Alveolar mimics with periodic strain and its effect on the cell layer formation

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Abstract

We report on the development of a new model of alveolar air-tissue interface consisting of an array of suspended hexagonal monolayers of gelatin nanofibers supported by microframes and a microfluidic device for the patch integration. The suspended monolayers are deformed to a central displacement of 40-80 μm at the air-liquid interface by application of air pressure in the range of 200-1000 Pa. With respect to the diameter of the monolayers that is 500 μm, this displacement corresponds to a linear strain of 2-10% in agreement with the physiological strain range in the lung alveoli. The culture of A549 cells on the monolayers for an incubation time 1-3 days showed viability in the model. We exerted a periodic strain of 5% at a frequency of 0.2 Hz during 1 hour to the cells. We found that the cells were strongly coupled to the nanofibers, but the strain reduced the coupling and induced remodeling of the actin cytoskeleton, which led to a better tissue formation. Our model can serve as a versatile tool in lung investigations such as in inhalation toxicology and therapy.

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Alveolar air-tissue interface model.docx available at https://authorea.com/users/298802/articles/428203-alveolar-mimics-with-periodic-strain-and-its-effect-on-the-cell-layer-formation
Nanofibers

Microframe

Pressure

Displacement

Radius

Bare gelatin nanofibers

Pressure

Displacement

A549-seeded culture patch

Pressure (Pa)

Time (s)

$P_{\text{atm}}$

$P_{\text{max}}$

(b)

(a)

Microframe Nanofibers

Bare gelatin nanofibers

A549-seeded culture patch

Displacement

Displacement

Displacement

Displacement

Displacement
The diagram illustrates the relationship between pressure (in Pa) and displacement (in µm) for a gelatin membrane. Different theories (including linear approximation, plate theory, and Laplace equation) are compared with experimental data. The graph shows that as pressure increases, displacement also increases, with the linear approximation and plate theory models closely matching the experimental data.
(a) i) $w = 0 \mu m$
ii) $w = 35 \mu m$
iii) $w = 70 \mu m$

(b) 120

Relaxed, $0 \mu m$
Half-depth, $35 \mu m$
Full-depth, $70 \mu m$
Theory

(c) 140

A549-cultured membrane
- Experiment
- Bare gelatin membrane

Displacement Profile (µm)
-200 -100 0 100 200
Radial Distance (µm)
Relaxed, 0 µm
Half-depth, 35 µm
Full-depth, 70 µm
Theory

Displacement (µm)
Pressure (Pa)
\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure.png}
\caption{(a) $Z=0$ (out-plan) \hspace{2cm} +3 \mu m \hspace{2cm} +6 \mu m \hspace{2cm} +10 \mu m$ (out-plan)
\hspace{2cm} (b) $Z=0$ (out-plan) \hspace{2cm} +3 \mu m \hspace{2cm} +6 \mu m \hspace{2cm} +10 \mu m$ (out-plan)}
\end{figure}
