PHASESPACE DESIGN LAB / CURRENT INVESTIGATIONS

Can We Keep the Lung Working as It Fills with Fluid?

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IN BRIEF

Fluid can accumulate in the lungs because pressure backs up from the left heart, because a blood–air barrier becomes leaky, or because normal clearance cannot keep pace. We began by asking whether microscopic surface geometry might concentrate excess water where it would interfere least with breathing. We built and ran capillary models, qualified a published molecular simulator containing pulmonary surfactant proteins SP-B and SP-C, and analyzed the authors' molecular trajectories. Some initially promising "gutters" added surprisingly little benefit. A reproducible molecular observation led somewhere else: water preferentially occupies lower regions of the compressed surfactant interface. But these nanometre-scale observations do not establish a treatment for pulmonary edema. Our most consequential finding may be a change in the design question itself: **where does excess lung water come from, and what controls its thickness, pressure, and exit?**

A small airspace, and a large hydraulic problem

A healthy alveolus has a very thin aqueous lining, a surfactant-coated air–water boundary, and an extraordinary density of nearby capillaries. Oxygen crosses the delicate air–blood barrier as we breathe. If the left ventricle suddenly struggles to accept or eject blood, pressure can rise backward through the left atrium and pulmonary veins. Fluid then filters out of pulmonary capillaries, first collecting in surrounding tissue and, if defenses are overwhelmed, entering the airspaces.[1,2]

The lung can therefore become congested while systemic blood pressure is relatively ordinary. In severe cases, the familiar crackling sounds heard by clinicians accompany fluid-filled or reopening airways. We became interested in what happens *before* that unmistakable stage, when the lung is still trying to preserve gas exchange as incoming fluid increases.

The water arrives from behind

In cardiogenic pulmonary edema, the incoming water originates in the blood, not in the inhaled air. Elevated pulmonary venous pressure pushes fluid across the capillary wall into the interstitium. Lymphatics initially increase drainage; if filtration outruns that reserve, fluid may cross the alveolar epithelium. An active epithelial sodium-transport system ordinarily helps reabsorb liquid from the airspace. Injury to that transport system makes clearance harder.[2,3]

There is another route into the problem. Acute congestion is not always a matter of carrying too much total body water. Sympathetic constriction can shift blood out of peripheral and abdominal venous reservoirs toward the heart and lungs; a left ventricle unable to receive that additional volume can produce pulmonary congestion rapidly. The 2026 European heart-failure guidelines explicitly distinguish fluid redistribution from total volume overload and emphasize treating the precipitating cause alongside congestion.[1]

Which surface are we changing?

Our first drawings placed water on an alveolar face and imagined making that face less wettable, with narrow preferred-wetting paths around its edges. But the anatomy forced a correction. The epithelial wall is always covered by a liquid lining; **surfactant principally occupies the moving air–water interface above that lining**. As edema water arrives from below, the interface rises or changes shape. If an airspace becomes completely liquid-filled, the local air–water boundary disappears, and with it the ordinary job of an interfacial surfactant monolayer.[3,5]

What should remain small is therefore not simply “wet area,” since the living surface is normally wet. A more physically relevant quantity is **the local thickness of the aqueous lining**, which we can denote $h(x,y)$. If extra water could be concentrated in some deeper regions while the lining stayed thin over much of the exchange surface, it might preserve shorter diffusion paths locally. Whether such a rearrangement is possible, stable, safe, or useful has not yet been demonstrated.

An alveolus has edges

We were drawn to the geometry because alveoli are neither perfect balls nor flat sheets. Three-dimensional imaging of human lungs reports median counts of approximately 12–15 planar facets per alveolus, broadly compatible with an old 14-faced foam-cell idealization.[4] Real alveoli share curved, deforming septa with neighbors. Our first models used an idealized 14-face cell and, subsequently, a local three-wall corner cut from it. This was an appropriate way to test capillary sorting without pretending we had reconstructed an entire living lung.

Giving unwanted fluid a gutter

In a capillary model, a surface may attract or discourage liquid through its contact angle. We asked whether a relatively non-wetting broad face, combined with more-wettable narrow junctions, would draw water away from the exchange surfaces. Surface Evolver was an attractive first instrument: with a fixed liquid volume, it can seek low-energy equilibrium shapes as wall geometry and contact-energy conditions change.

We executed **169 Surface Evolver equilibrium cases** across a strip, crossing tracks, and idealized three-dimensional alveolar-corner geometries. In the canonical corner at the highest fluid burden tested, changing uniform wall contact angle from 90° to 120° increased our geometrically defined dry broad-face fraction from about **68.8% to 78.1%**. The direction was intriguing, but those are model surfaces and model contact angles, not measurements of functioning alveoli.

When we added junction bands that were more wettable than the broad faces, more liquid generally appeared near those junctions. That did not translate into a comparably large additional area benefit. Strongly attractive gutters sometimes drew the wet region farther outward, producing a larger footprint. Five aggressively patterned cases even extended beyond the local corner patch, a useful sign that the simplified geometry was becoming inadequate.

A useful number became much smaller

Our first narrow-band analysis seemed to show an additional dry-face gain of about 9.6 percentage points. That result did not survive inspection. The patterned cases had been scored with a finite-width junction band, but their uniform controls had been scored with a zero-width band. Changing the band changed the denominator of the measured broad-face fraction. The comparison was invalid.

We retained the original simulated contact lines and repaired the measurements without rerunning Surface Evolver. Uniform controls were re-scored at matching virtual band widths. The strongest corrected individual gain was about **0.26 percentage points**, in one sheared geometry with a 15% junction band, while junction capture increased about **3.35 percentage points**. The original large gain was an artifact; the genuine incremental benefit was small and sensitive to geometry.

That correction saved us from spending further effort optimizing an imaginary success. We also screened artificial ridges, pillars, and needle-like nanostructures. Some analytical Cassie-style calculations predicted strong liquid exclusion, even for dimensions resembling observed surfactant assemblies. Yet those calculations assume rigid surface features and stable air pockets. Lung surfactant is a deformable lipid–protein system. The analytical result was a reason to investigate softness, not evidence that nanoneedles would work in a lung.

Reusing a published surfactant model

A much better starting point was already public. Liekkinen, Javanainen and colleagues simulated compression of lipid monolayers containing SP-B or SP-C, alongside compression and expansion of protein-free controls, and compared aspects of their behaviour with experiments.[6] Their Zenodo deposit contains starting molecular structures, force-field information, run inputs, energy data and trajectories.[7] We acquired the required files, built GROMACS 2020.7 on our Mac, successfully read both published run inputs, and rebuilt fresh SP-B and SP-C inputs from the authors' released text files. The published and rebuilt systems passed zero-step execution checks. **That established an inherited runnable model; it did not reproduce the authors' five-microsecond trajectories.**

We then analyzed five published compression-energy records. SP-B changed the mechanical stress–area response considerably relative to SP-C and to a protein-free control. At strong compression the pressure-derived estimate behaved unusually, making a scalar surface-tension reading difficult to interpret without looking at the three-dimensional structure. We therefore recovered selected late-compression coordinates rather than commission a costly new molecular trajectory.

The water in the folds

Research by Collada, Pérez-Gil and colleagues gave those structures biological context. Their neutron-reflectometry work shows SP-B promoting subsurface membrane reservoirs connected to the interfacial film; other experiments emphasize that multilayers require continuing lipid–protein supply and that breathing-like deformation can reorganize the film.[8–10] In mice with reduced SP-B, a separate study also found disturbed alveolar lining-fluid balance during ventilation, although that finding does not prove any particular nanoscale drainage mechanism.[11]

In our analysis of the published Liekkinen coordinates, SP-B-rich regions were associated with folds and lower-height regions of the molecular interface rather than simply with projecting peaks. Water that met our operational penetration criterion was also enriched in those lower regions. At the final compressed snapshot, our initial analysis reported about **1.61-fold** water enrichment in valley regions; a no-protein comparator also showed valley preference, so ordinary geometry explains some of the sorting.

What 270 configurations actually mean

We later re-examined five SP-B snapshots under **270 combinations** of grid resolution, margin, leaflet and valley threshold. Low-height regions had greater locally measured water penetration than high-height regions throughout that sensitivity sweep; forty historical measurements were reproduced to numerical precision. But these were 270 ways of analyzing *the same published molecular evidence*, not 270 independent experiments or new molecular-dynamics runs. Nanometre-scale hydration of surfactant folds is also not the same as bulk pulmonary edema.

What we have actually done

Our work combines a targeted literature and simulator search, locally developed capillary and analytical models, reproducibility qualification of an inherited molecular system, and new analyses of published coordinates. The Surface Evolver programme produced 169 equilibrium cases; a further 324 and 1,035 analytical microtopography configurations screened idealized structures. We reconstructed the published Liekkinen compression histories and analyzed molecular topography, then completed the 270-configuration robustness audit in the ChatGPT sandbox. Every stage has preserved code or results and an explicit evidence record.

We attempted a new controlled aqueous-loading experiment on the inherited SP-B system, but the returned attempts available for this report stopped at GROMACS preprocessing. We do not report them as successful molecular experiments. We have performed **no lung-on-chip, animal, or human edema intervention study**, and we have not measured oxygen transfer through our proposed geometries.

A different set of places to intervene

We once imagined temporarily making surfactant rougher, either by amplifying its own folding, adding molecules that co-assemble with it, or introducing a separate scaffold. Those remain possible questions about interfacial material behaviour. They are no longer our entire intervention map. A congested lung can also be helped upstream by reducing pulmonary filling pressure, redistributing circulating blood, or removing sodium and water through the kidneys. Within the lung, epithelial ion transport and lymphatic drainage help clear fluid that has already escaped the vasculature.[1–3]

The interesting design question is how those processes couple. An alveolar geometry that briefly tolerates extra liquid might buy time for pressure relief. An active clearance mechanism might be more valuable than a passive reservoir. An intricate surfactant texture might remain mechanically important without determining where most of the edema fluid resides.

A test that would teach us something either way

Our next candidate model would place an epithelial boundary beneath a variable-thickness liquid film and a deformable, surfactant-coated air–water interface above it, with septal junctions represented explicitly. We would hold incoming liquid volume fixed while comparing realistic wall geometry, capillary forces and clearance rates. The main outcome would be **how much exchange surface remains close to its normal thin-film state**, accompanied by measures of liquid bridging, interface stability, and modeled oxygen diffusion. Grotberg and Romanò's capillary–interstitial edema equations provide one possible physiological starting point.[2]

A favorable result would identify a physically useful regime for further biological testing. An unfavorable result would redirect our modelling toward pressure and clearance mechanisms, rather than establish which intervention best protects a living lung. Either outcome would improve the direction of the next experiment.

Sources and methodological notes

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Method note. Published physiological and molecular findings are attributed to their original sources. Surfacesim outputs described here are our own computational investigations or re-analyses of deposited data; the latter do not constitute independent replications of the original molecular-dynamics trajectories. The 169 Surface Evolver cases are equilibrium models. The 1,359 analytical microtopography configurations assume idealized surface physics. The 270 hydration configurations reuse five correlated snapshots from one published SP-B replicate, and cannot be counted as independent confirmations.

Run identifiers for the principal reproducible evidence are 277v2–v4a (capillary equilibrium and metric correction), 277v5–v6 (analytical microtopography), 277v8d (GROMACS rebuild qualification), 277v9–v11 (published-data analysis), and 277v14 (sandbox robustness). This letter does not claim a treatment, a clinical benefit, or an experimentally established mechanism for water removal. Bibliographic identities and the attributed scientific claims were checked against publisher, PubMed, and dataset records on 9 November 2026.