JOHANNES KEPLER UNIVERSITÄT LINZ

HABILITATIONSKOLLOQUIUM
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(INSTITUT FÜR BIOPHYSIK)

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Raum: UG1 in der Gruberstraße 40

Water transport through narrow membrane channels

Macroscopic laws of hydrodynamics do not apply to narrow biological channels. Since the discovery of water channels more than a quarter of a century ago, the physical laws of water flux through sub-nanometer wide channels remained elusive. To obtain water flow determinants, we quantified the unitary water permeability p_f of a diverse set of water facilitators, including cation selective peptides (gramicidin), a potassium channel (KcsA), aquaporins (AQP1, AQP4, AQP5, AQZ, GlpF) and the sodium glucose transporter (SGLT1). Therefore, we measured (i) the amount of fluorescently labeled and reconstituted proteins in the vesicular membrane by both fluorescence correlation spectroscopy (FCS) and high-speed atomic force microscopy, and (ii) the intensity of scattered light as a means to assess vesicular water efflux via our new adaptation of the Rayleigh-Gans-Debye equation (1). The FCS based registration of solute dilution in the immediate vicinity of an epithelial cell monolayer allowed online visualization of the pharmacologically induced inhibition of water channeling proteins. Using these methods we made the following observations: 1. Both potassium channels and the sodium-glucose cotransporter (SGLT1) are able to conduct water at rates comparable to that of AQP1 (2, 3). 2. The number of hydrogen bonds a water molecule may form inside narrow channels serves as the major determinant of p_f (1). 3. Positively charged residues near the channel mouth may increase p_f two or three times, conceivably by lowering the dehydration penalty at the channel mouth (4). 4. Transition state theory provides a useful link between p_f and the activation energy for single-file transport (5).

(1) **A Horner**, F Zocher, J Preiner, N Ollinger, C Siligan, SA Akimov, P Pohl. *The mobility of single-file water molecules is governed by the number of H-bonds they may form with channel-lining residues.* Science Advances, 1, 2, e1400083, 2015

(2) **A Horner**, L Erokhova, N Ollinger, C Siligan, P Pohl. *The Sodium Glucose Cotransporter SGLT1 Is an Extremely Efficient Facilitator of Passive Water Transport.* J. Biol. Chem., 291, 18, 9712-9720, 2016

(3) T Hoomann, N Jahnke, **A Horner**, S Keller, P Pohl. *Filter gate closure inhibits ion but not water transport through potassium channels.* PNAS, 110, 26, 10842-10847, 2013

(4) **A. Horner***, C. Siligan*, A. Cornean, P. Pohl. *Positively charged residues at the channel mouth boost single-file water flow.* Faraday Discussions, DOI: 10.1039/C8FD00050F, 2018

(5) **A. Horner,** P. Pohl. *Comment on "Enhanced water permeability and tunable ion selectivity in subnanometer carbon nanotube porins"*. Science, 359, eaap9173, 2018