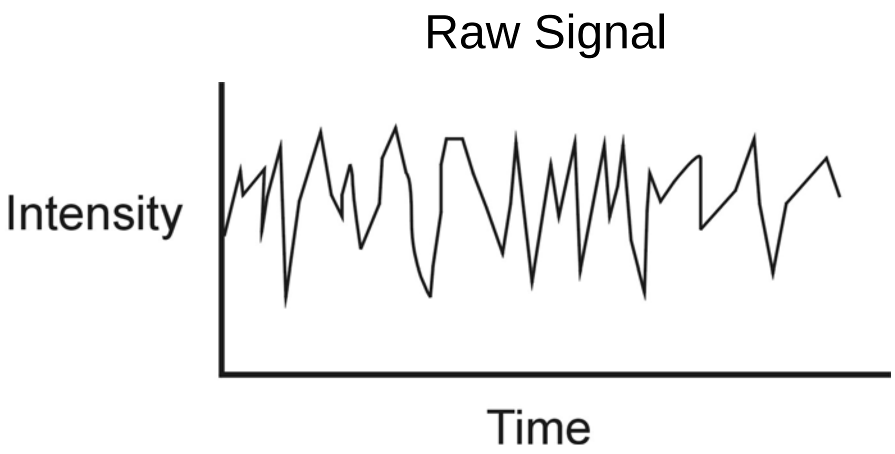


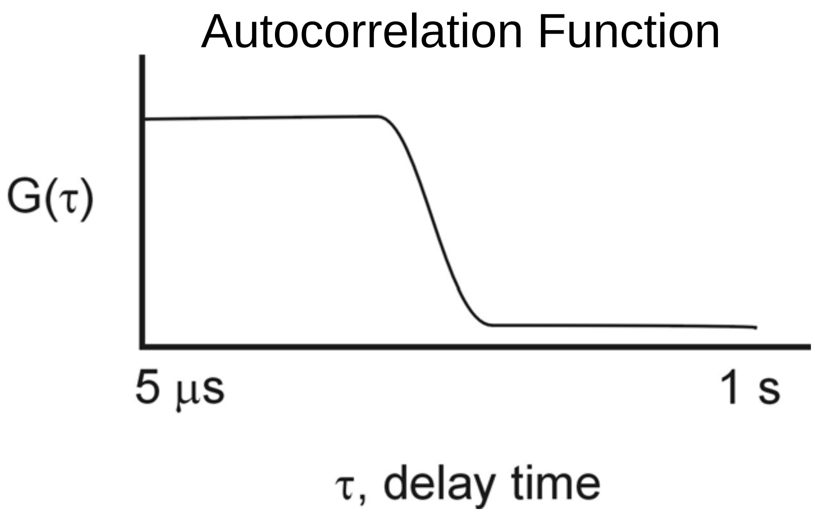
Available characterization tools

Optical microscopy and fiber optic compatible techniques such as spectroscopy and light scattering

-- The continuous flow design is expected to allow for ***automated*** evaluation of the relationship between ***reaction conditions*** and resulting ***products***.

What is Dynamic Light Scattering (DLS)?





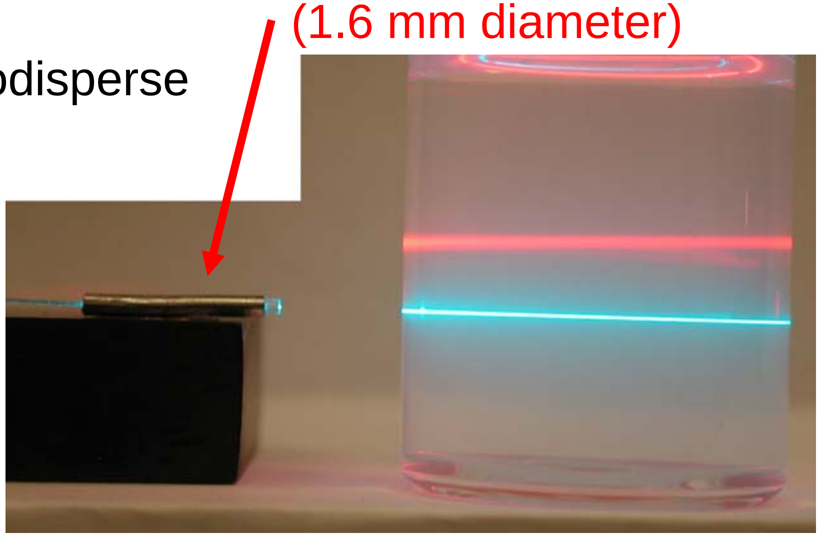
-- Fitting to the autocorrelation function gives the diffusion coefficient, which is used to determine the ***hydrodynamic radius*** of spherical particles.

Practical specifications:

-Ideal tool for examining dilute solutions of monodisperse particles with diameters of 20-500 nm.

- Can give particle sizes of +/- 5% in as little as a few seconds.
- It can be integrated into a microfluidic device with fiber optic probes, without reducing data quality.

Fiber optic probe (1.6 mm diameter)



Microfluidic Challenges

Aqueous samples + room temperature = Many existing microfluidic techniques

-- Molded PDMS attached to glass, Selectively cured thiolene resin between glass slides, embossed plastic thermally bonded to a surface…

Polymer synthesis

High temperatures and ***organic solvents*** for long times
Goal = no swelling or leaking

> A typical ATRP synthesis of polystyrene is done in toluene at 90 °C for multiple hours, and continuous production may be desired for several days.

DLS

Rigid, black material

In general…

Inexpensive, simple to make, and potential for a transparent surface

Microfluidic Solutions

Kapton glued onto machined aluminum with chemically resistant epoxy

780 μm wide channels,
path length >5.5 m

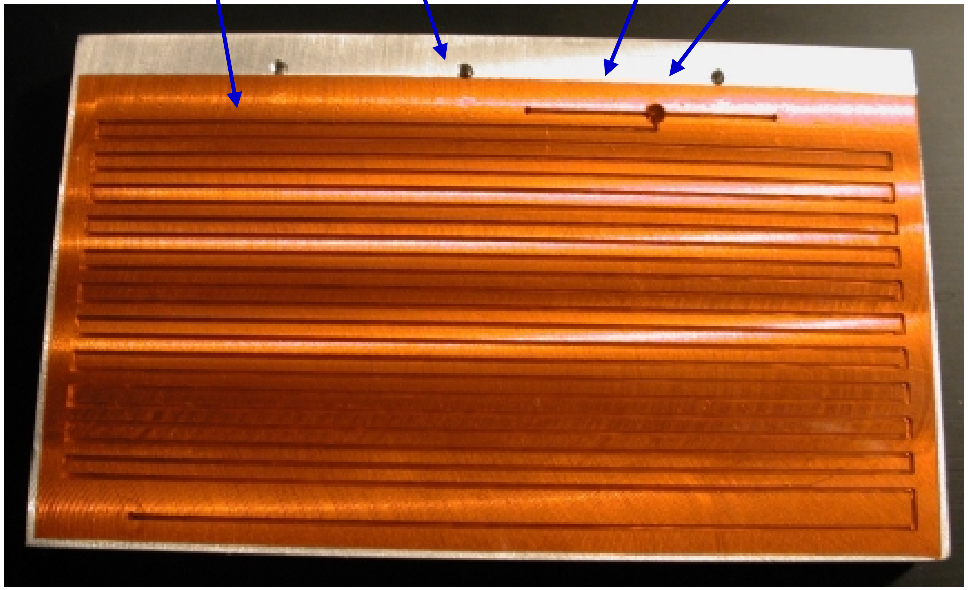
3 inlets for reagents

Inlet with mixing
at midpoint

2 heating cartridges
+ thermocouple for
temperature control

Mixing chamber
with stir bar

Exit



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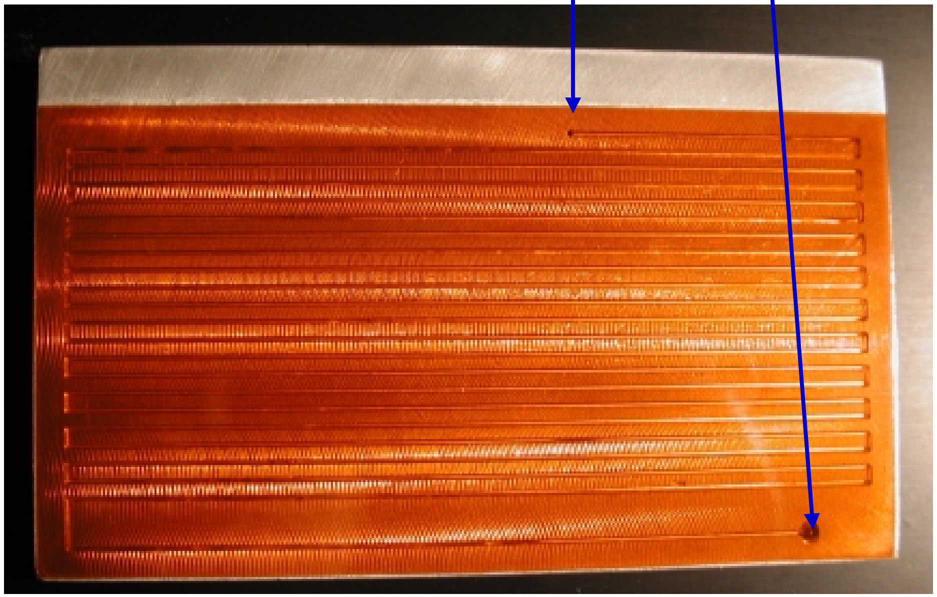

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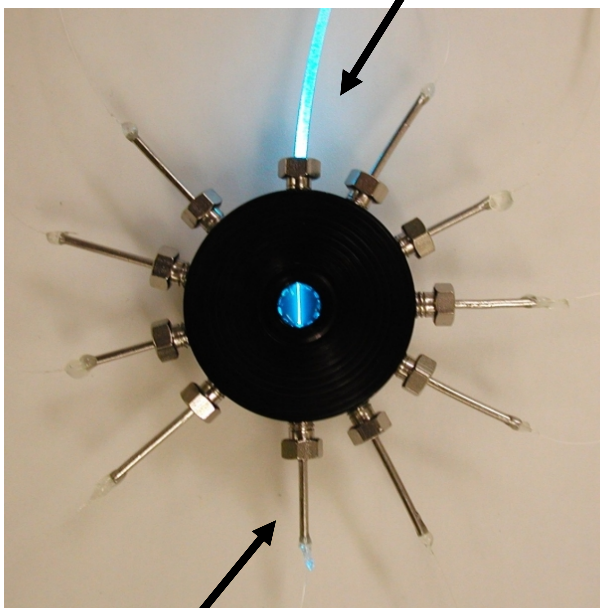
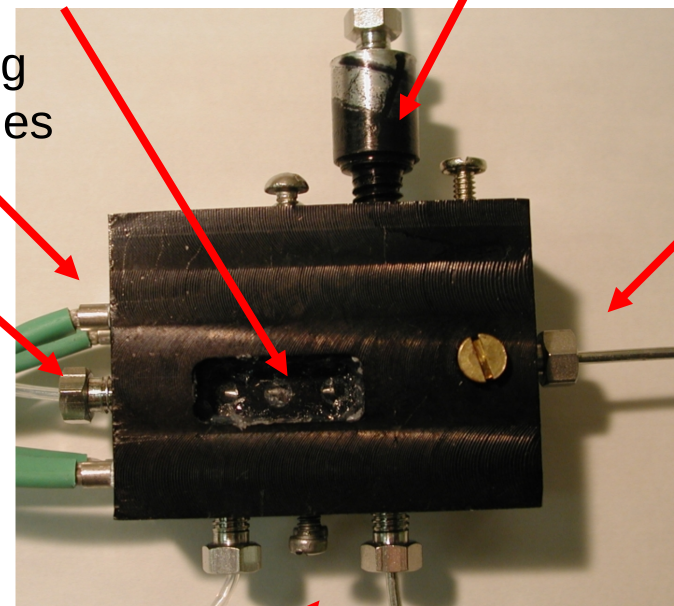
Microfluidic Solutions

DLS works well with ***aluminum anodized black***



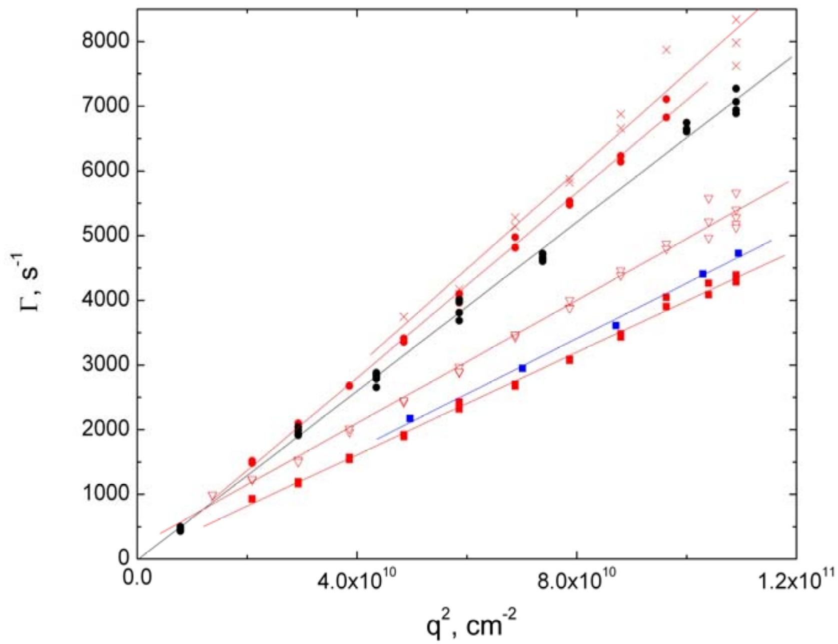


Note: the internal measurement chamber is not visible from the outside

Microfluidic fiber optic DLS works…

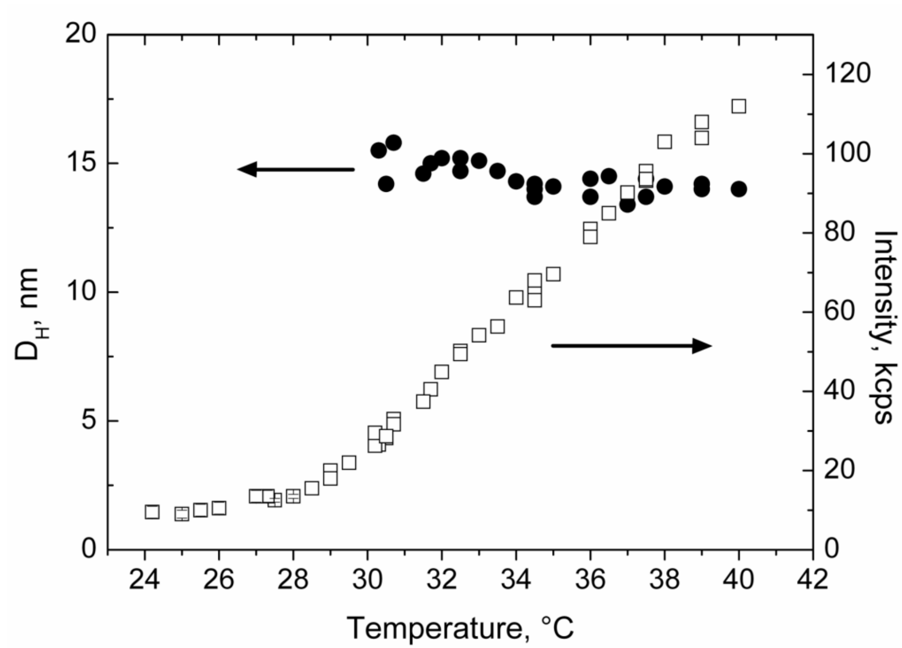
All of the devices have been successfully calibrated with latex size standards

Calibration of multiangle devices



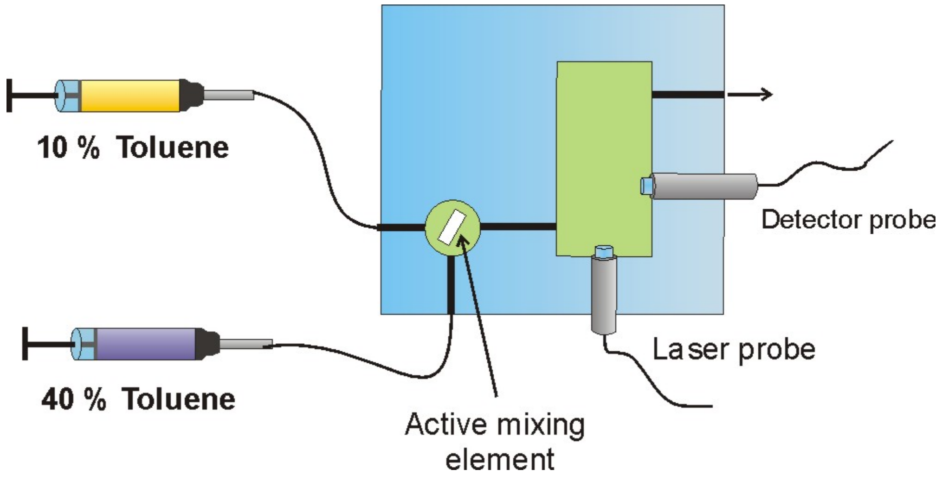
- ■ 107 nm latex, inline rotation
  $D_m = 4.28 \times 10^{-8}$ cm^2/s
  $D_H = 105$ nm
- ● 64 nm latex, fixed angles
  $D_m = 6.51 \times 10^{-8}$ cm^2/s
  $D_H = 69.1$ nm
- ■ 107 nm latex, out of plane rotaton
  $D_m = 3.96 \times 10^{-8}$ cm^2/s
  $D_H = 114$
- ● 64 nm latex, out of plane rotation
  $D_m = 7.16 \times 10^{-8}$ cm^2/s
  $D_H = 62.9$ nm
- × SB(5-5), out of plane rotation
  $D_m = 7.51 \times 10^{-8}$ cm^2/s
  $D_H = 19$ nm
- ▽ SB(9-9), out of plane rotation
  $D_m = 4.75 \times 10^{-8}$ cm^2/s
  $D_H = 30$ nm

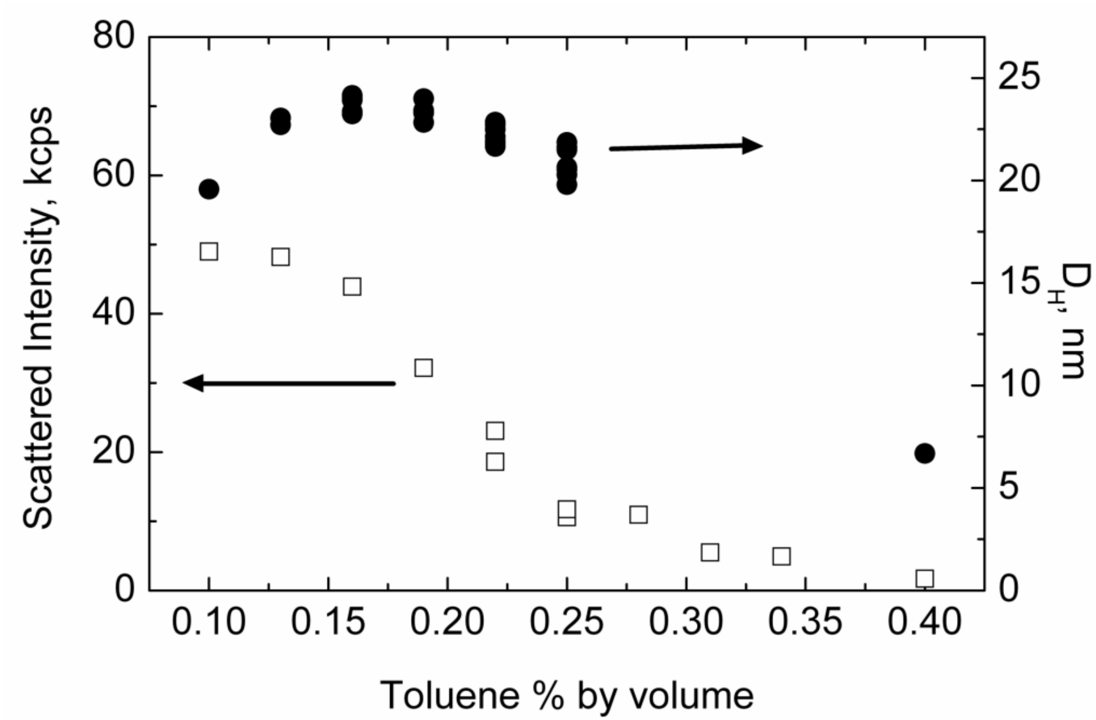
Temperature control



Aqueous PEO-PPO-PEO block copolymers form micelles above 30°C.

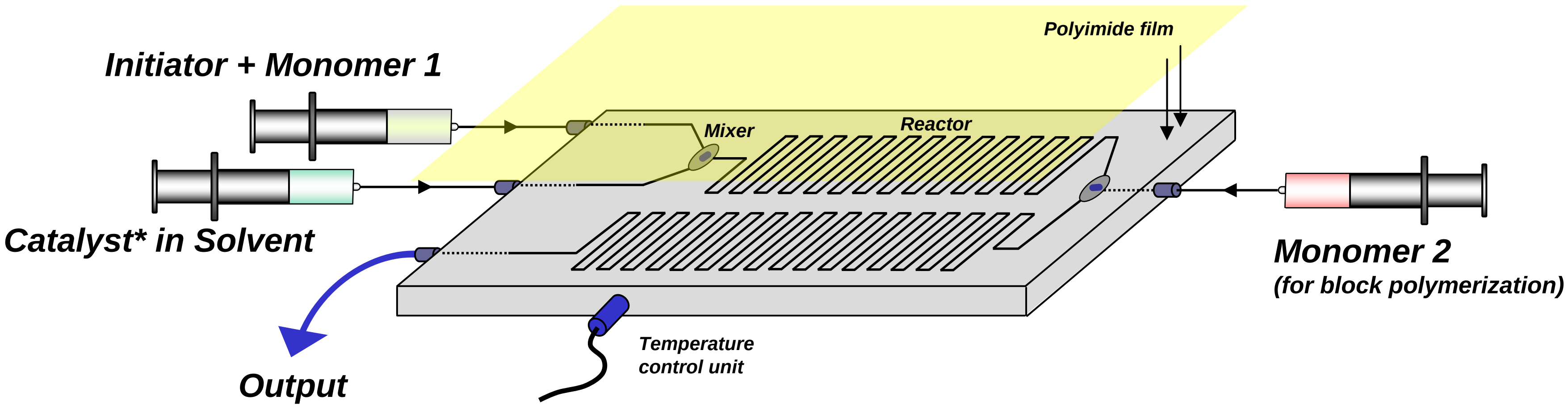
High-throughput DLS measurements





Toluene is a neutral solvent for the polystyrene and polyisoprene blocks causing the micelles to dissolve.

Microfluidic polymer synthesis



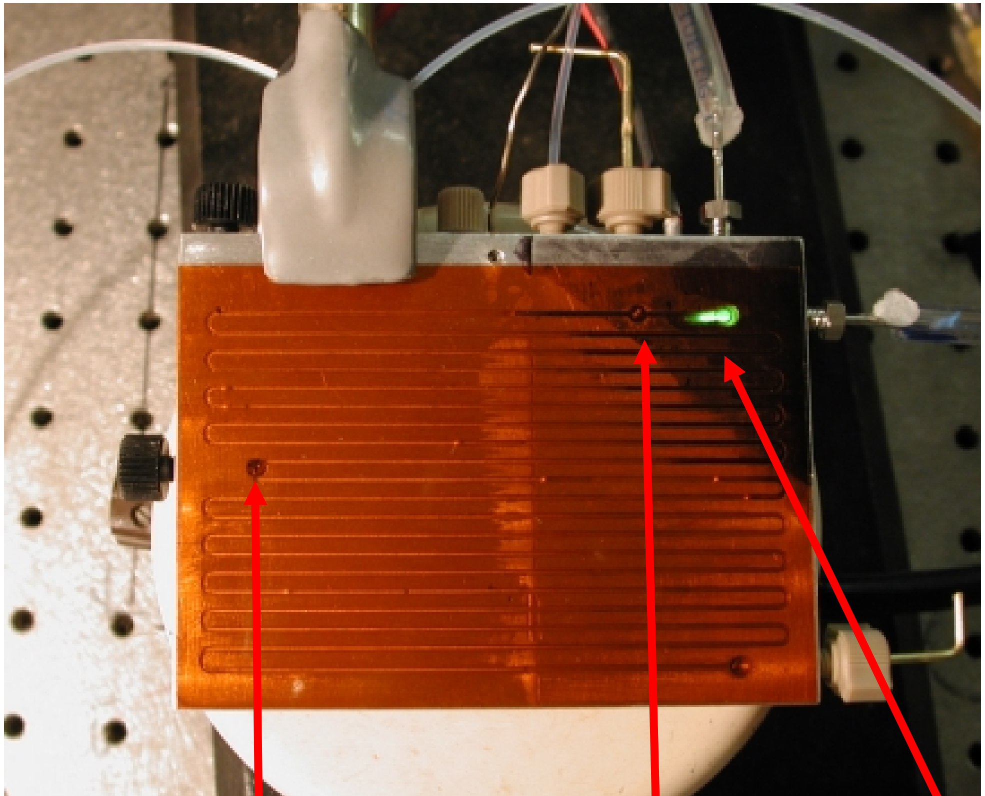
Initiator/Monomer (equiv)	Solvent	Condition (°C/min)	Yield[a] (%)	M_n [b]	M_w/M_n [b]
PEBr[1]/Styrene (50)	anisole (20 %)	90/160	59	4300	1.09
EBiB[2]/Benzyl methacrylate (300)	anisole (50 %)	40/120	47[c]	20700	1.34
MBP[3]/*n*-Butyl acrylate (100)	MEK (50 %)	70/240	48	5900	1.13

*One equiv of CuBr/PMDETA complex to initiator was used.

[a] Determined by gravimetry. [b] Measured by SEC using PS standards. [a] Determined by ^{1}H NMR.

[1]PEBr; 2-phenylethylbromide, [2]EBiB; ethyl 2-bromoisobutylate, [3]MBP; methyl 2-bromopropionate

Integration of DLS and Synthesis



2 –sided device
3.6 m channel 780 μm x 780 μm
Particle sizing conducted at device exit

Fully automated

Computer controlled syringe pumps and data acquisition

DLS

Mixing chamber towards end for surface functionalizing

Mixing chamber for diluting products

Silica nanoparticle synthesis – Stöber Method

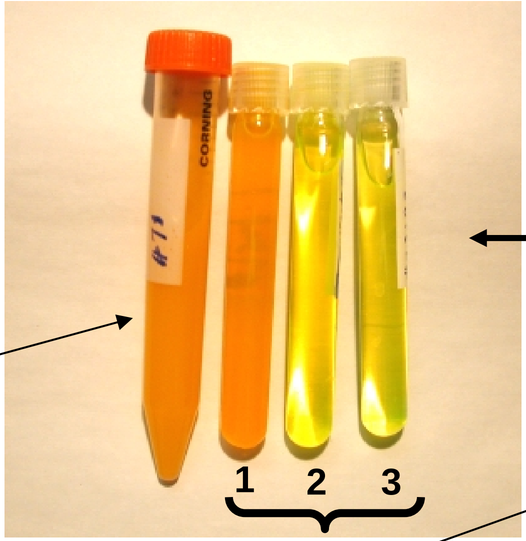
Ethanol
Ammonia
Tetraethyl orthosilicate (TEOS)
Water

Silica nanoparticles (100 nm - 800 nm) often monodisperse

W. Stöber, A. Fink, E. Bohn, J. Coll. Int. Sci., 26 (1968) 62.

Size determined by reagent ratios and temperature.

Functionalized triethoxy silanes are used to modify the silica surfaces
-- They are simply added at the late stages of particle growth



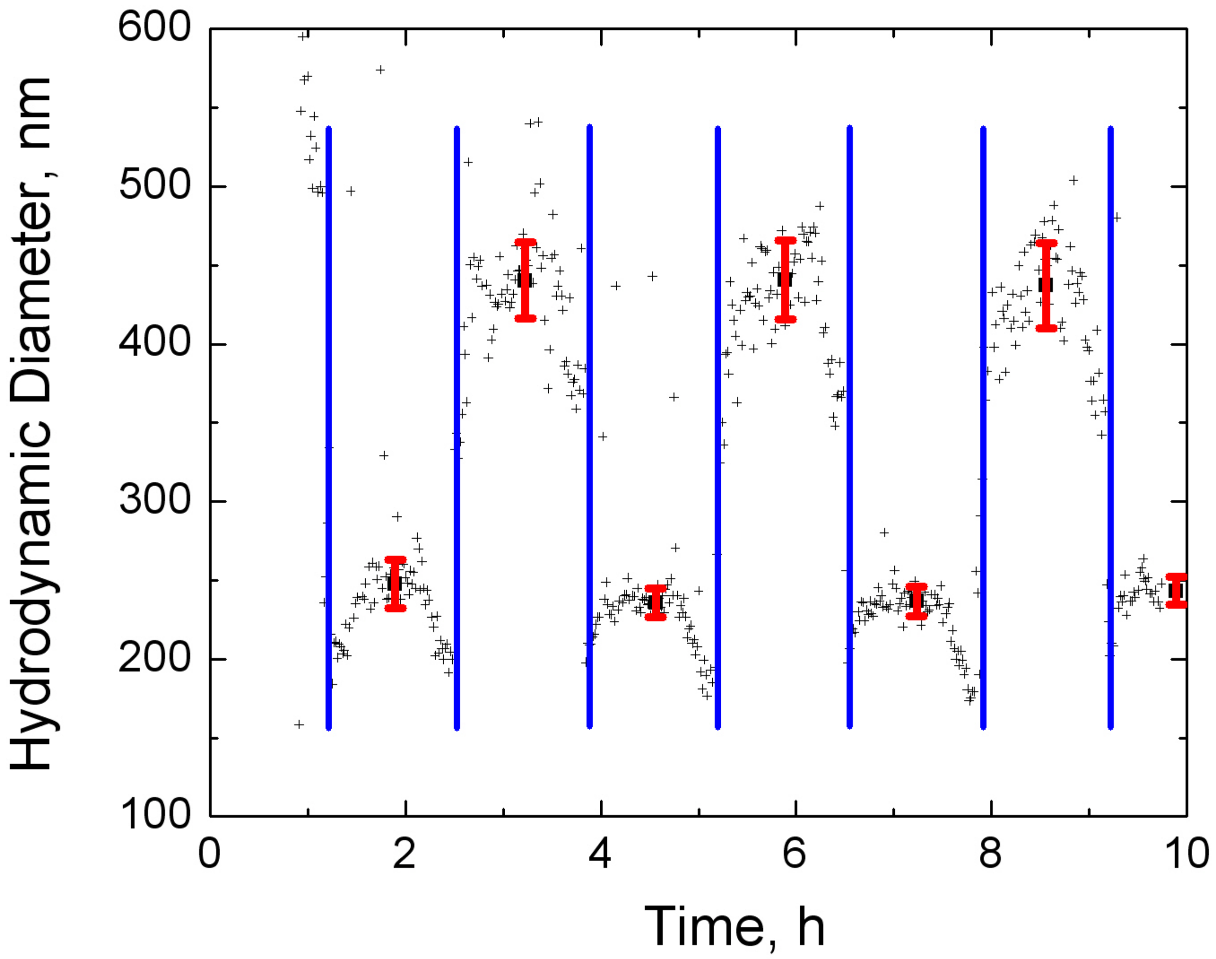
particles

Silica particles coated with fluorescein. The particles remain fluorescent after repeatedly centrifuged and redispersed in ethanol.

Supernates reduce in intensity as free dye is removed

Integrated synthesis and DLS measurements

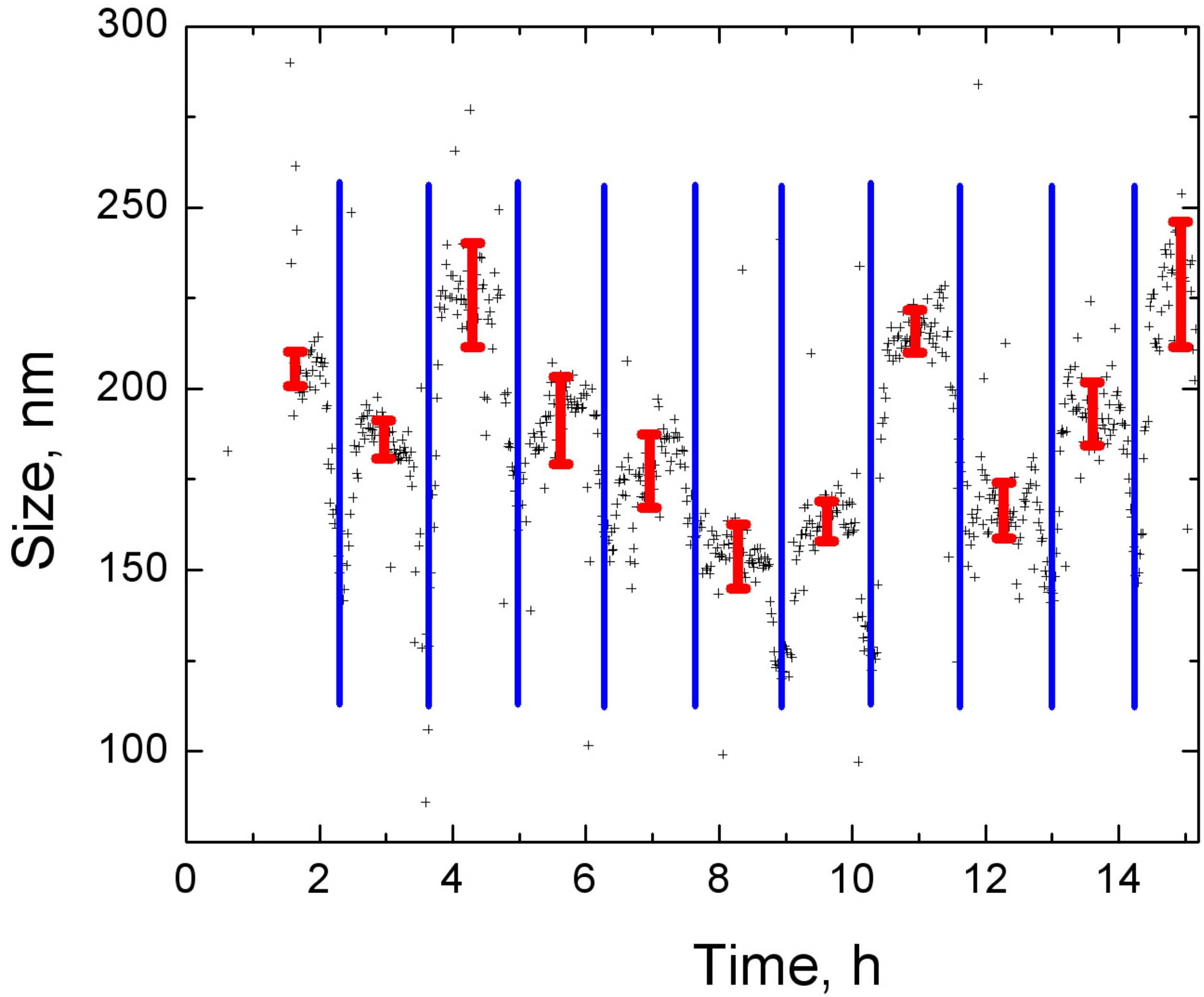
Alternately flowing two reagent compositions
Cycling between 60 min reagents, 20 min ethanol purge



Composition 1 (smaller) = 11.9 M [H_20], 0.040 M [TEOS], 0.50 M [NH_3]
Composition 2 (larger) = 9.5 M [H_20], 0.032 M [TEOS], 0.75 M [NH_3]

Reagent composition – particle size relationship

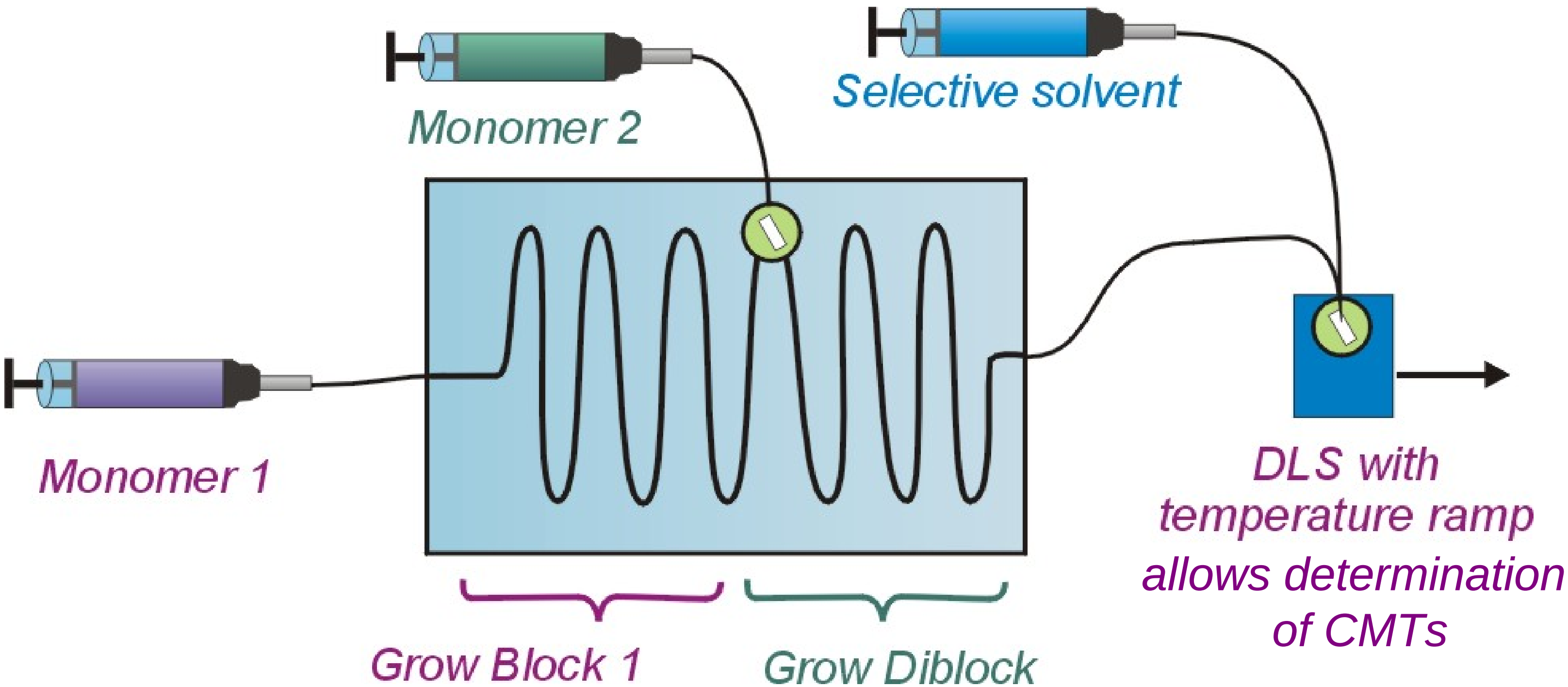
Consecutively flowing various reagent compositions
Cycling between 60 min reagents, 20 min ethanol purge



Silica particle sizes

[TEOS], M	*[NH_3], M*	*[H_20], M*	*D_H, nm*	*St. Dev., nm*	*Rel. St. Dev.*
0.035	0.36	11.3	154	9	6 %
0.035	0.41	13.3	163	6	3 %
0.035	0.41	2.9	166	8	5 %
0.035	0.50	7.2	177	10	6 %
0.035	0.41	11.3	186	5	3 %
0.035	0.50	9.2	191	12	6 %
0.035	0.50	11.3	193	9	5 %
0.035	0.50	11.3	206	5	3 %
0.035	0.59	2.9	216	6	3 %
0.035	0.59	11.3	226	14	6 %
0.035	0.59	12.3	229	17	8 %
0.040	0.50	11.9	240	12	5 %
0.032	0.74	9.5	439	25	6 %

Micelle formation



Preliminary results for the synthesis of poly(styrene -*b*- stearyl methacrylate) showed self assembly in dodecane --- 130 nm structures. Too large for micelles.

Previous work on this copolymer also found large structures, which were explained as “micelle clusters”.

Pitsikalis, M., et al. Macromolecules **2000**, *33*, 5469-5469.

Summary

Components for microfluidic synthesis and characterization of nanoparticles have been assembled and used

Fiber optic dynamic light scattering
- Used for high throughput measurements on stock solutions

Robust continuous flow reactor
- Demonstrated synthesis of several polymers in organic solvent

Silica nanoparticles
- Fully automated production and size characterization
- Reproducible sizes, and good resolution
- Examined compositions resulting in 150-440 nm

This tool is expected to allow for automated examination of the synthesis and self assembly of block copolymers in dilution solutions