WARSAW UNIVERSITY OF TECHNOLOGY
Faculty of Chemical and Process Engineering

STUDY OF THE INTERACTIONS BETWEEN O_2 NANOBUBBLES AND THE PULMONARY SURFACTANT

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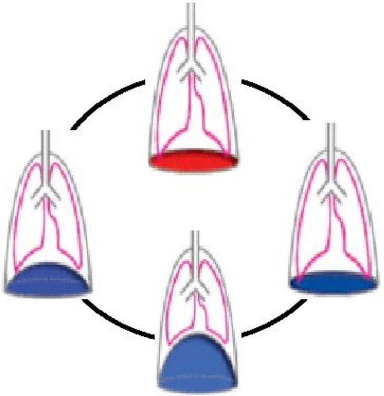
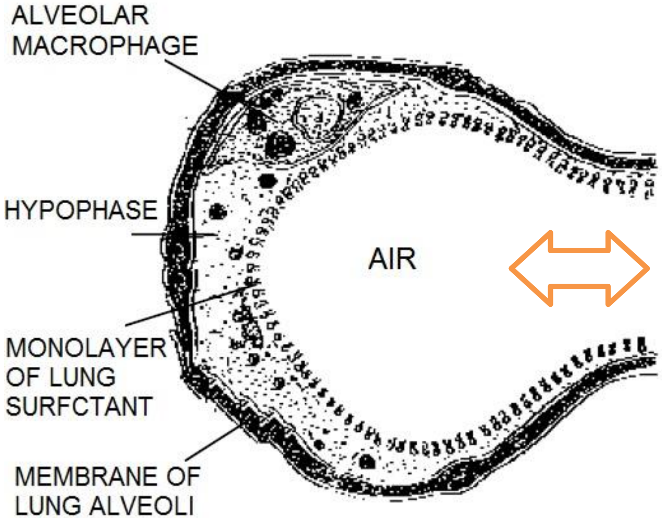
Introduction



Pulmonary surfactant (PS) forms the natural barrier exposed to inhaled matter: not only air contaminants but also to **therapeutic aerosols**, which should overcome it to produce clinical effects. Inhalable drug aerosols produced, e.g., in nebulizers contain sufficiently small droplets to reach alveoli, where they may interact with the PS.

From engineering point of view, lungs form the surface with elastic properties which can respond to continuous variations of air pressure.

Due to the fact that the liquid-gas interface is subjected to repeated cycles of compression and expansion, it is important to study potential influence of new components of inhaled drugs on the PS under dynamic breathing-like conditions.



Structure of the pulmonary surfactant

The aim of the work

• **POTENTIAL DRUG COMPONENT – Aqueous Dispersion of Oxygen Nanobubbles (NBs)**

The physicochemical properties of nanobubbles:

- diameter below 1 μm
- huge surface-to-volume ratio
- very high internal gas pressure

Potential medical application in inhalation therapy:

- aerosol drug carrier
- additional function of oxygen supplementation
- component of liquid drug formulation

This research is focused on the measurements of the dynamic surface-active properties of the pulmonary surfactant model (MPS) in the presence of ADON.

Methods

Investigation of the influence of NBs on the dynamic Surface-active Properties of lung liquids

- **Prediction of the physiological changes in the lungs**

Studies on the effects of NBs on the model pulmonary surfactant (MPS):

- MPS: **Infasurf** * (calfactant) - multi-component model containing proteins and lipids (* donated by ONY Biotech, USA)

- two liquids containing O_2 NBs:
  - Aqueous Dispersion of Oxygen Nanobubbles (ADON)
  - 0.9% Saline Dispersion of Oxygen Nanobubbles (SDON)

NBs produced by membrane technique and characterized by DLS *(Odziomek et al., 2022)*

Studies done for the concentration of NBs dispersions predicted from the calculated alveolar deposition of inhaled droplets in the alveoli:

0.018 ml / ml of MPS mixture

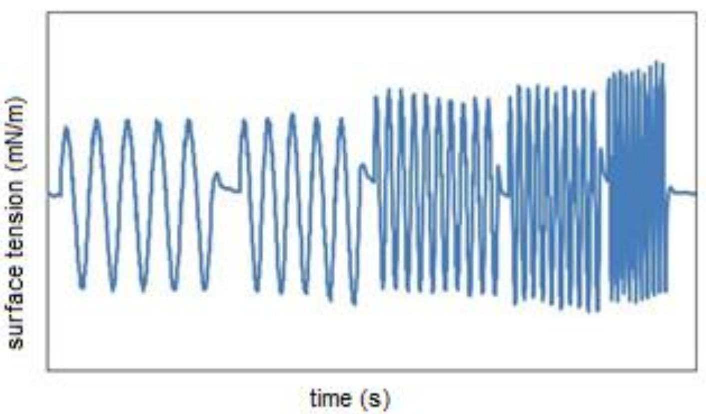
Methods

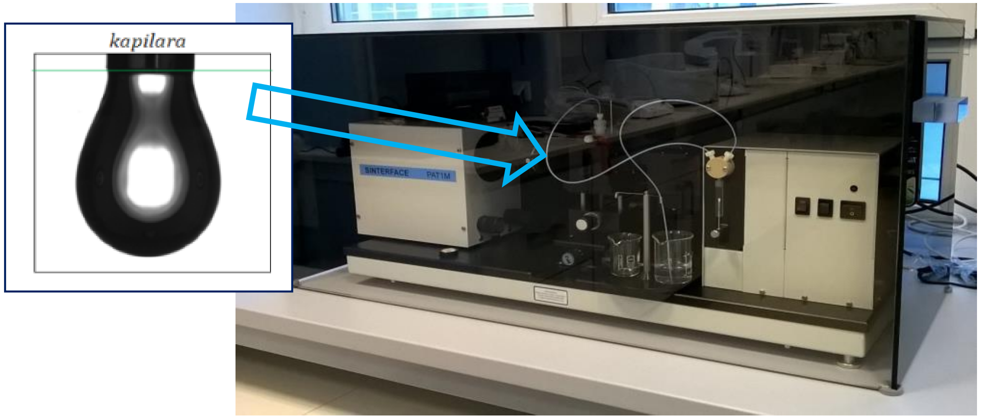
Investigation of the influence of NBs on the dynamic surface-active properties of lung liquids

- **Prediction of the physiological changes in the lungs**

Study on the effects of NBs on MPS:

- sinusoidal oscillations of the liquid-gas surface (pulsation drop method)
- determination of rheological parameters of the liquid-gas interface (μ_d i ε_d)



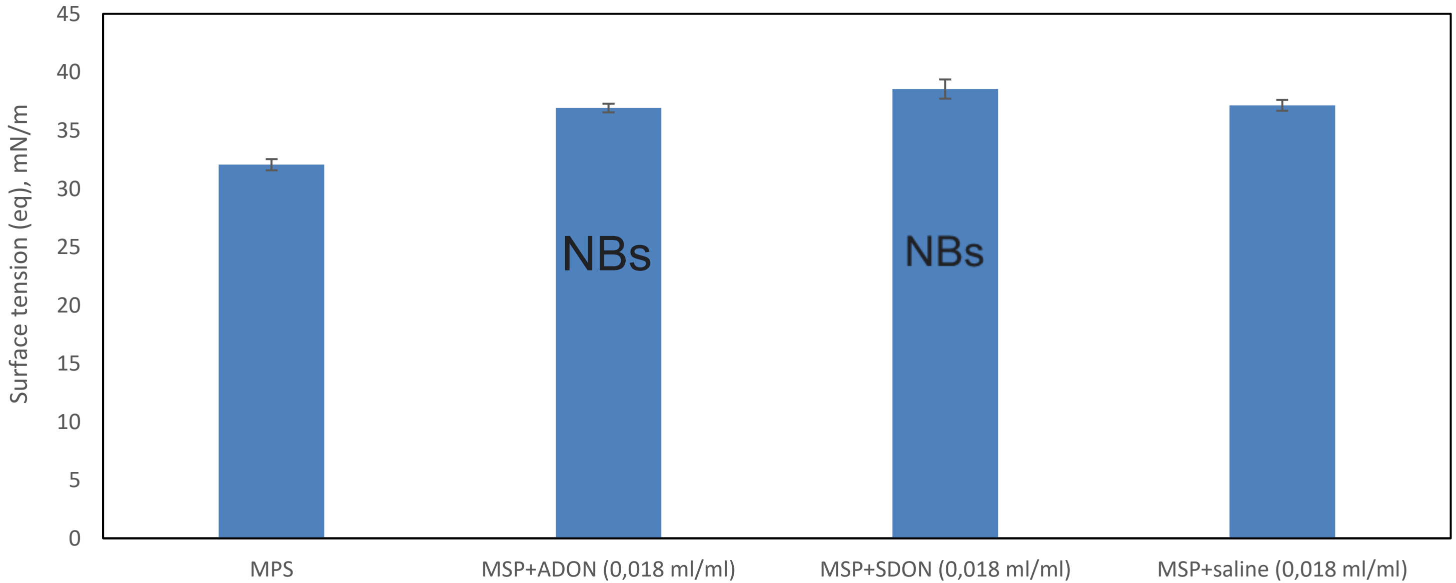


Profile Analysis Tensiometer *PAT-1M* (SINTERFACE, Germany)

Results

Investigation of the influence of NBs on the dynamic Surface-active Properties of lung liquids

The equilibrium surface tension (10 min) of MPS was only slightly increased due to the presence of salt ions and / or NBs.



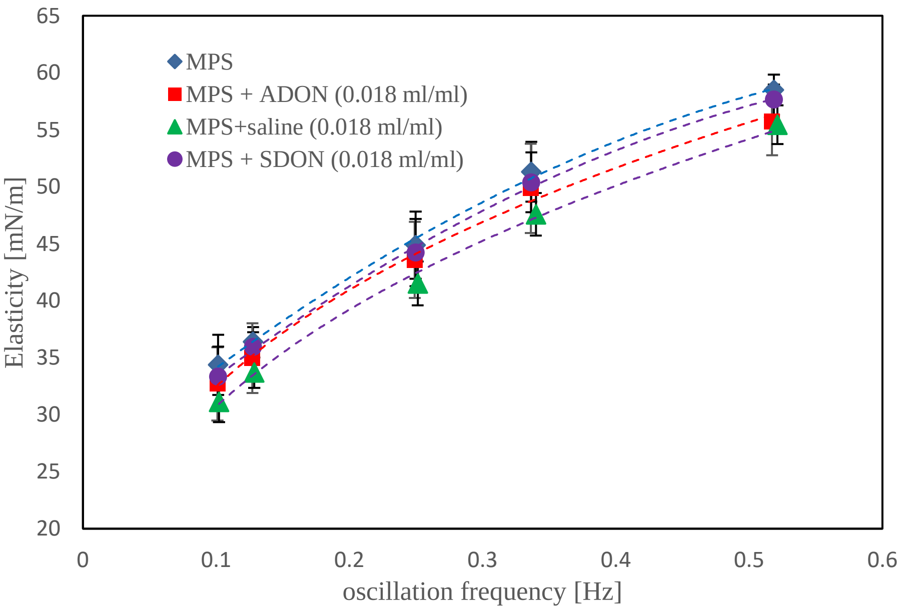
Average equilibrium surface tension σ_r of MPS and in the presence of NBs or saline (36.6˚C, t ~ 600s)

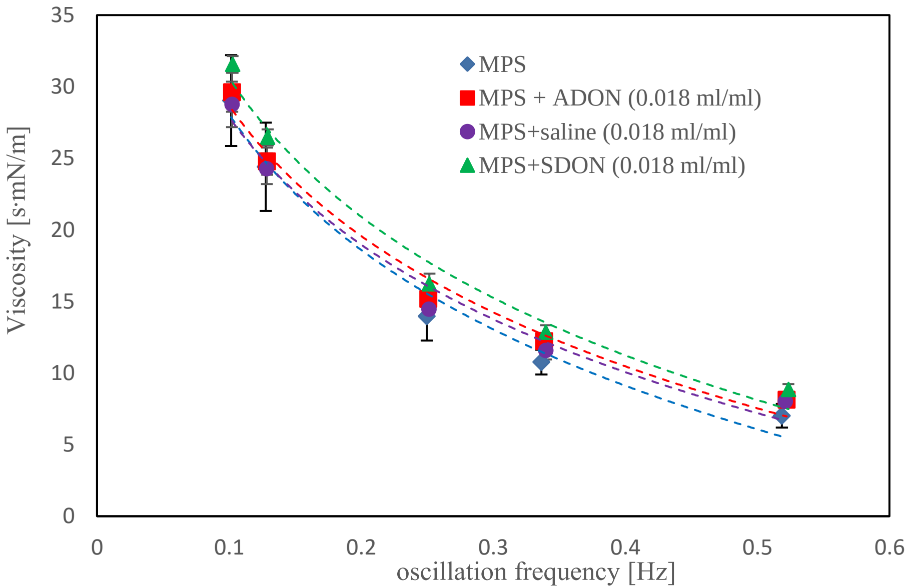
Results

Investigation of the influence of NBs on the dynamic Surface-active Properties of lung liquids

MPS: Higher oscillation frequencies result in a decrease in the surface viscosity and an increase in the elasticity (viscoelastic nature of the air-liquid interface).

Interactions: The effective rheological parameters in the MPS system after adding ADON or SDON follow the trends observed for pure MPS. The elasticity is slightly reduced.





Dilational surface elasticity (ε_d) and viscosity (μ_d) of the liquid-gas interface in the presence of MPS and additives (36.6°C)

Conclusions

- Model calculations indicate that nebulized **aerosol droplets containing NBs may reach the alveoli**. So they may influence the properties and function of the pulmonary surfactant.

- Prediction of the physiological changes in the lungs, first, should be verified by *in vitro* tests conducted under dynamic conditions (simulation of breathing cycle). Dynamic characteristics of the MPS system during oscillations allowed to determine dilatational surface viscosity and elasticity as a function of oscillation frequency. The observed relationships confirm the viscoelastic nature of MPS interface.

- The presence of NBs has a minor effect on the dynamic characteristics of the air-liquid interface. Unchanged surface viscosity suggests the absence of additional intermolecular interactions, related, e.g., to formation of H-bonds between the surfactant adsorbed on the surface and water molecules. Small reduction in the elasticity suggests only a slight decrease of the amplitude of the surface tension variations during cycle.

- It can be concluded that inhaled O_2-NB dispersions should be safe for the pulmonary surfacant.