BRAVE ANALYTICS

NANOPAT:

Process & Lab Analytics with OptoFluidic Force Induction (OF2i)

A BRAVE new way in time-resolved particle characterization for PAT and LAB

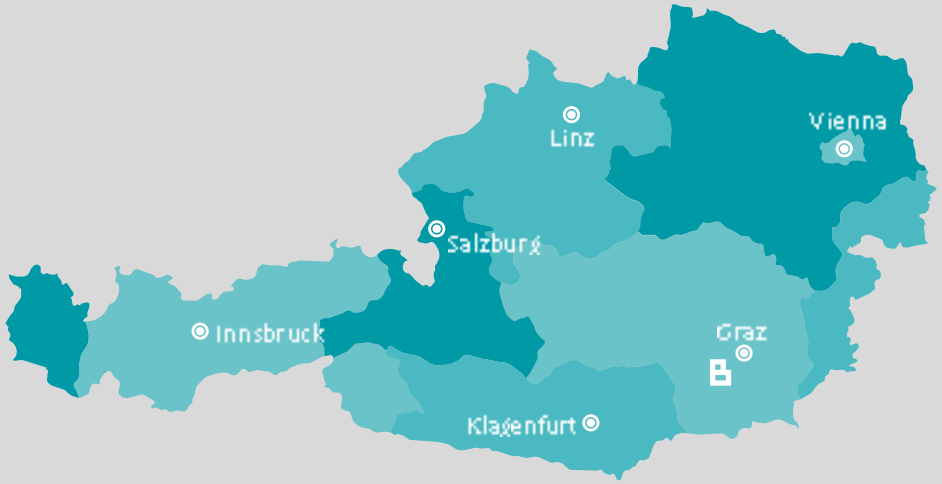
B1 Process Sensor

B2 Lab Device OF2i INSIDE

Ing. Dr. Christian HILL, MA

nanomedicine Biophysics
Med Uni Graz
Bundesministerium Digitalisierung und Wirtschaftsstandort
austria wirtschafts service aws
FFG Promoting Innovation.
LightMatters OPTOFLUIDIC ANALYSIS
I.E.C.T HERMANN HAUSER
NanoSyn
FUNDED BY
Federal Ministry Republic of Austria Climate Action, Environment, Energy, Mobility, Innovation and Technology
European Commission
MOZART

BRAVE
ANALYTICS



ZWT-GRAZ-AUSTRIA



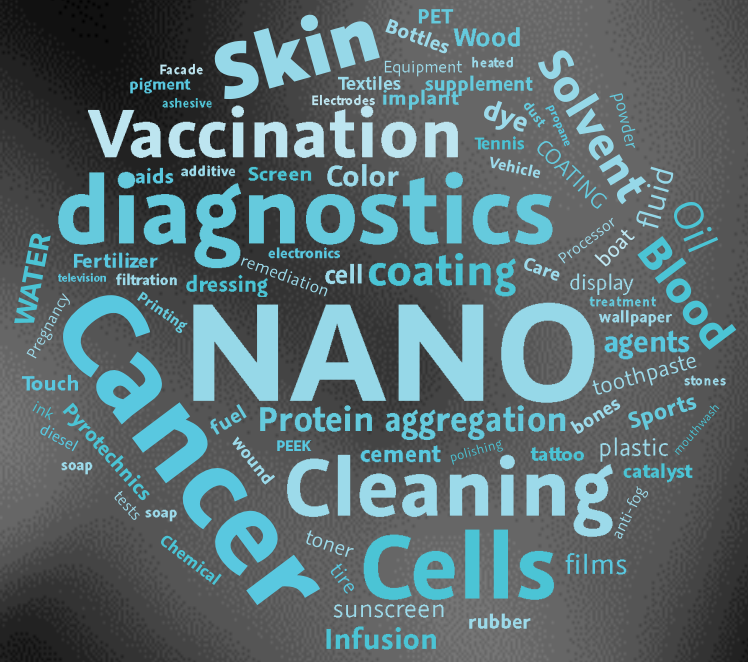


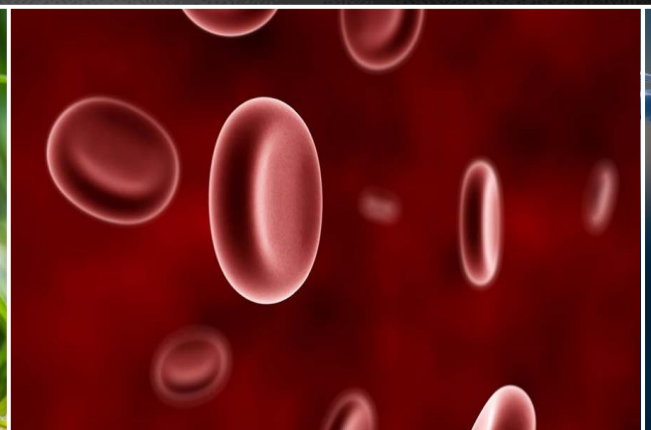
BRAVE ANALYTICS

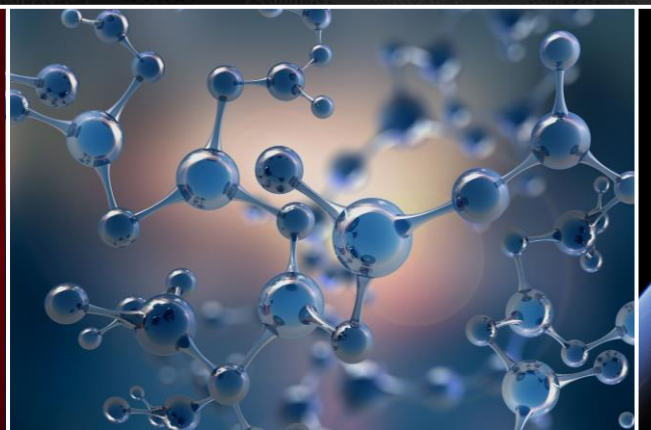
Med Uni Graz *Pioneering Minds*

a BRAVE problem to solve

...modern nanoparticle research and productions need continuous and real-time characterization for waste reduction and performance control...

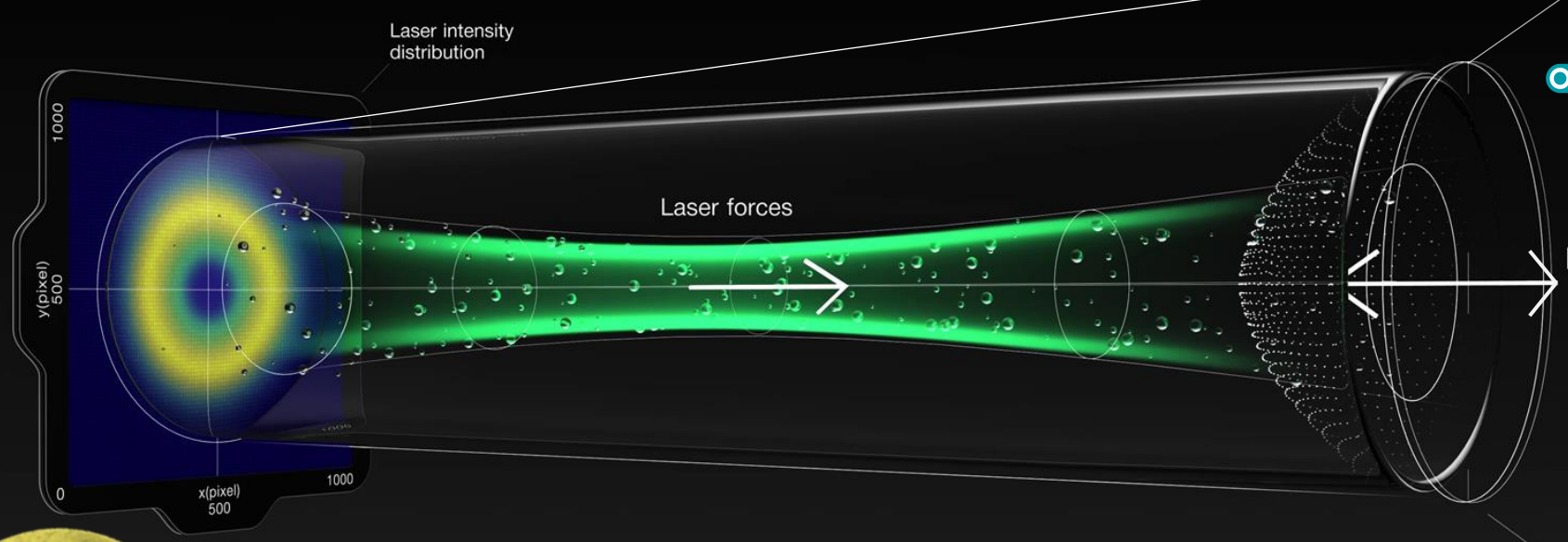






Combining Biophotonics & µ-Fluidics

OF2i®



Based on NOBEL PRIZE 2018 PHYSICS Ashkin et al.

...breaking the barrier of Brownian Motion with actively induced optical and fluidic forces...

BRAVE ANALYTICS

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The BRAVE products

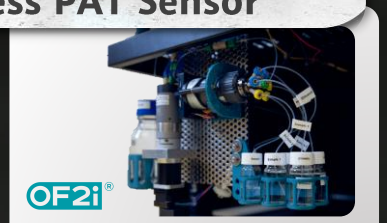
launch Q1/23

B2 Lab Device OF2i INSIDE

OF2i®
OEM detector module

Planned launch 2023/24

B1 Process PAT Sensor



OF2i®
OEM online sample prep.-dilution module

ACTIVE PRINCIPLE REAL TIME RESULTS

CONTINUOUS PARTICLE SIZING

WIDE SIZING RANGE

AUTOMATED & INTEGRABLE

HIGH SENSITIVITY

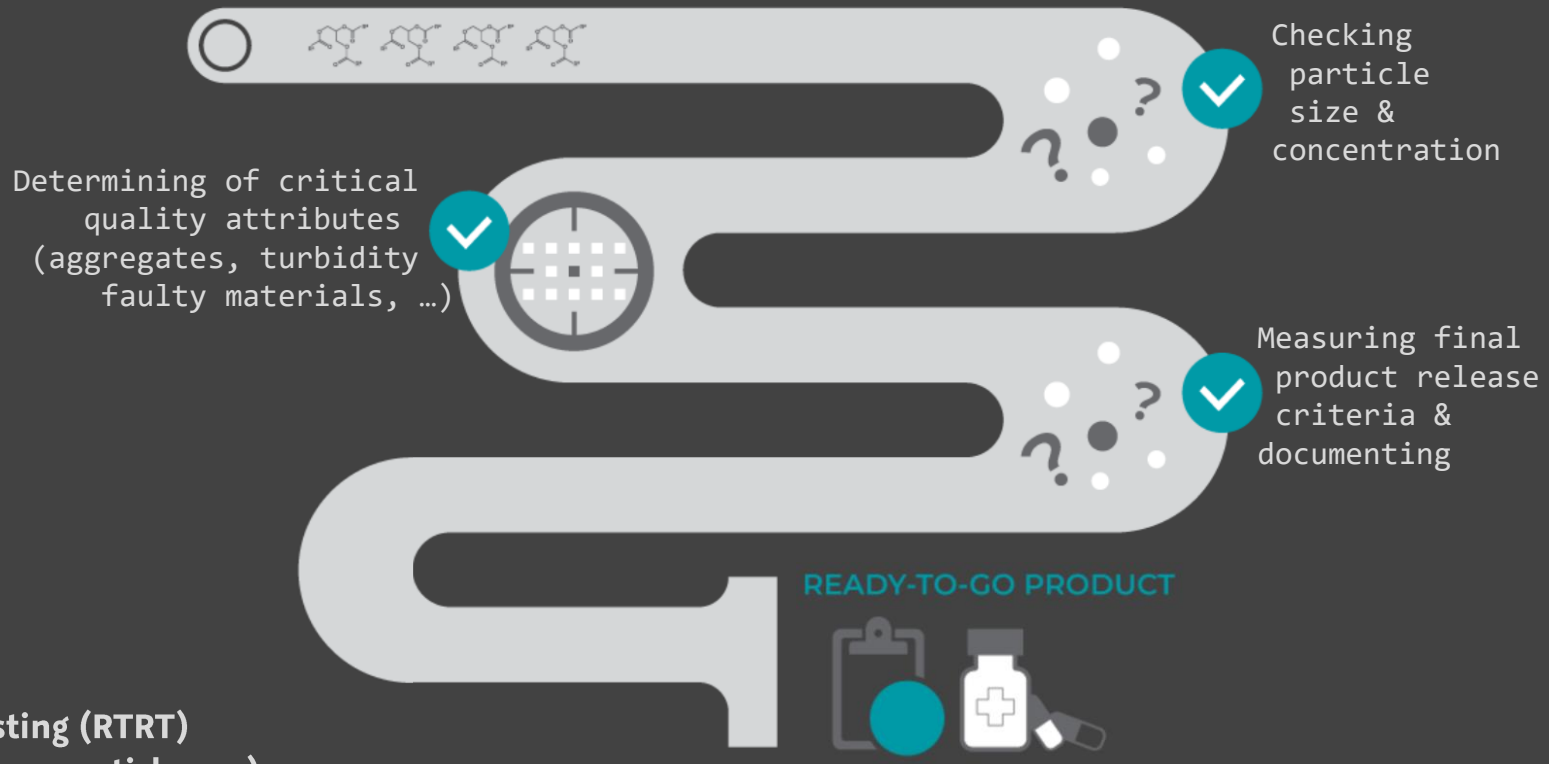
BRAVE ANALYTICS

OF2i® in action

Areas of Application

- In Process Quality Control (IPQC) & Realtime Release Testing (RTRT)
- Predictive Maintenance (detection of faulty materials, rear particles, ...)
- Monitoring of Critical Quality Attributes (CQA)
- Identification of Critical Process Parameters (CPP)
- Basic research

Continuous Production



OF2i® Automated Process Analytical Technology (PAT)

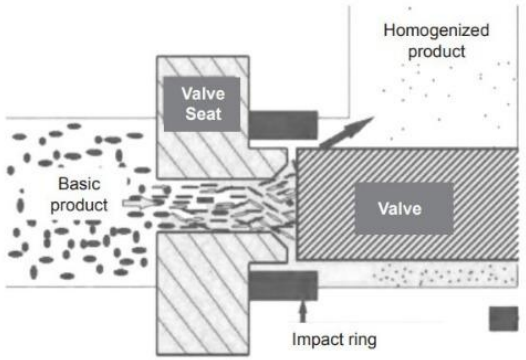
BRAVE ANALYTICS

a BRAVE use case
FRESENIUS KABI

Continues detection of High-Pressure - Homogenization states

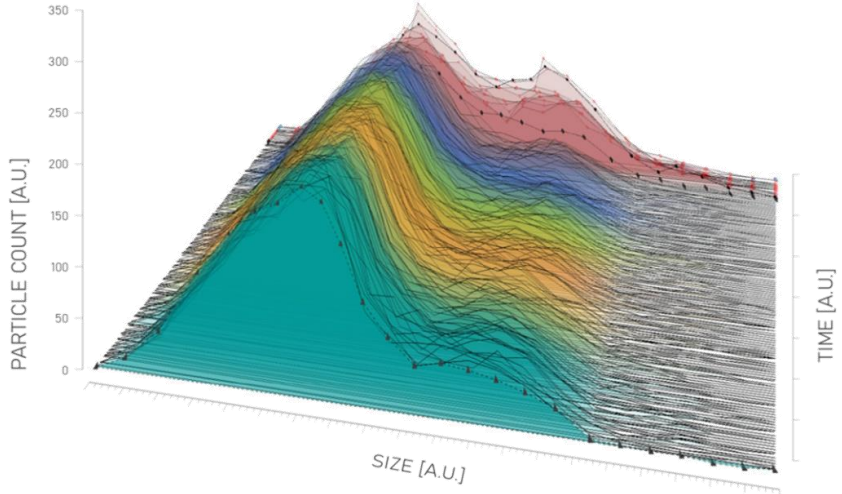
To replace offline quality control and go towards real-time release testing (RTRT) for liquid pharmaceutical formulations

Emulsions with a particle size from 100 nm to 600 nm undergoing high-pressure homogenization processes



Basic principle of high pressure homogenization procedures. Pre-emulsified products are transported via high pressure, generating high shear forces on particles.

Emulsion Products for intravenous application of pharmaceuticals, parenteral nutritioun, and other emulsion products



OF2i time resolved online characterization as number based size distributions of different processing steps in looped emulsion production.

1. Tech. pic. Ref: Korpro Corp. /product/high-pressure-homogenizer-applications/648/
2. Exemplary pictures Copyright by Sonic Corporation

Preliminary, unpublished data

BRAVE
ANALYTICS

a BRAVE use case
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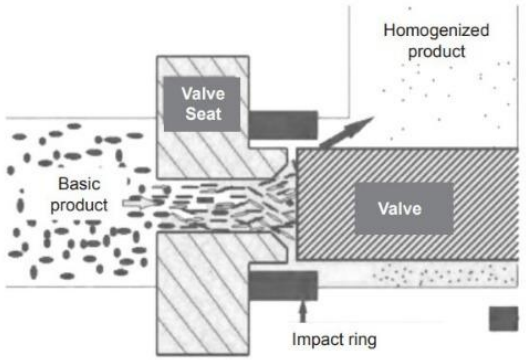

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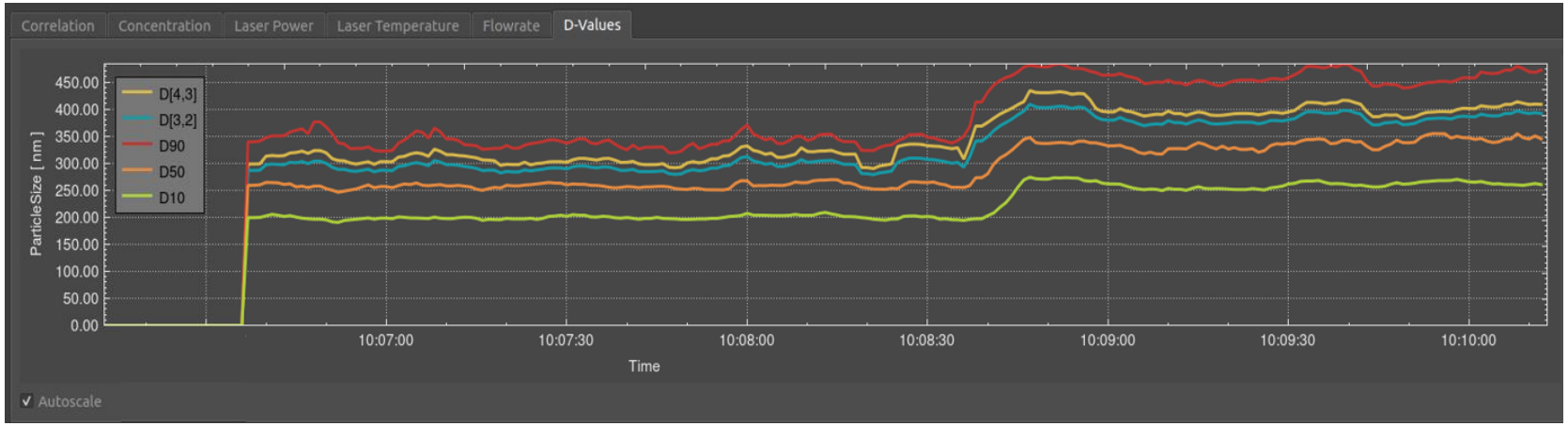
OF2i® Particle characterization over trajectories



1. Tech. pic. Ref: Korpro Corp. /product/high-pressure-homogenizer-applications/648/

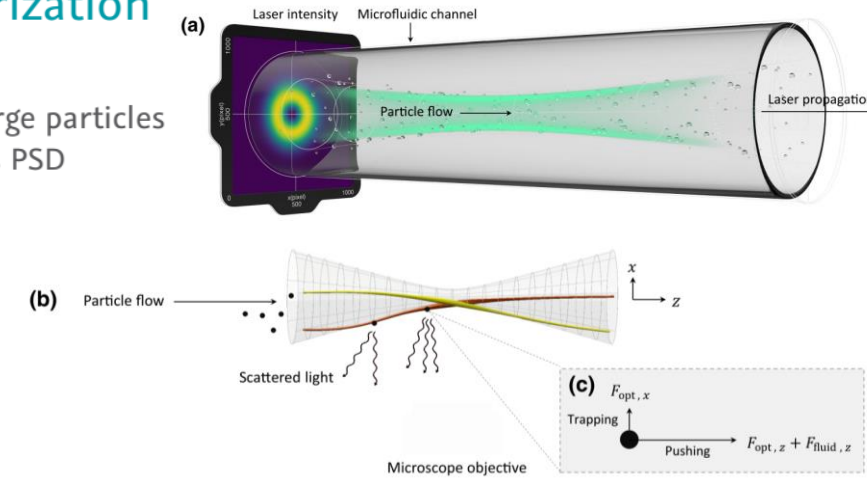
Preliminary, unpublished data

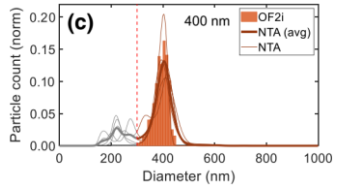
BRAVE ANALYTICS

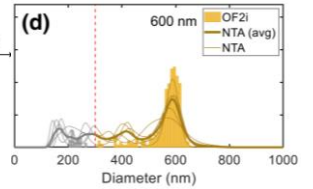
...Particle Analytics you can count on

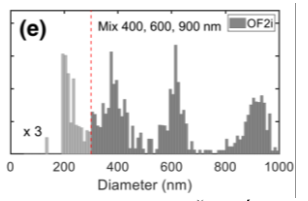
BA2 Analyzer for ultra-low concentration measurement and time-resolved nanoparticle characterization

- Determines ultra-low concentrations and single large particles
- Delivers automated, time-resolved and continuous PSD
- Detects large-particle tails and LPC









MARKO ŠIMIĆ *et al.*

PHYS. REV. APPLIED **18,** 024056 (2022)

Specifications

Continuous, time-resolved sample scans on up to 4K particles/min*

Measuring statistics as number-based hydrodynamic size distribution.

Particle sizing range: 20 nm to 50 µm (module-dependent).

For nanosuspensions, nanoemulsions and colloidal formulations (liquid continuous phase; solid or liquid dispersed phase).

BRAVE ANALYTICS

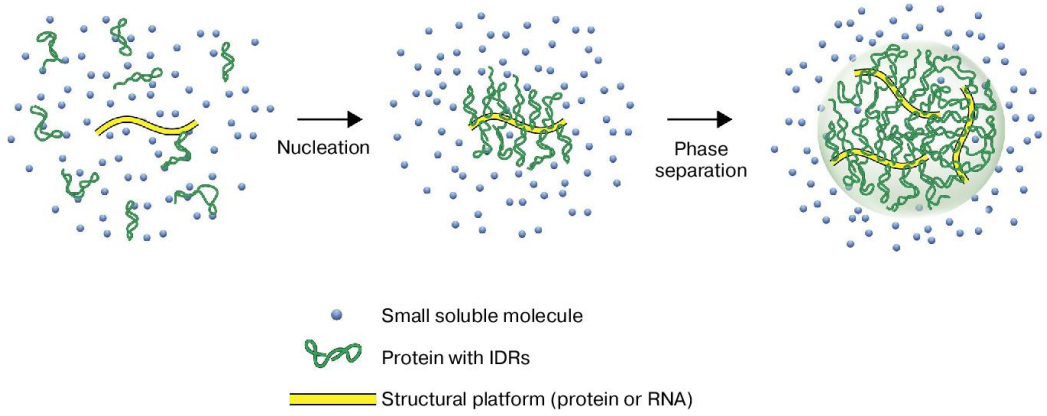
a BRAVE use case

Research on (dys)regulation and drug targeting of the early processes of biomolecular condensate formation

Understanding dynamic liquid-liquid phase separation (LLPS) processes by observing the formation and size distribution of the proteins as they change over time

Buffer with protein and various amounts of RNA (0.02 µM to 0.2 µM) added (sample < 100µl)

group of
Univ. Prof. Dr. Tobias Madl,
Professor of Integrative Structural Biology and Metabolomics



Measurement	Conc. Protein [µM]	RNA [µM]
1	X/10 µM	-
2	X µM	-
3	-	0,2µM
4	X µM	0,02µM
5	X µM	0,04µM
6	X µM	0,06µM
7	X µM	0,08µM
8	X µM	0,1µM
9	X µM	0,15µM
10	X µM	0,2µM

Razin, S.V., & Gavrilov, A.A. (2020). The Role of Liquid–Liquid Phase Separation in the Compartmentalization of Cell Nucleus and Spatial Genome Organization. *Biochemistry (Moscow), 85*, 643-650.

Preliminary, unpublished data in cooperation with Med Uni Graz

BRAVE ANALYTICS

a BRAVE use case

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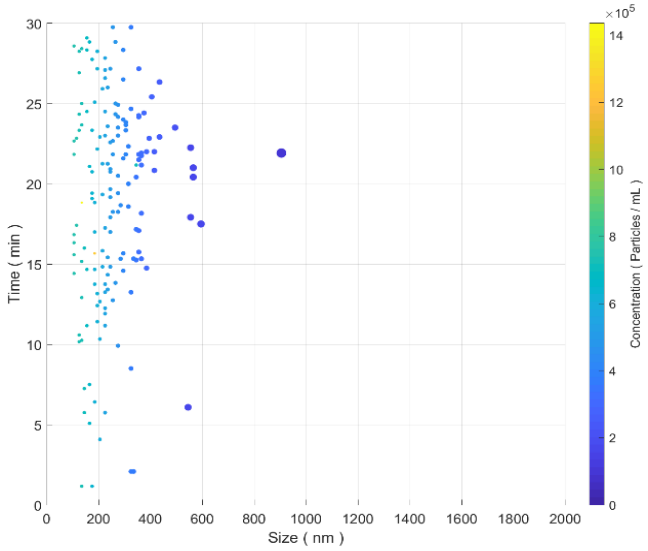

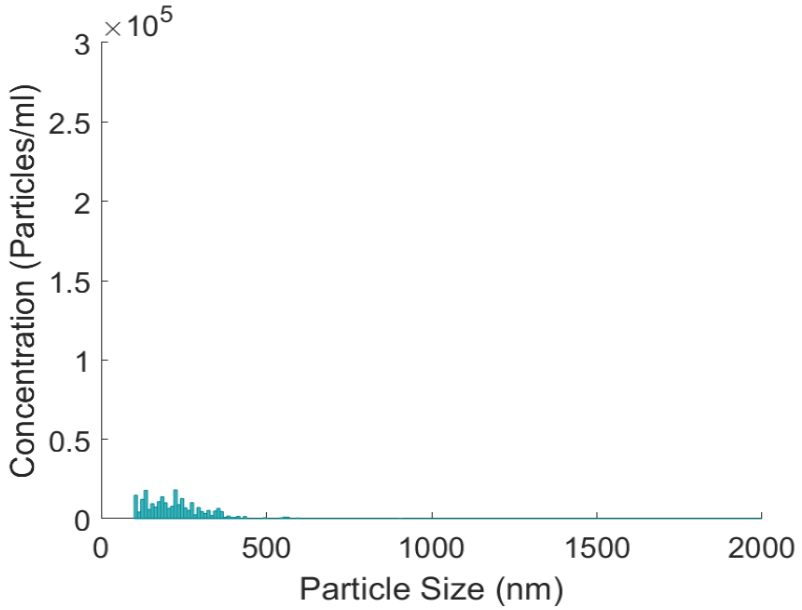

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9	X µM	0,15µM
10	X µM	0,2µM

Protein + RNA 0,06µM, 2D-Histogramm (left), Particle size distribution (right)

Preliminary, unpublished data in cooperation with Med Uni Graz

BRAVE
ANALYTICS

a BRAVE use case

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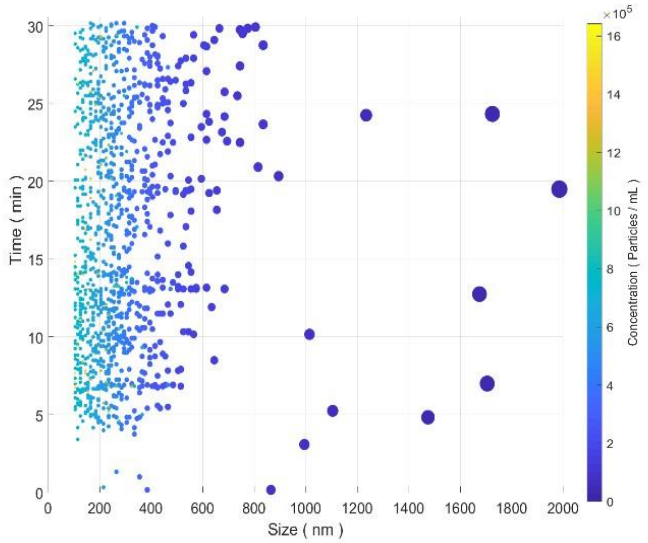

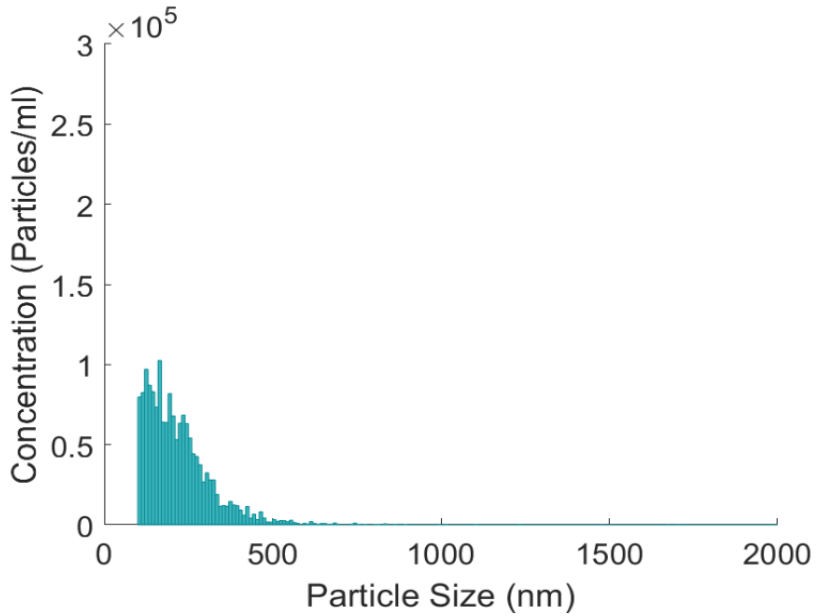

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7	X µM	0,08µM
8	X µM	0,1µM
9	X µM	0,15µM
10	X µM	0,2µM

Protein + RNA 0,15µM, 2D-Histogramm (left), Particle size distribution (right)

Preliminary, unpublished data in cooperation with Med Uni Graz

WE ARE

BRAVE

The BRAVE team

FLUIDINOVA
THE NANO-HYDROXYAPATITE SPECIALIST

creative nano

LIGNOVATIONS

Med Uni Graz

MONTAN UNIVERSITÄT
WWW.UNILEOBEN.AC.AT

SIMVANTAGE

human. technology. styria.

FRESENIUS KABI

I.E.C.T
HERMANN HAUSER

BRAVE
ANALYTICS

B1 SENSORS FOR REAL-TIME ONLINE NANOPARTICLE CHARACTERIZATION

- Robust industrial 19" rack PC
- BRAVE B1 detector module
- BRAVE B1 laser module
- Detector liquid handling module
- Customizable sample preparation and adjustable on-line dilution system
- Service parts and maintainance compartment

SPECS

Particle sizing range: 10nm – 50µm*

Measuring statistics as number weighted hydrodynamic size distribution

For nanosuspension, nanoemulsions and colloidal formulations:

- continuous phase → liquid
- dispersed phase → solid or liquid

Measuring time specifications:

- continuous, 1x sec sizing data update
- lag time for bypass system: 4 – 20sec*

OPERATION and APPLICATION REQUIREMENTS

Bypass continuous sampling:

- optimal 0.7ml/min (minimum 5µl/min)
- concentration range sizing: minimum 10^4 objects/ml – optimal > 10^{10} objects/ml

BRAVE
ANALYTICS

www.braveanalytics.eu

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Entrance B
8010 Graz – AT

www.braveanalytics.eu

Contact us

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+43 (0) 680 30 34 759

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gerhard.prossliner@braveanalytics.eu

NANOPAT

NanoPAT project has received funding from the European Union's HORIZON 2020 research and innovation programme under grant agreement n°862583.

nanomedicine Biophysics
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Bundesministerium Digitalisierung und Wirtschaftsstandort
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MOZART

BRAVE ANALYTICS

Med Uni Graz *Pioneering Minds*

a BRAVE introduction

ENSEMBLE METHOD

DLS, LD, SLS, Acoustics, ...

Measuring properties of the whole sample, which are resolved in time, space or frequency

FRACTIONATING METHOD

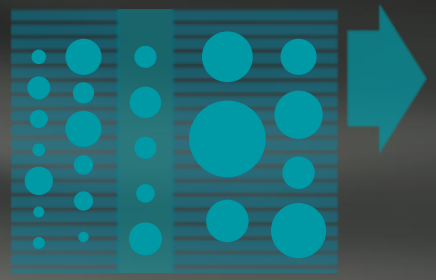
FFF, SEC, AUC, ...

Measuring of the quantity of each size fraction

COUNTING METHOD

Microscopy, NTA, LOD, FACS, ...

Measuring properties of each single particle



OF2i®

patented optical parallelization

Measuring properties of particles ensembles at the same time continuously

(up to 4k #/min resolution)

LOWER RESOLUTION

"Less" capable

HIGHER RESOLUTION

Increased certainty, "most" capable

BRAVE ANALYTICS

a BRAVE use case

Production of non-nanoLignin particles under “regulatory” constraints: OF2i – SEM – NTA – DLS comparison study

Identifiable constituent particles (primary particles) as aggregates/agglomerates
>50 % particles number-based size distribution

group of
Dipl.-Ing. Dr. techn. Miltner, Martin,
Dipl.-Ing. Dr. techn. Beisl, Stefan
+ Team of Lignovations GmbH
Technopark 1 / A-3430 Tulln

Colloidal lignin particles

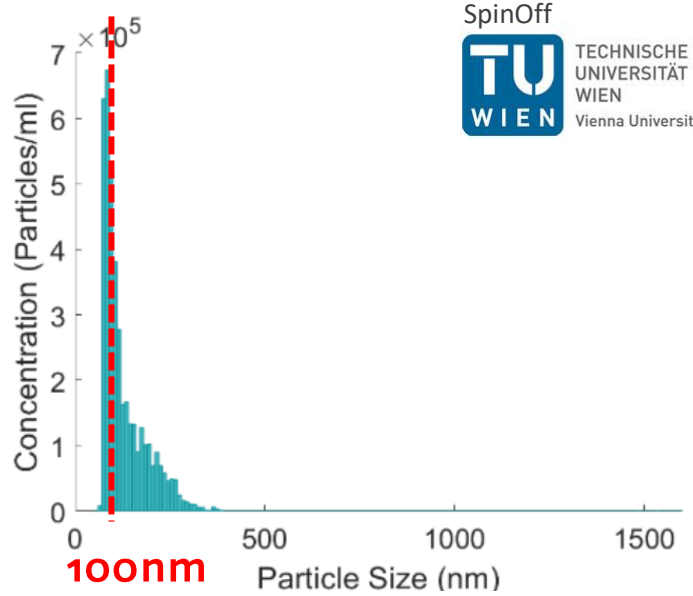
production from wheat straw, nutshells, hemp and feedstocks

UV-Protection…

…emulsifier

SpinOff

TU WIEN TECHNISCHE UNIVERSITÄT WIEN Vienna University of Technology



Preliminary, unpublished data in cooperation with lignovations

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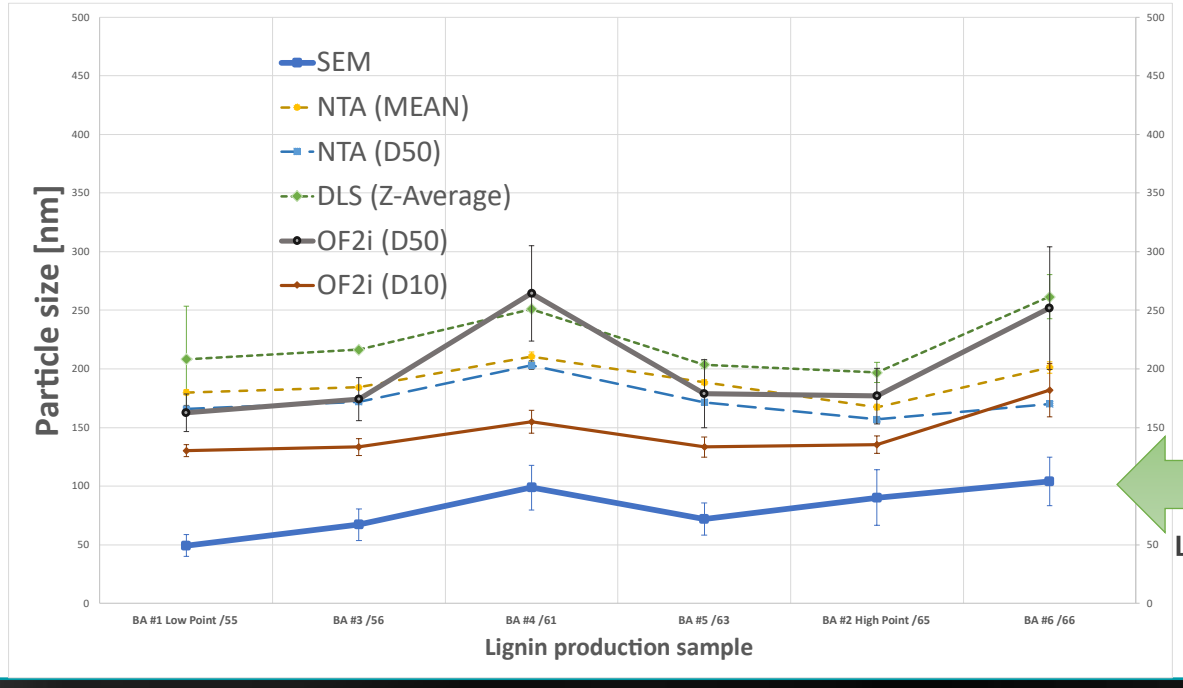
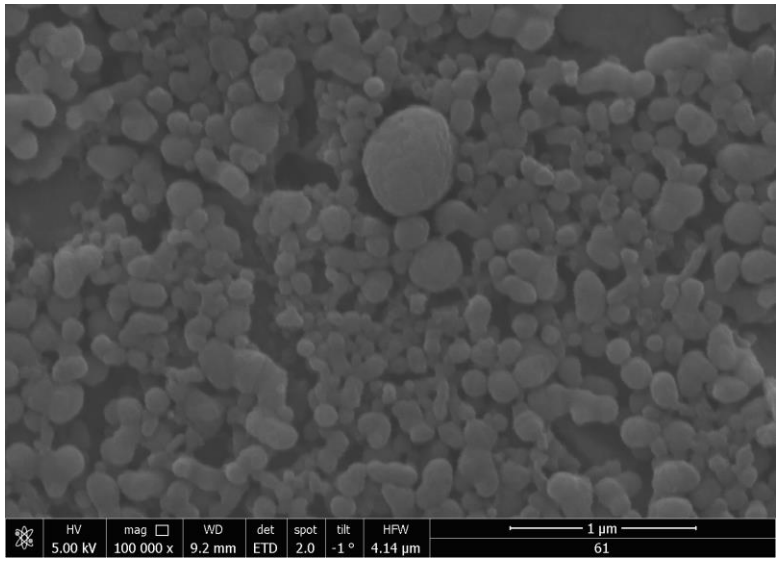


Lignovations SEM data



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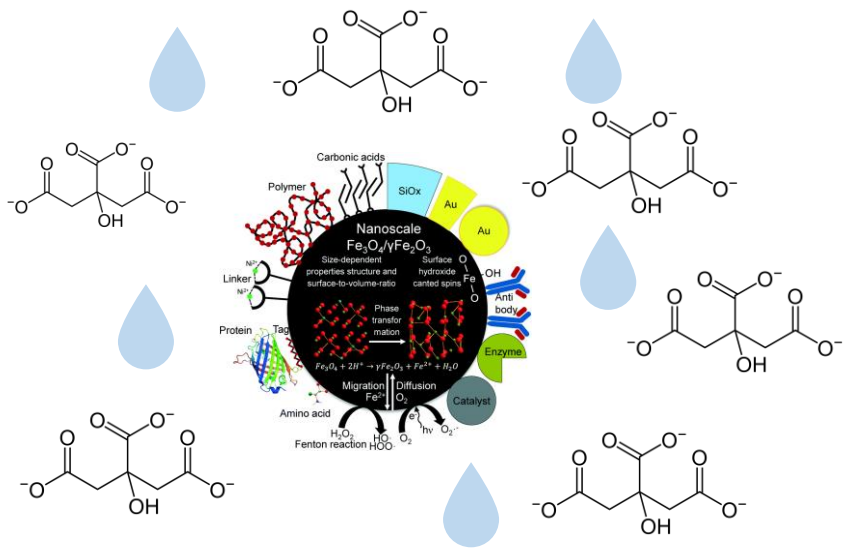
BRAVE ANALYTICS

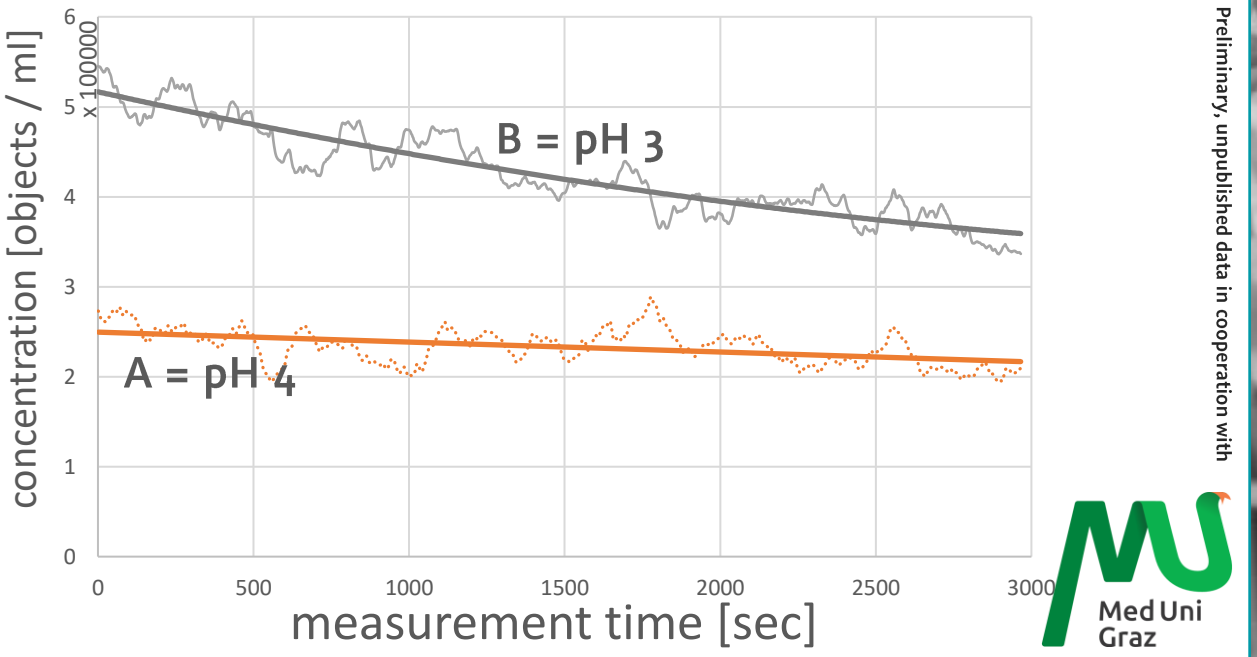
a BRAVE use case

Time resolved characterization of Dissociation dynamics for coated Iron-Oxid nanoParticles in acidic buffer systems

To understand the particle dissociation dynamics within different acidic pH conditions
Particles (ION_PVA) are in citric Buffer (200mM) with A pH 4 and B pH 3

group of
Ass.-Prof. Dr. Sebastian Schwaminger,
Division of Medicinal Chemistry
Research Focus: Circulation and vascular research





Preliminary, unpublished data in cooperation with

Med Uni Graz

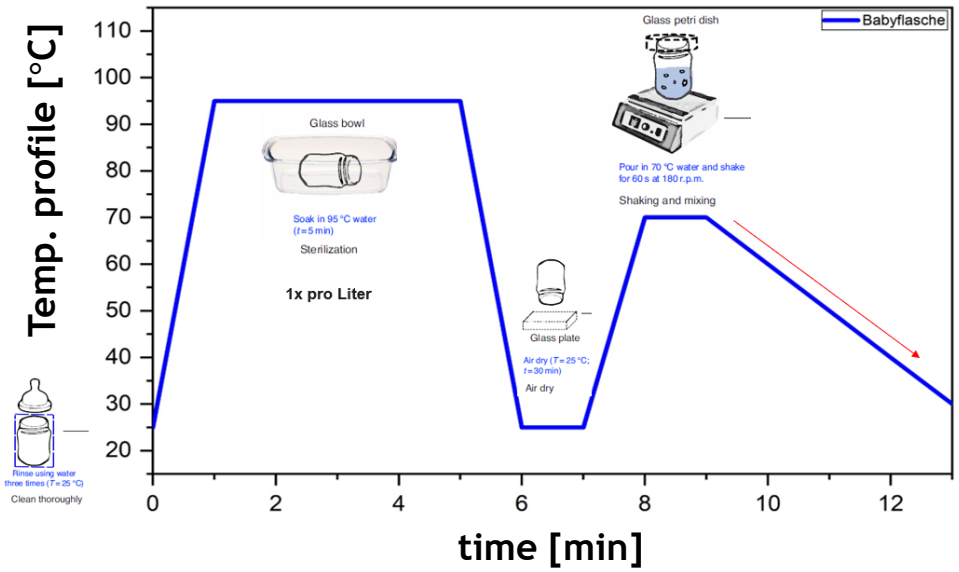
Schwaminger, S. P., Bauer, D., Fraga-García, P., Wagner, F. E., & Berensmeier, S. (2017).
Oxidation of magnetite nanoparticles: impact on surface and crystal properties. CrystEngComm, 19(2), 246-255.

BRAVE ANALYTICS

a BRAVE use case

Quality control: Low concentrated samples

Nano Plastics – Plastic leaching processes (e.g. plastic bottles, plastic implants, pure water quality, ...)



0,2l direkt vermessen

OF2i®

RAW - signal (concentration measurement)

unpublished data in cooperation with

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BRAVE ANALYTICS

a BRAVE use case

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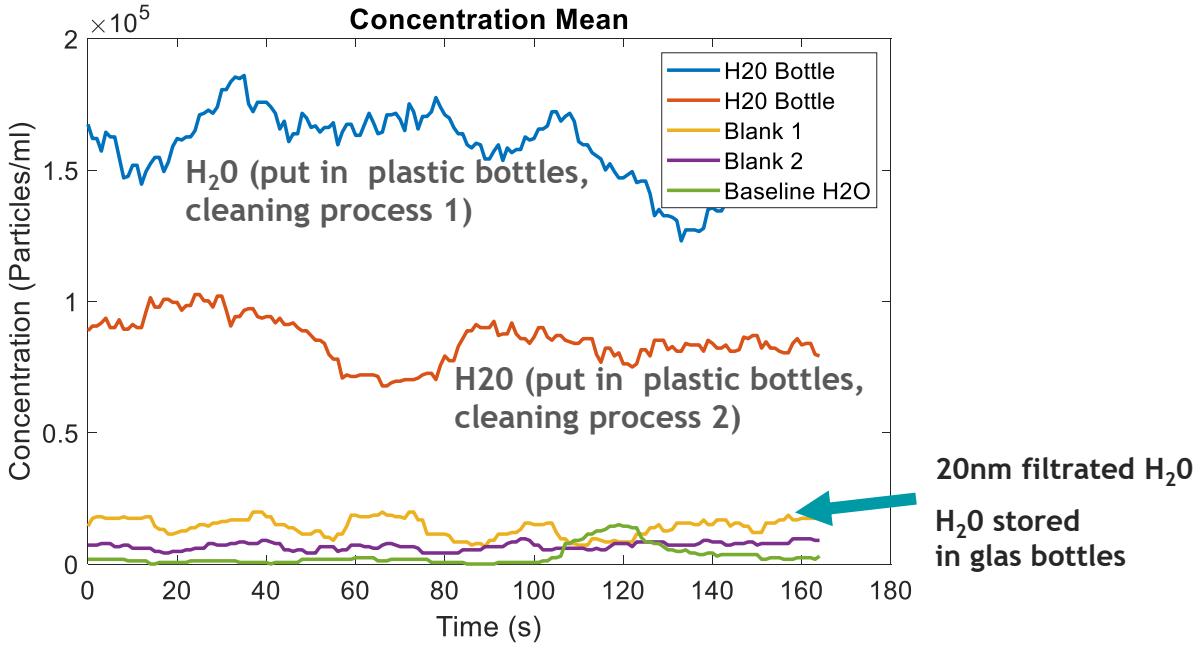

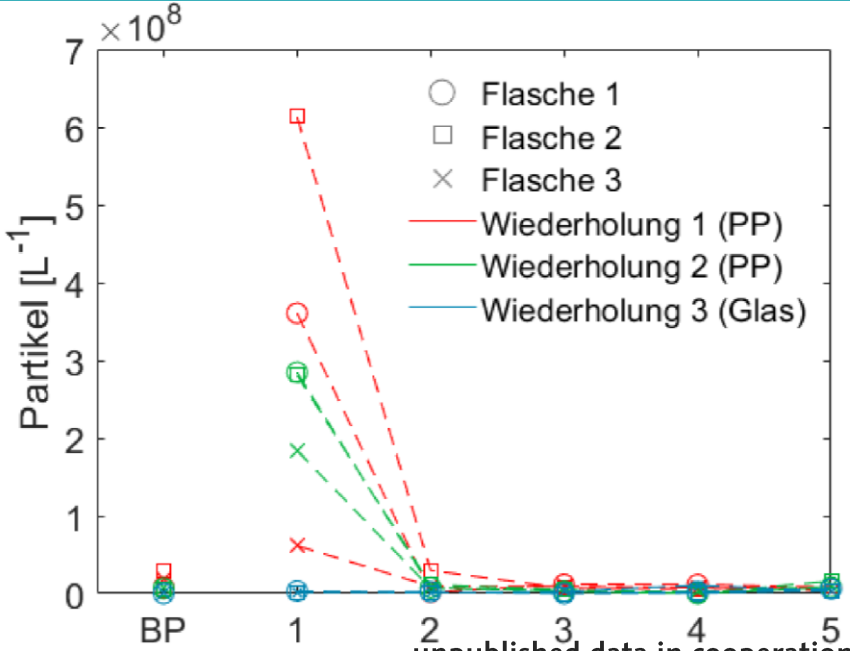

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