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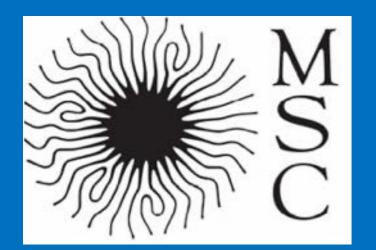


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Microrheological study of human respiratory mucus





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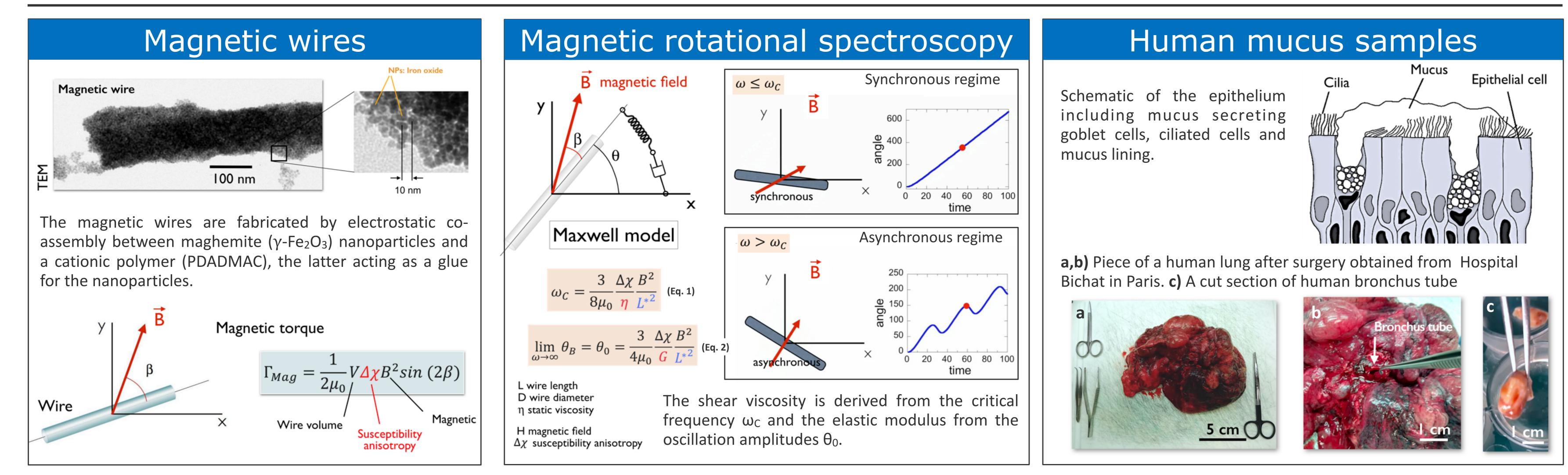
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ABSTRACT

Mucus is a viscoelastic gel secreted by the pulmonary epithelium in the tracheobronchial region of the lungs. The coordinated beating of cilia moves mucus upwards towards pharynx, removing inhaled pathogens and particles from the airways. The efficacy of this clearance mechanism depends primarily on the rheological properties of mucus. Here we use magnetic wire based microrheology to study the viscoelastic properties of human mucus collected from human bronchus tubes. The response of wires between 5 and 80 µm in length to a rotating magnetic field is monitored by optical time-lapse microscopy and analyzed using constitutive equations of rheology, including those of Maxwell and Kelvin-Voigt. The static shear viscosity and elastic modulus can be inferred from low frequency ($3 \times 10^{-3} - 30$ rad s⁻¹) measurements, leading to the evaluation time. This relaxation time is found to be widely distributed, from one to several hundred seconds. Mucus is identified as a viscoelastic liquid with an elastic viscosity of 100 \pm 40 Pa s. Our work shows that mucus exhibits secondary

inhomogeneities associated with the relaxation time of the mucin network that may be important for its flow properties. The results of this work were published in the journal Soft Matter, under the reference : M. Radiom, R. Hénault, S. Mani, A.G. Iankovski, X. Norel, J.-F. Berret, Magnetic Wire Active Microrheology of Human Respiratory Mucus, Soft Matter 17 (2021) 7585-7595.

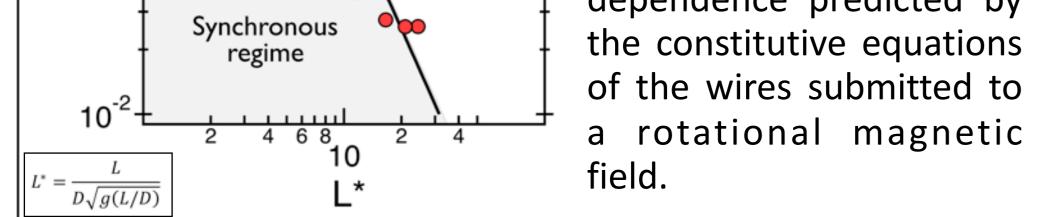
INTRODUCTION



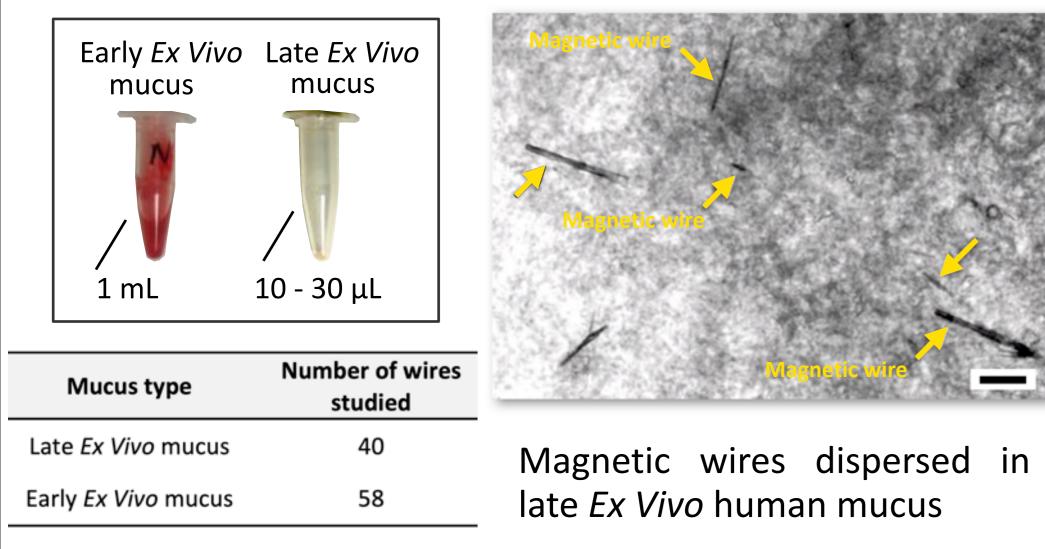
RESULTS

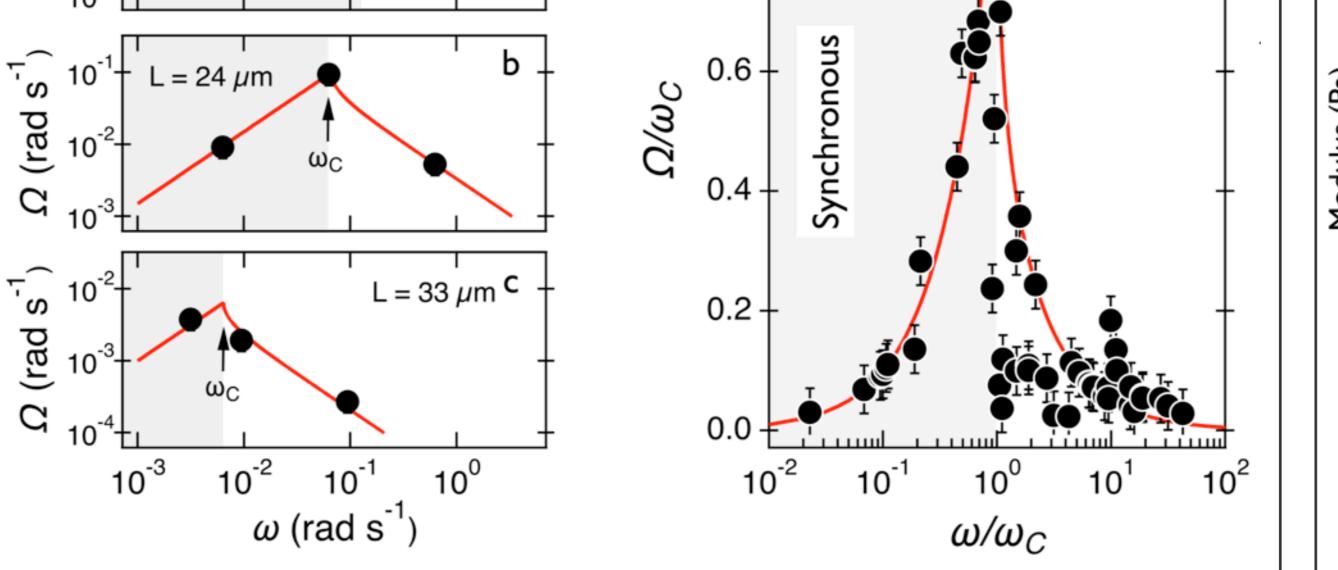
Comparison with literature

Magnetic wire technology Optical time-lapse microscopy Summary $\omega = 0.0094 \text{ rad s}^{-1}$ Left panels: Chronographs $(20^{\circ})^{\circ}$ *Complex fluids studied by Magnetic Rotational spectroscopy* $\omega = 0.0094 \text{ rad s}^{-1}$ Viscosity and elasticity schemes **Rheological class of** Quantities Ref. **Complex fluids** materials measured going rotation in late Ex , Eq. 2 Maxwell fluid Vivo mucus as a result of Surfactant wormlike micelles η, G, τ Α Ea. 1 200 400 600 an external magnetic field t (s) G_{eq}, G Soft solid Polysaccharide gels rotating with a frequency °-' $\omega = 0.94$ rad (rad) Living mammalian cells η, G, τ Viscoelastic liquid С of 0.0094 and 0.94 rad s⁻¹. ad) (rad Newtonian liquid 20 µm η, G_{eq}, G Pulmonary surfactant Soft solid θ_{o} $\omega = 0.94 \text{ rad s}^{-1}$ ວ ອ_{10⁻²} Right panels: Time series of Newtonian liquid η, G_{eq}, G DNA and NAP proteins 12 Soft solid 16 orientation angle $\theta(t)$ in the [A] L. Chevry et.al., Phys. Rev. E 88 (2013) 062306 - [B] F. Loosli et.al., ChemPhysChem synchronous and asynchro-10 17 (2016) 4134-4143. - [C] J.-F. Berret, Nat. Commun. 7 (2016) 10134 - [D] L.-P.-A. Thai $2 + \omega = 9.4 \text{ rad s}^{-1}$ nous regimes. The average 10 rotational velocity is shown et.al., ACS Nano 14 (2020) 466-475 - [E] O. El Hamoui et.al., Biomacromolecules 21 (2020) 3668-3677. 10 10 by the straight lines and the o Validation of wire constitutive equations oscillation amplitudes by arrows. t (s) Elastic modulus Viscosity **Relaxation time** 20 µm Mucus type Asynchronous η (Pa s) G (Pa) τ **(s)** 10⁰ regime Late Ex Vivo mucus 100 ± 40 2.5 ± 0.5 47 ± 12 Viscosity determination $3 \Delta \chi B^2$ Magnetic rotational Early Ex Vivo mucus 180 ± 30 4.4 ± 0.5 49 ± 6 $8\mu_0 \eta L^{*2}$ \sim spectroscopy performed ່ທ (rad ີ່ທ¹⁰⁻¹⁻ on water-glycerol viscous $L = 10 \,\mu m$ 10-7 Comparison with literature fluid of static viscosity 250 (rad β mPa s revealed the $1/L^{*2}$ Model 0.8 -Cystic fibrosis *n* = 177 Mucus G dependence predicted by sputum Synchronous



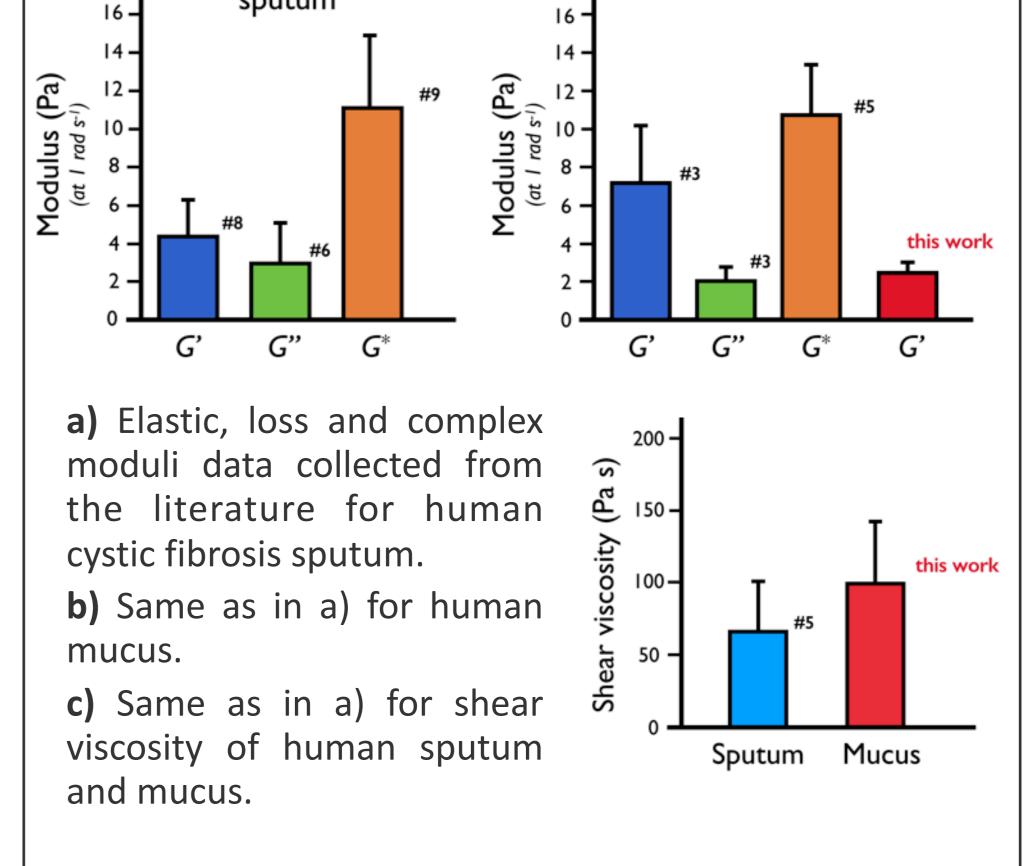
Magnetic wires dispersed in human mucus samples





Left panels: Average rotational velocity of several wires with length between 10 μ m and 33 μ m, showing the dependence of ω_c on the wire length.

Right panel: Average rotational velocity of wires normalized by the critical frequency ω_c plotted *versus* normalized frequency. The continuous line comes from the model developed for fluids of finite viscosity.



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REFERENCES

CONCLUSION

R. Bansil and B. S. Turner, Adv. Drug. Deliv. Rev., 2018, 124, 3-15 B. Button, H. P. Goodell, E. Atieh, Y.-C. Chen, R. Williams, S. Shenoy et al., PNAS 2018, 115, 12501-12506 B. S. Schuster, J. S. Suk, G. F. Woodworth and J. Hanes, Biomaterials, 2013, 34, 3439-3446 J.-F. Berret, Nat. Commun., 2016, 7, 10134 L.-P.-A. Thai, F. Mousseau, E. Oikonomou, M. Radiom and J.-F. Berret, ACS Nano, 2020, 14, 466-475 M. Radiom, R. Hénault, S. Mani, A.G. Iankovski, X. Norel, J.-F. Berret,

Soft Matter 17 (2021) 7585-7595

In this work we propose a new active microrheology technique to determine the rheological characteristics of human respiratory mucus. The probes used are remotely actuated magnetic wires of lengths between 5 and 80 µm, i.e. much greater than the size of the microcavities observed in mucus samples. Human mucus is identified as a viscoelastic liquid with an elastic modulus of a few Pa and a static viscosity of the order of 100 Pa s. This work also shows that mucus exhibits strong inhomogeneities associated with the relaxation times of the mucin network.