COMBINING IN SILICO AND IN VITRO TOOLS FOR ASSESSING INHALATION HAZARD OF SODIUM DODCEYL SULPHATE EXPOSURE

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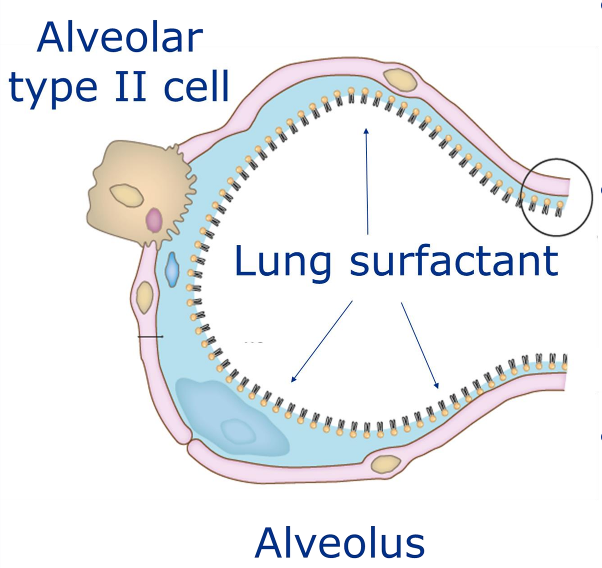
Key Questions:

1. Can we study the effects of Sodium Dodecyl Sulphate (SDS) exposure on lung surfactant function *in vitro* ?

***2.* Can we study the effects of SDS on the visco-elastic properties of lung surfactant?**

3. Can we use this information to address future inhalation hazard of SDS aerosols as an alternative to animal testing?

Lung Surfactant

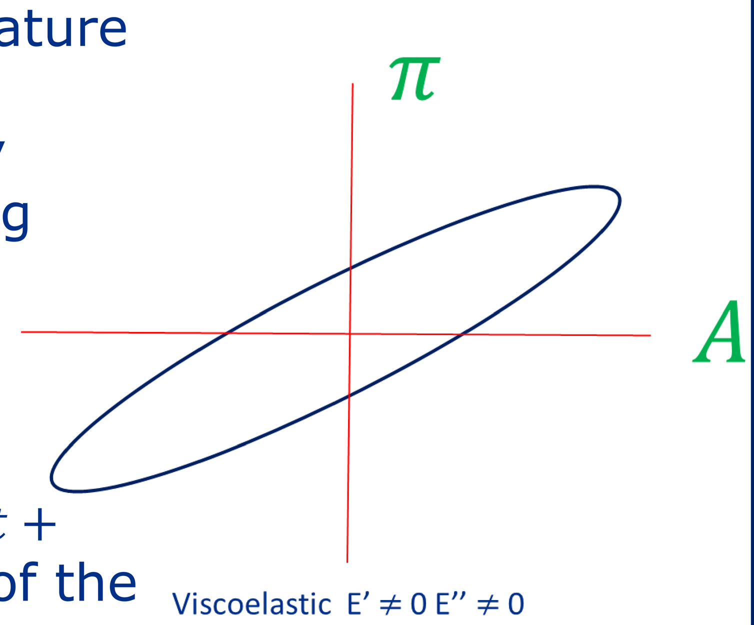


Sørli 2018

- Film at the air-liquid interface composed of 90% lipids + 10% proteins.
- **Function: surface tension regulation** allowing effortless **breathing** and prevent lung collapse.
- Lung surfactant function inhibition leads to alveolar collapse resulting in difficulty in breathing.

Investigating viscoelastic properties of lung surfactant

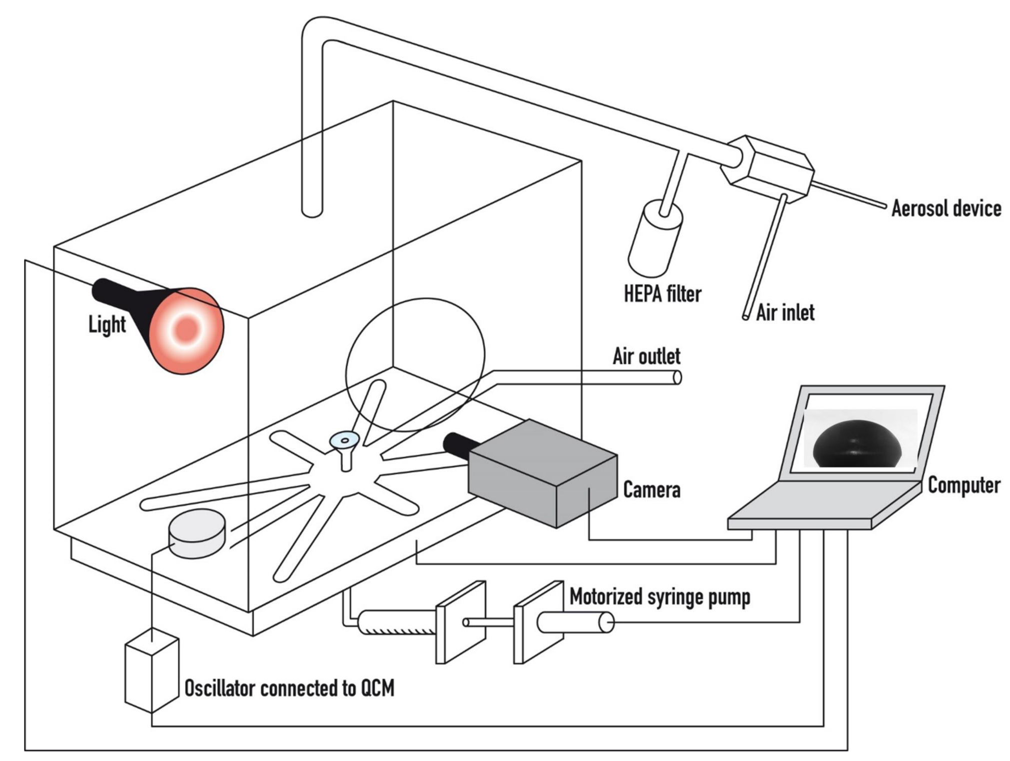
- Lung surfactant is viscoelastic in nature
- The Fourier Transform Tensiometry method : periodic oscillation of lung surfactant drop
- Area : $A(t) = A_0 sin\ \omega t$
- Surface pressure : $\pi(t) = E' A_0 sin\ \omega t + E'' A_0 cos\ \omega t$, ω mode of oscillation of the droplet size



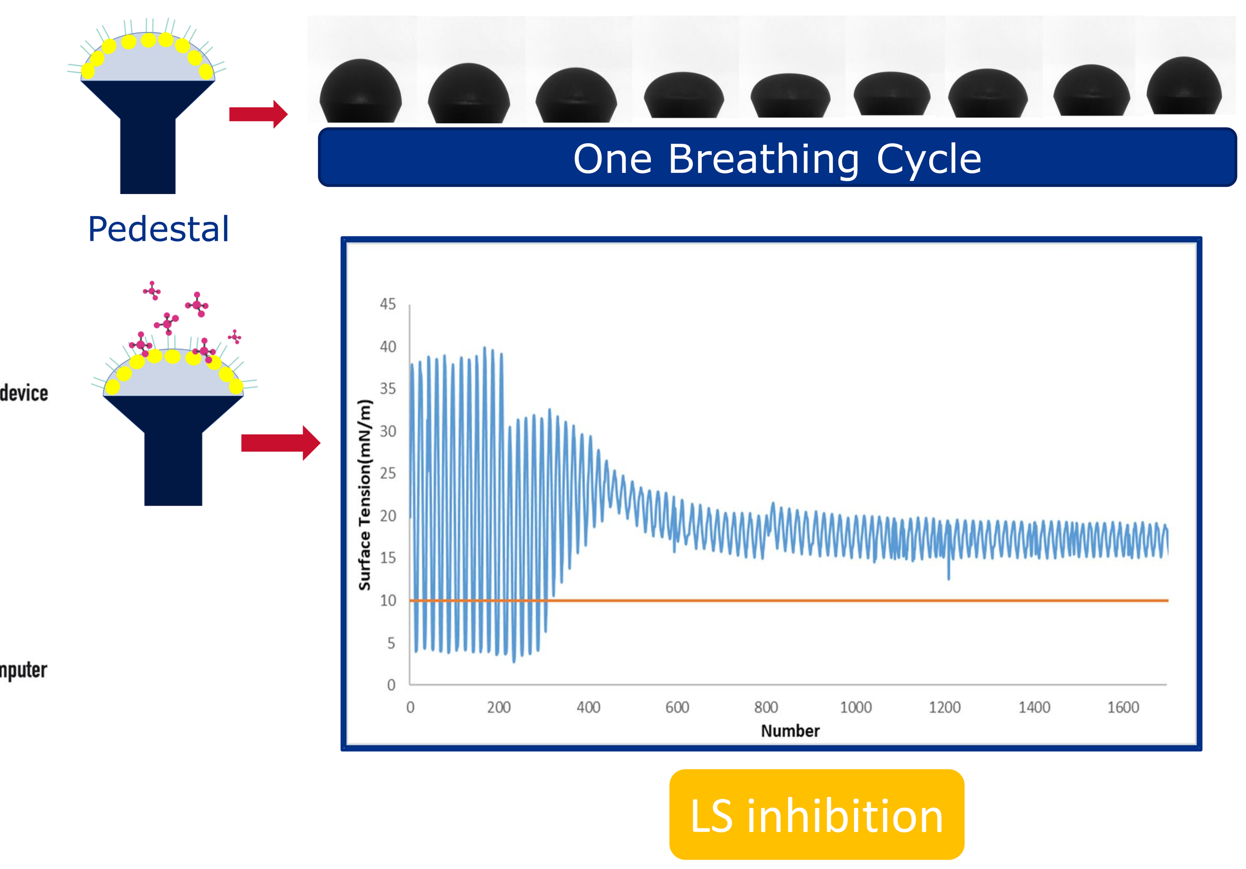
- Viscoelastic properties determined by E' = storage moduli, E'' = loss moduli.
- Complex modulus $E^* = E' + i\ E''$

Methodology

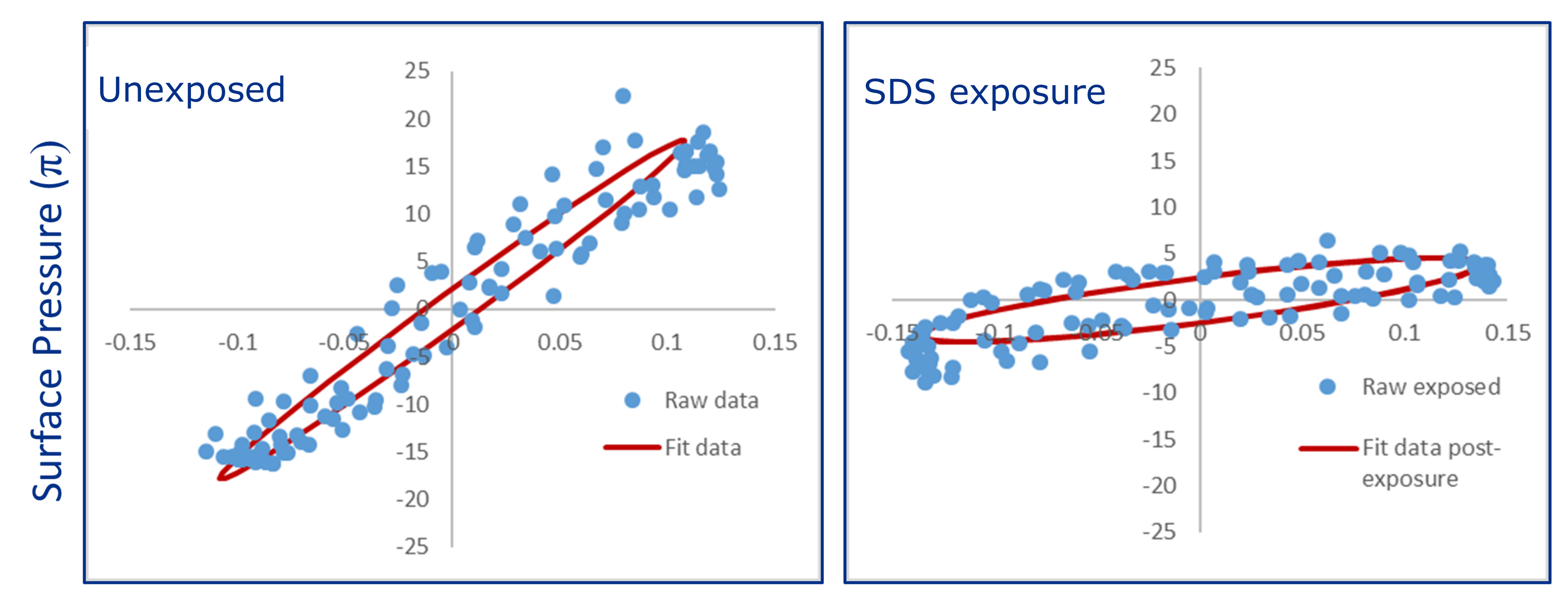
a)*In vitro* LS bioassay : based on the constrained drop surfactometer



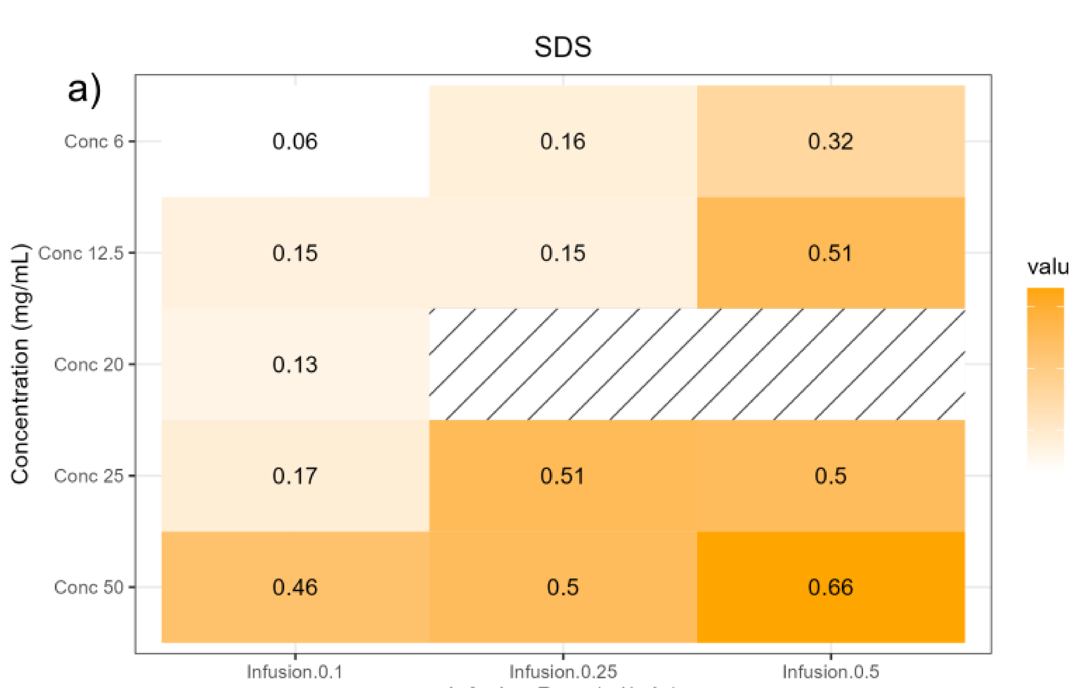
b) Measurement of LS function



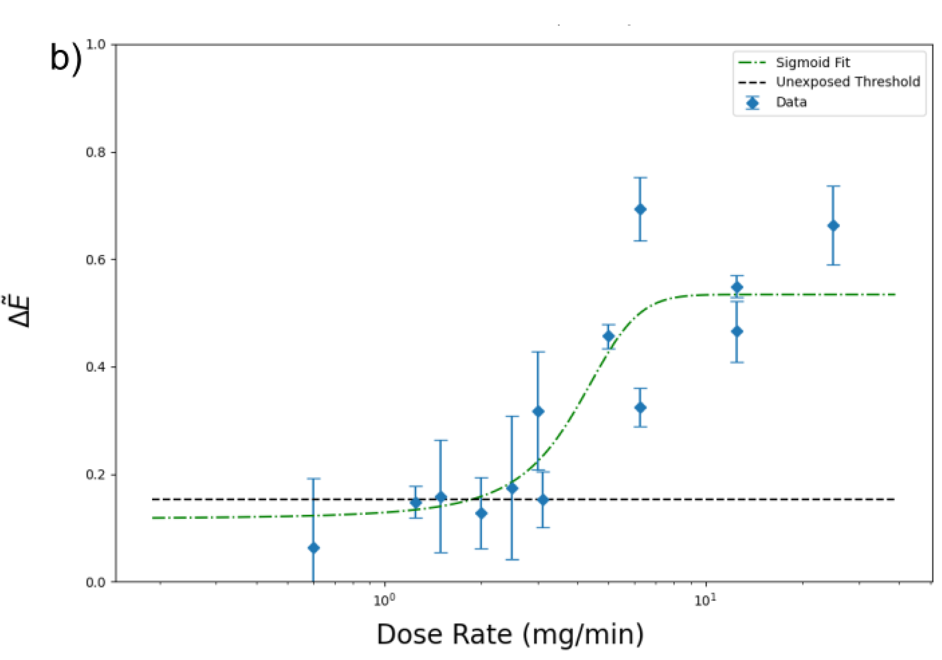
c) The Fourier Transform Tensiometry Method



Results



a) Surfactant inhibition is determined by the normalized changes of the complex modulus.



b) Inhibition of lung surfactant is correlated to the dose rate.

Conclusions

- The effects of SDS exposure on lung surfactant function *in vitro* is inhibitory at increasing concentrations and infusion rates.
- The Fourier Transform Tensiometry method allows to study the changes in the viscoelastic properties of lung surfactant when exposed to aerosolised SDS.
- Furthermore, the complex modulus from the method can be used to quantify lung surfactant function inhibition
- Inhibition of lung surfactant function on interaction with SDS aerosols in dose rate dependent.

References :
Da Silva et al., Curr. Res. in Tox., 2021
Sørli et al., *Am. J. Respir. Cell Mol. Biol.* 2016
Sørli et al., *Int. J. Pharm.* 2018

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