National Research Centre for the Working Environment

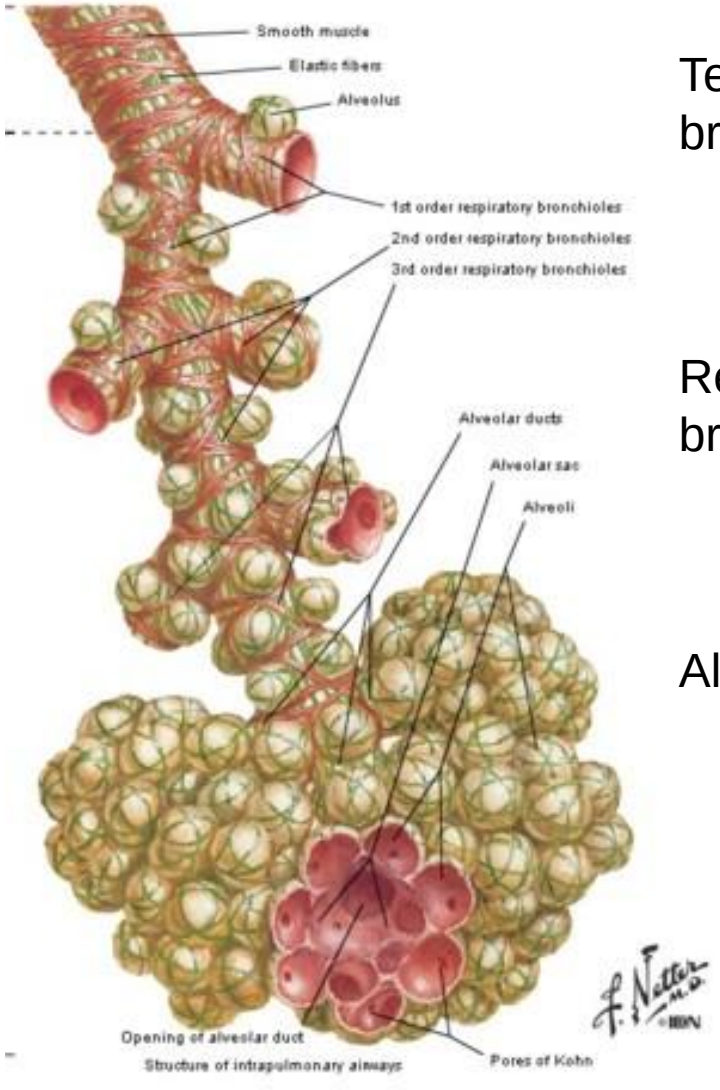
nanoPASS

The Work planned in nanoPASS to support the Weight of Evidence of AOP302: Lung Surfactant Function Inhibition Leads to reduced Lung Function

Senior researcher Jorid B. Sørli

22th of November 2023

The respiratory part of the lungs

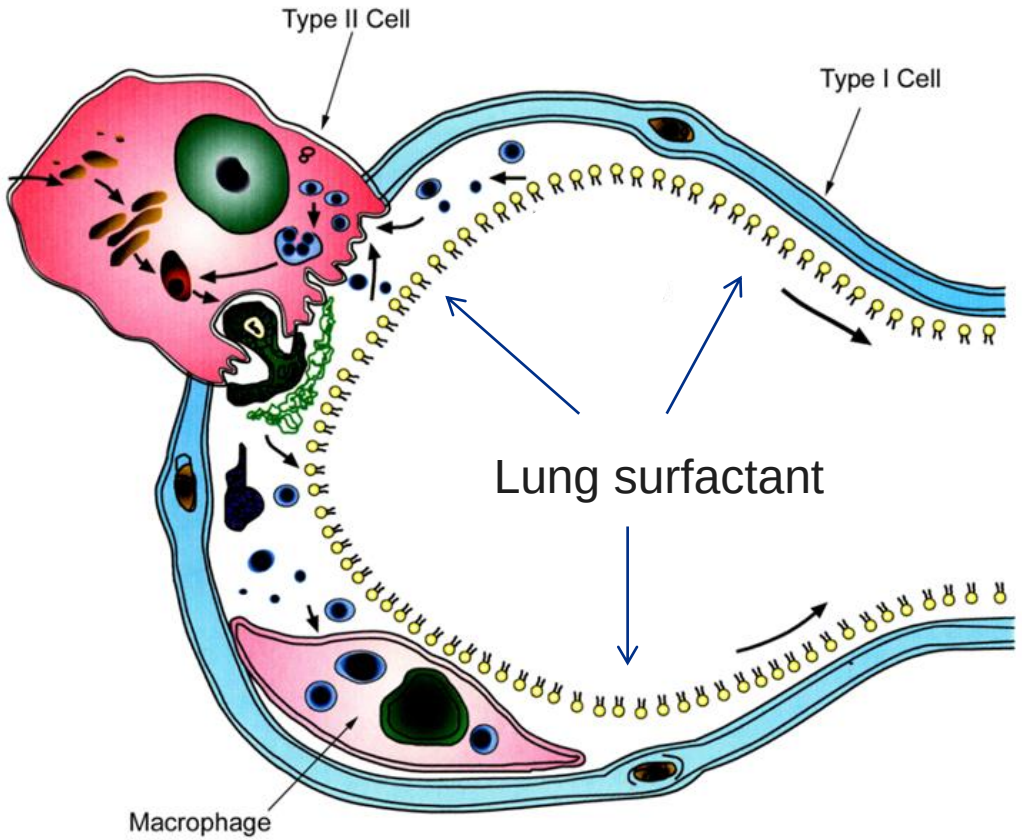


http://www.sharinginhealth.ca/respiratory/respiratory.html

Terminal bronchioles	0.4 mm
Respiratory bronchioles	0.25 mm

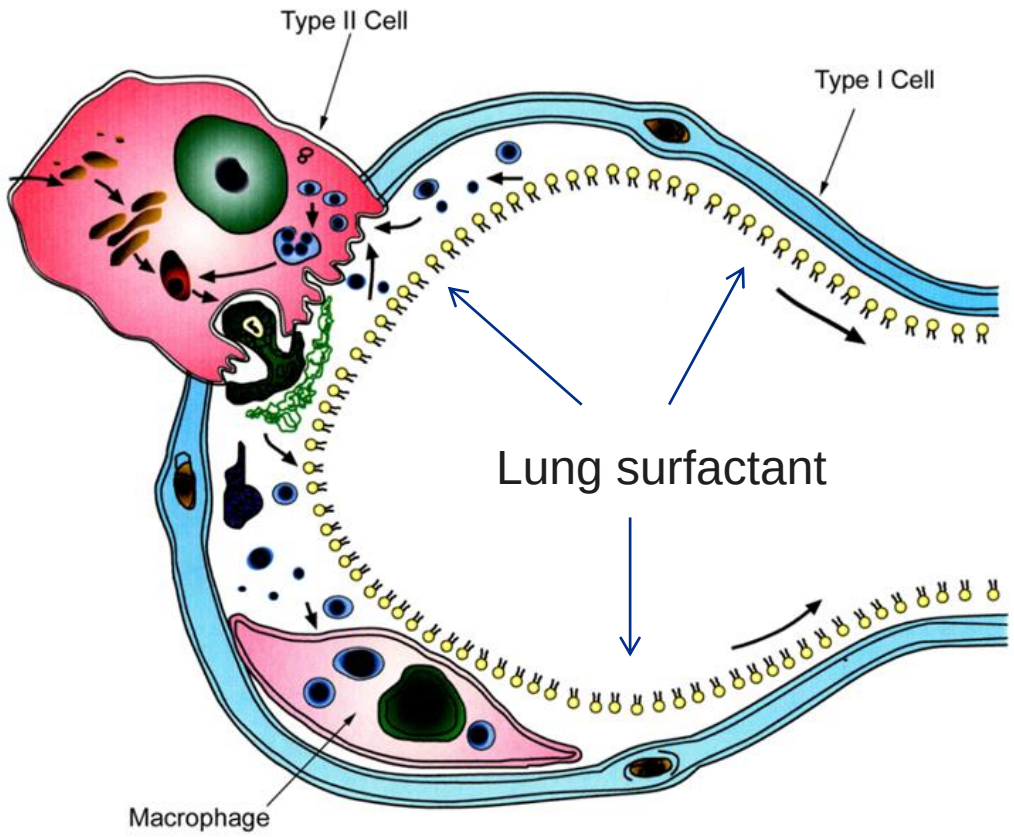
Alveoli

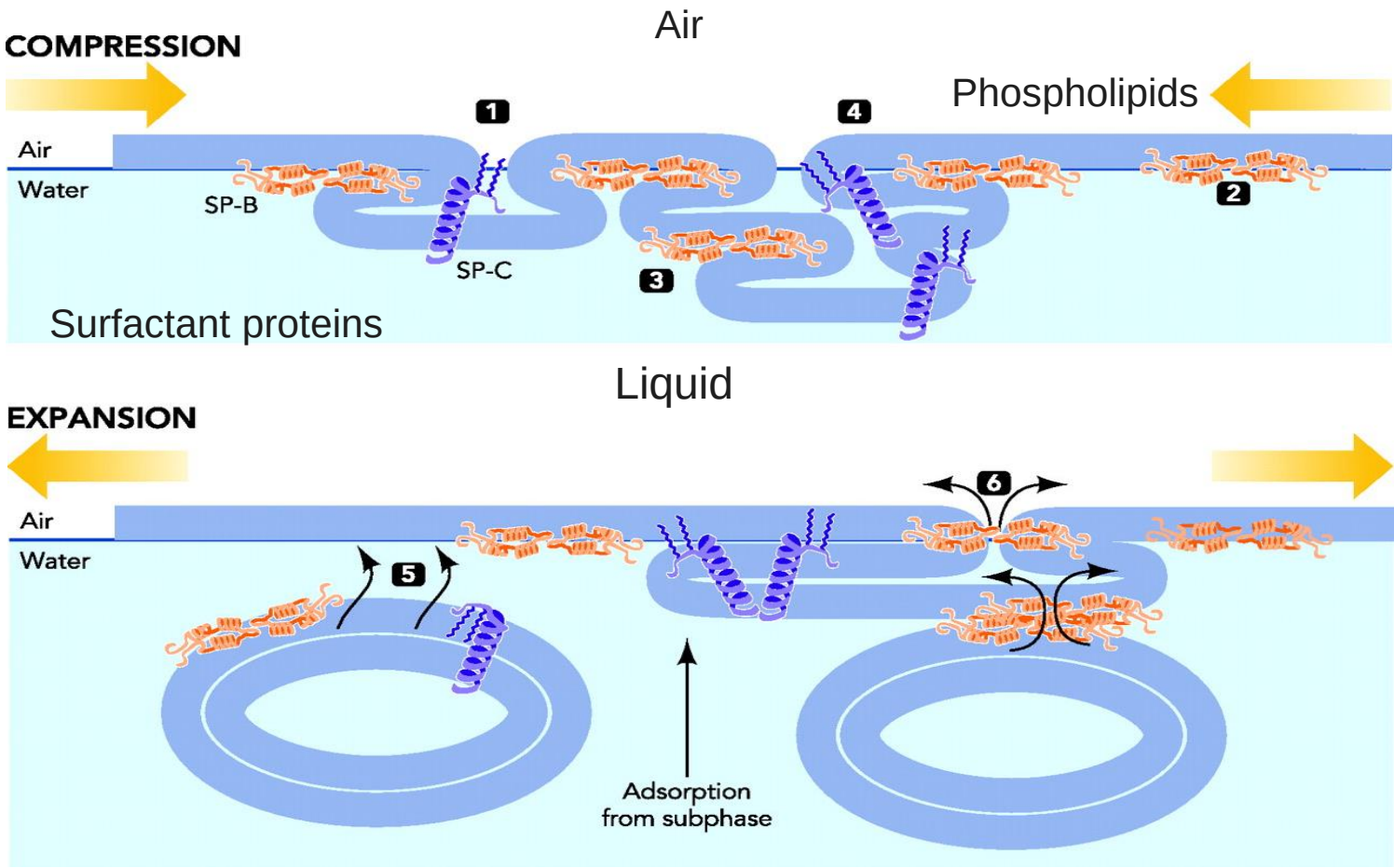
- ~0.2 mm (constantly changing)
- 480 million alveoli
- Surface area ~70 m^2



http://usmle.biochemistryformedics.com/respiratory-distress-syndrome-case-discussio

Lung surfactant function





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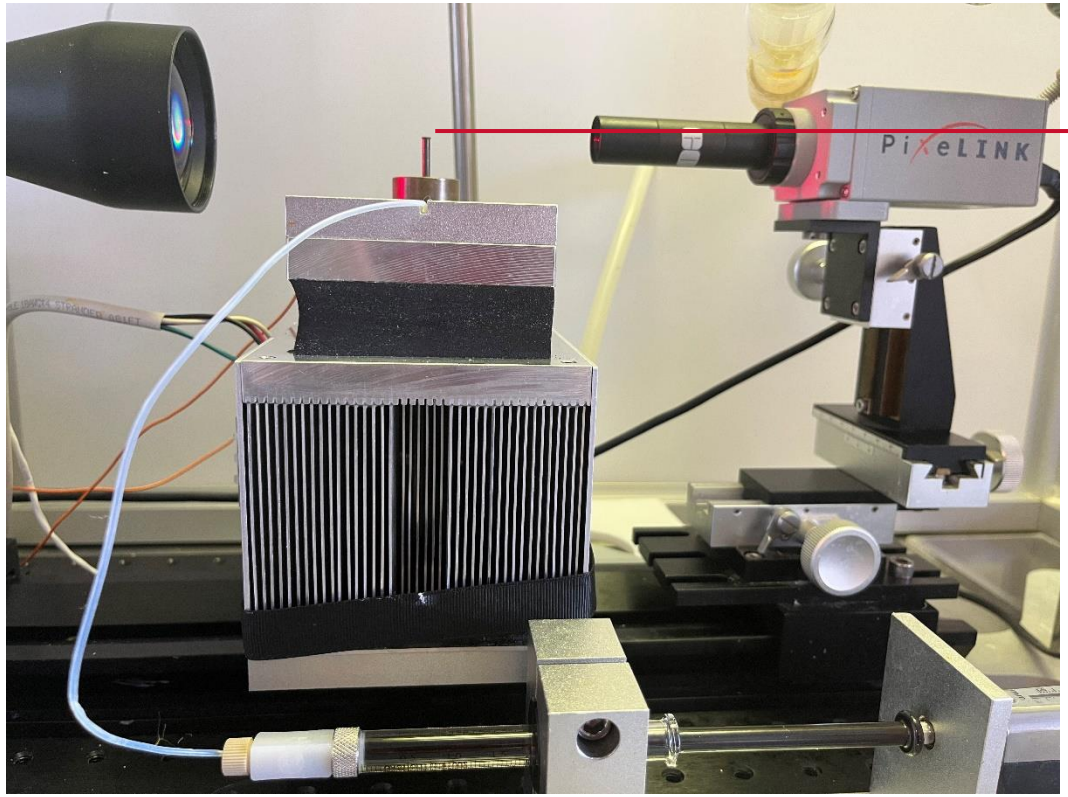
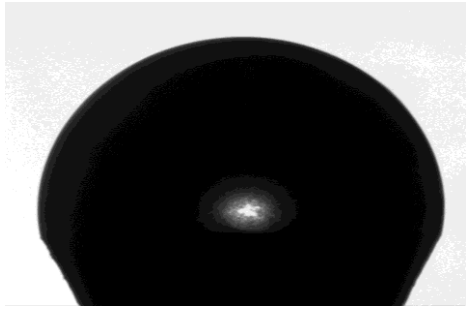
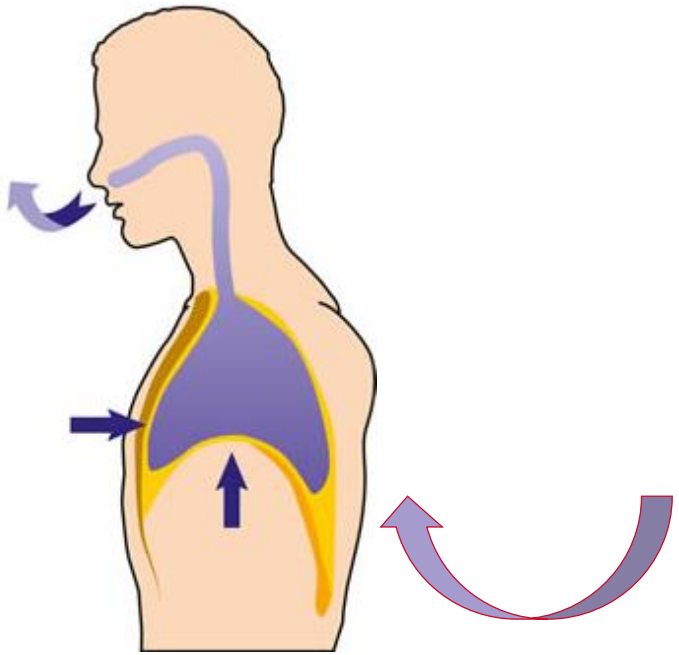
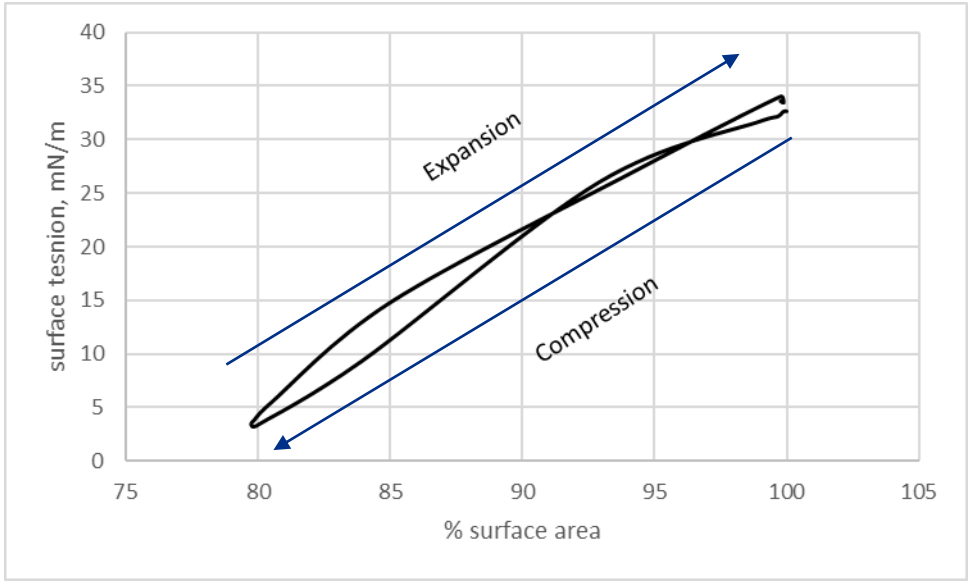
Perez-Gil & Weaver, Physiology, 2010

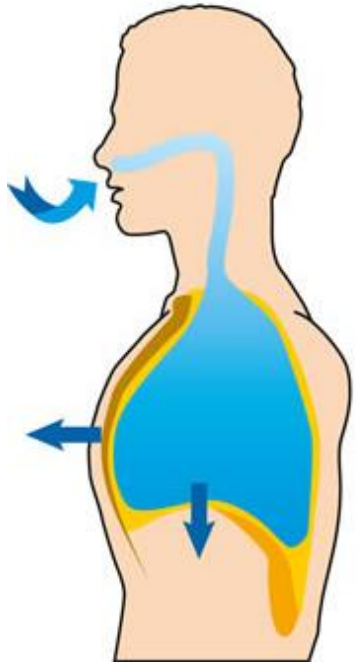
In the lab

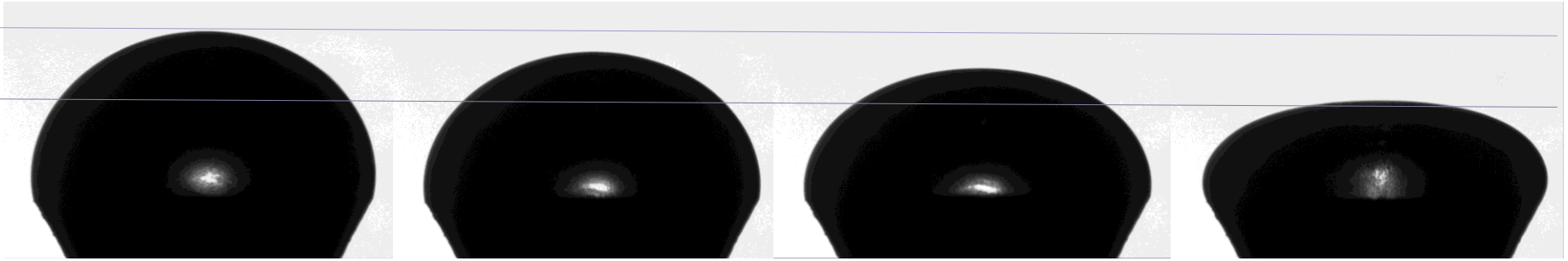


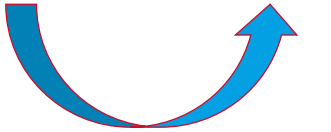


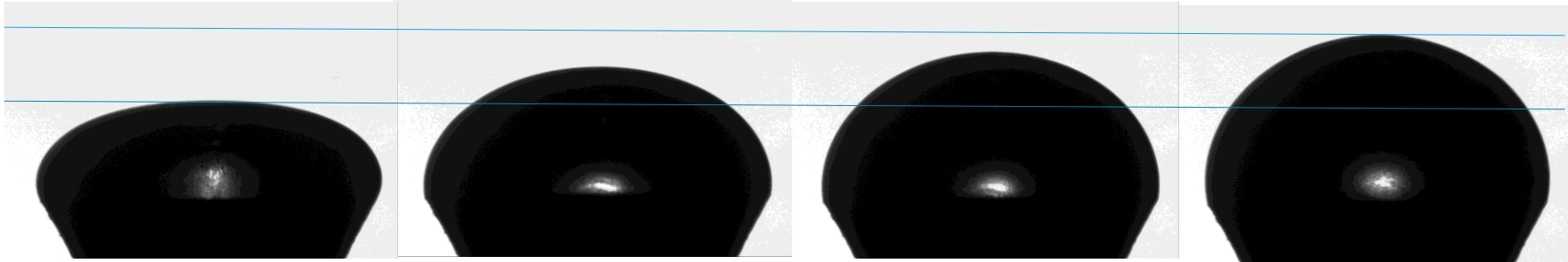












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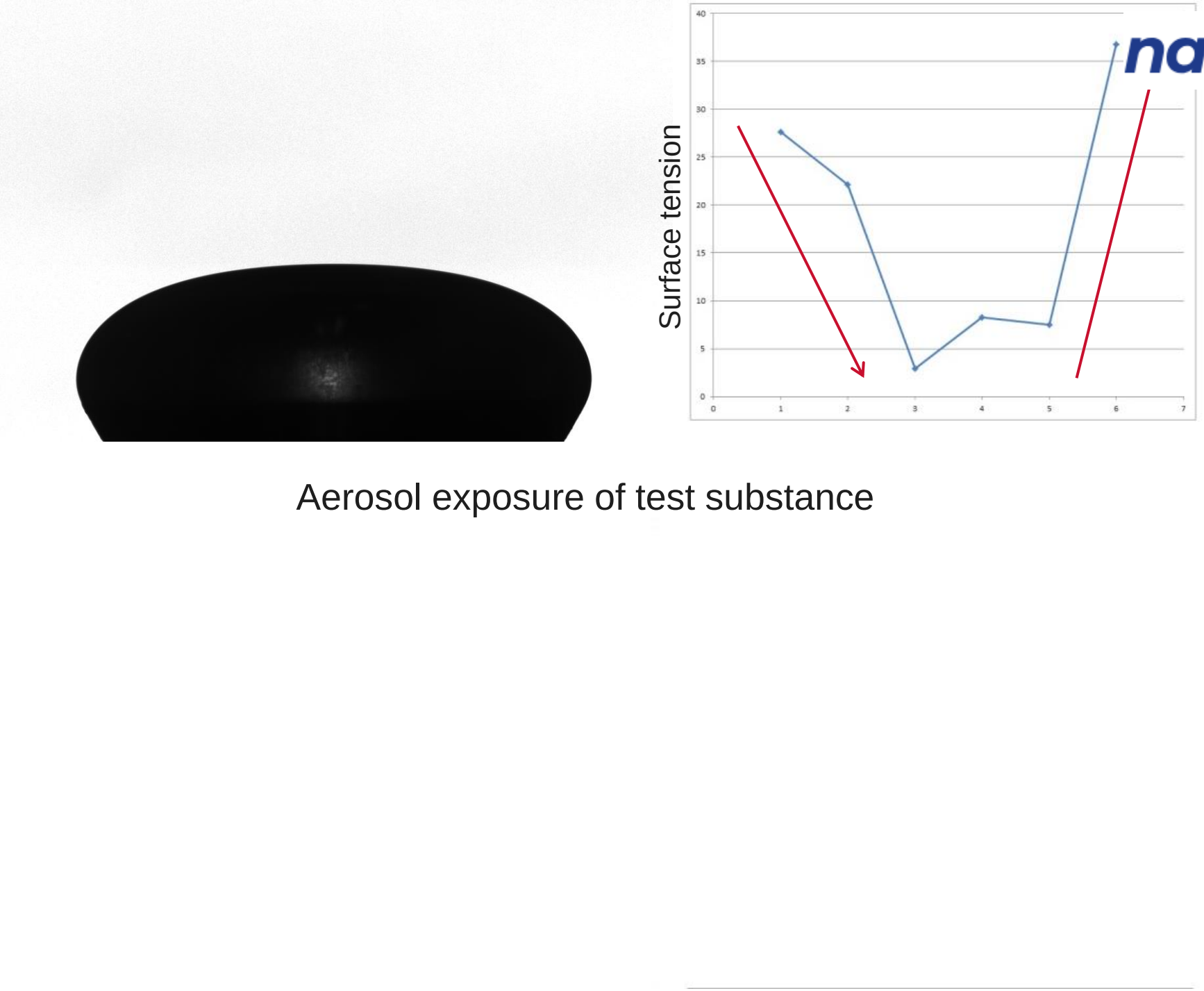
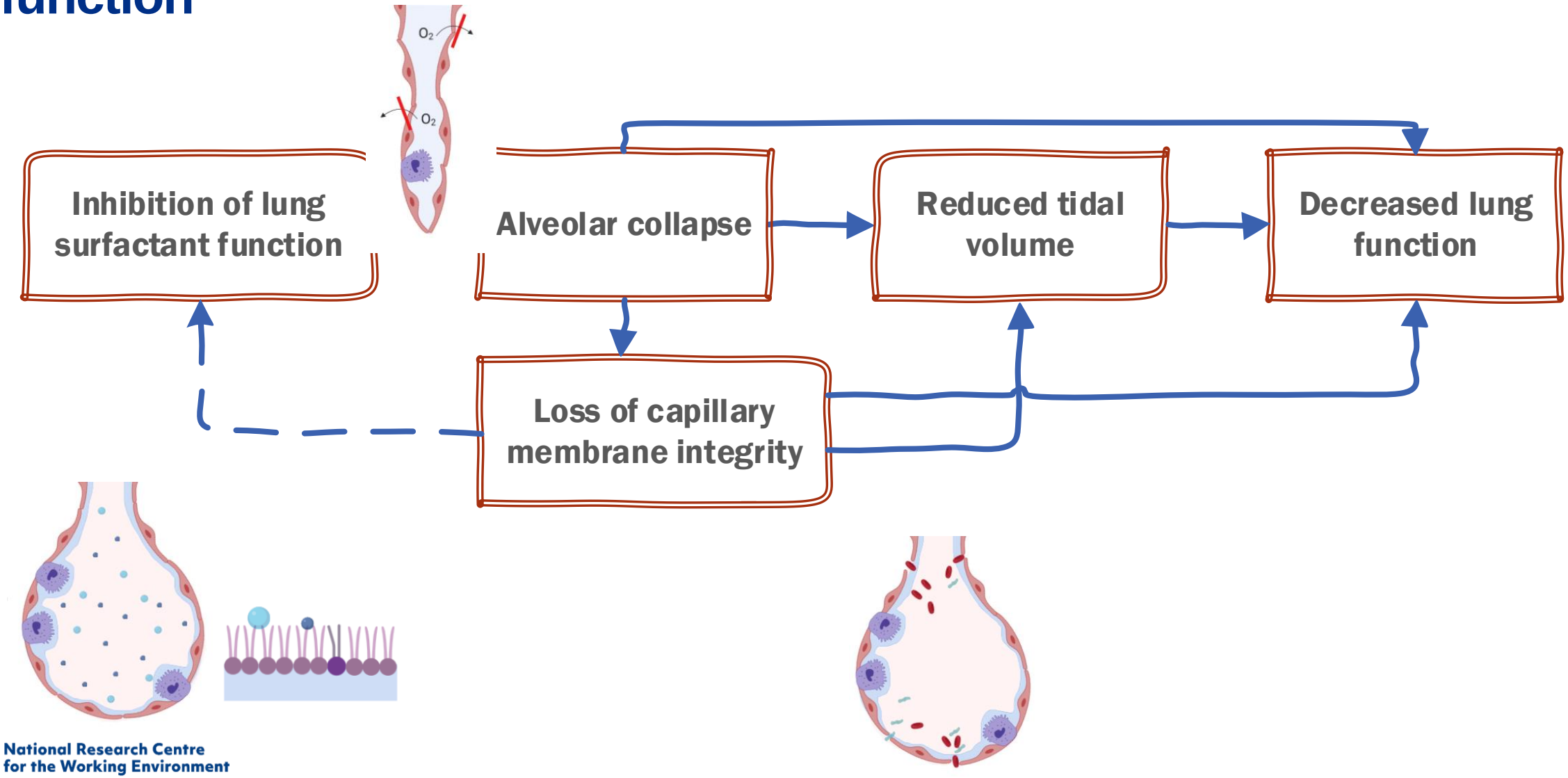


Minimum surface tension!

Aerosol exposure of test substance

AOP 302: Lung surfactant function inhibition leading to reduced lung function



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Created with Biorender

Da Silva et al 2021 CrTox

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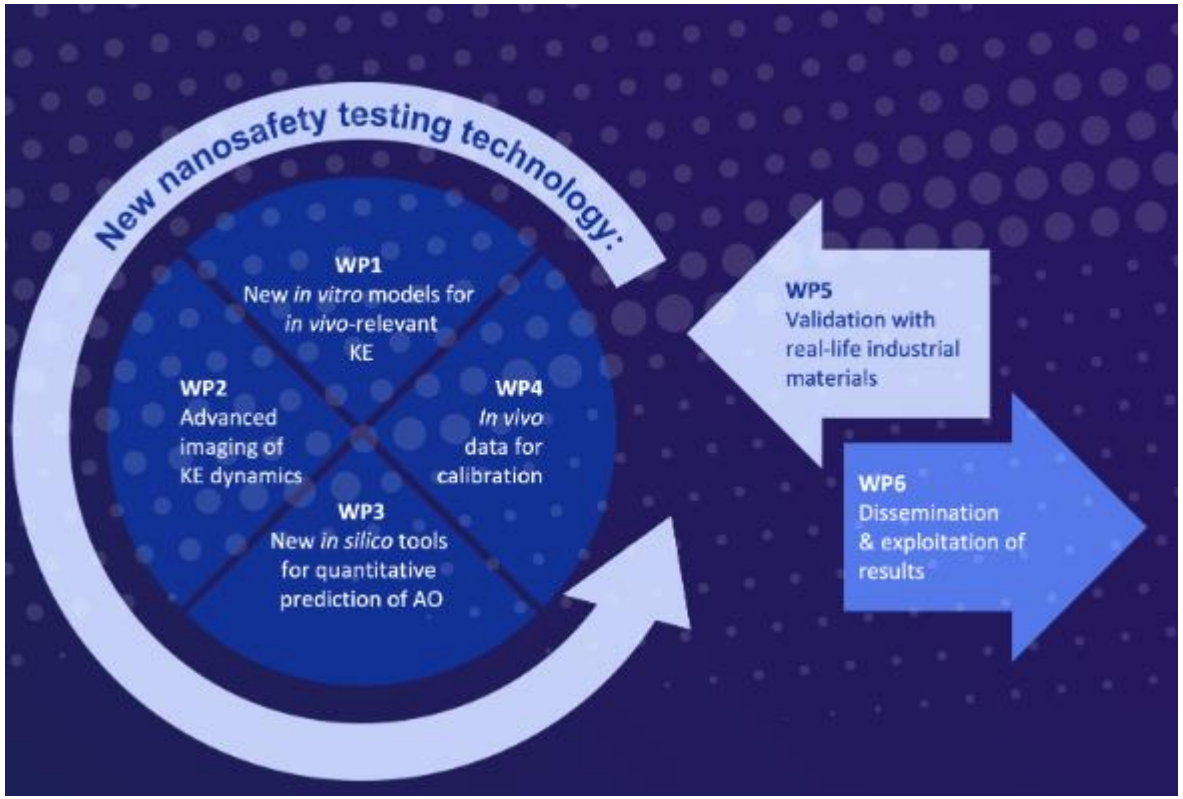
- **Objective 1: Develop new *in vitro* models relevant for prediction of *in vivo* adverse outcomes (AOs)**.

- **Objective 4: Calibrate and validate the *in vitro* adverse outcome prediction models with *in vivo* data**
- - historical data, and case studies with cement, nanoplastics, electronics waste material, and advanced materials for catalysis and medical applications, collected at different stages of their life cycle.



Effect of substances on lung surfactant function

- Case: impregnation products
- Predictiveness of the in vitro method
- Combining the in vitro method with exposure modeling
- Planned work in nanoPASS

Impregnation products as an example

- Make surfaces dirt and water repellent
- Used both by consumers and workers

Human poisoning cases

- People frequently experience respiratory problems after using impregnation sprays, even if the instructions for use are followed
- Often sold in pressurized cans -> creates aerosol droplets that are small -> penetrate deep into the lungs
- Symptoms (shortness of breath, coughing, tightness in the chest, difficulty breathing) occur shortly after application
- Most recover with supportive care

Case

- Used 2 spray cans on her new sofa
- Windows and doors open
- Sprayed 30 min
- Coughing, tightness in the chest, difficulty breathing, headache, nausea, fever

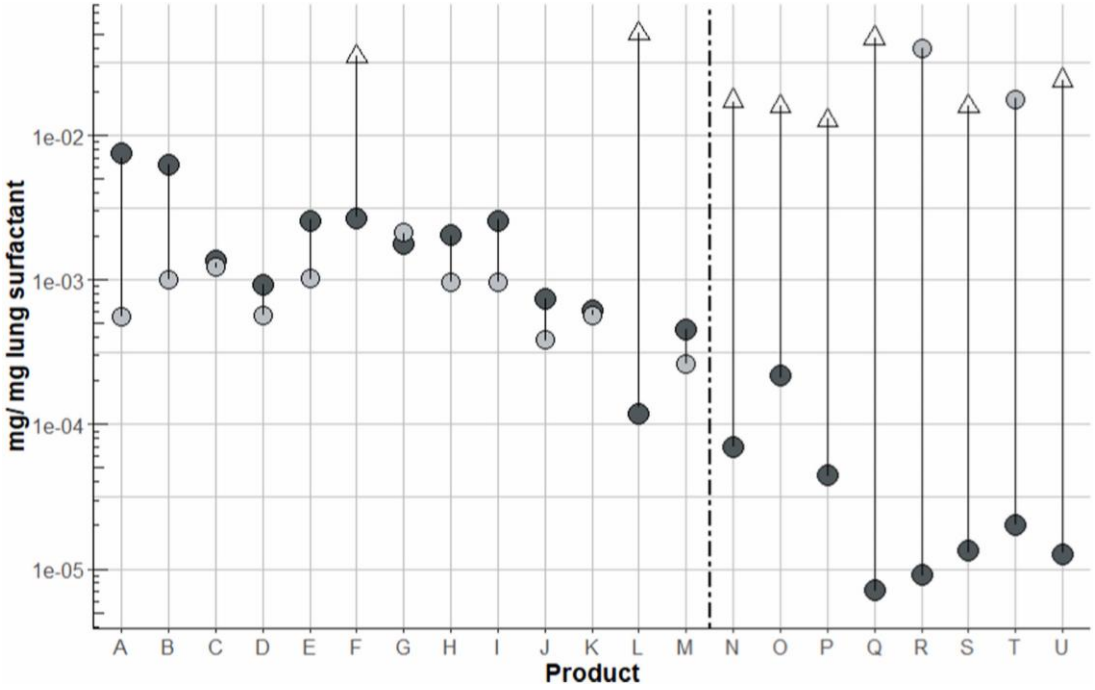
Predictiveness of measuring lung surfactant function inhibition

Chemical or product	Lung surfactant function measure	In vivo comparison	Type of data	n	Predictiveness
Impregnation products	CDS	Breathing pattern changes in mice Human data	Whole body plethysmographs Accidental exposure	22 7	Sensitivity: 100% Specificity: 63%

Da Silva, 2021, DOI: 10.1016/j.crtox.2021.05.002.
Sørli, 2018, DOI: 10.14573/altex.1705181.
Sørli, 2018, DOI: 10.1016/j.ijpharm.2018.08.031.
Sørli, 2016, DOI: 10.1165/rcmb.2015-0294MA.

Combining in vitro assay and exposure modelling

- 13 products for impregnation
- 8 cleaning spray products
- Exposure assessment in chamber
- Estimating alveolar deposited dose by modelling
- Test for lung surfactant function inhibition



Impregnation Cleaning

- Deposited alveolar dose in use scenario
- Inhibiting dose
- Margin of safety

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Risk assessment of consumer spray products using *in vitro* lung surfactant function inhibition, exposure modelling and chemical analysis

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Work planned in NanoPASS

- Test particles from industrial cases for lung surfactant function inhibition
- Compare with data generated in the rest of the consortium
- Integrate data in weight of evidence for AOP302

- **Challenges**
  - Dose estimation is possible, but sometimes challenging. Does not always compare to in vivo estimated doses
  - Only tests one toxicological target in the lungs and needs to be combined with other in vitro methods

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Thank you for your attention