USING THE QCM-D TECHNOLOGY TO CHARACTERIZE MEMBRANE WATER PERMEABILITY

Transport of water molecules through cell membranes is crucial for many vital functions in living organisms. The human body consists of ca. 70% water, which needs to be transported to tear ducts, saliva glands, kidneys, brain, lungs and blood, etc. Additionally, the outermost layer of the skin regulates hydration by modulating the uptake and release of water. Methods for studying such processes are therefore relevant for skin related cosmetics, pharmacy and many other medical applications. In this work the QCM-D technology was successfully applied to such studies.

INTRODUCTION

The outermost layer of the skin, the *Stratum Corneum* (SC), is responsible for water transport into and out of the skin in order to regulate the hydration and prevent dehydration. Additionally, it protects the underlying tissue from infection and damage caused by external factors. Normally the SC layer is roughly 10-40 μm thick and under extended immersion in water its increased hydration is revealed by the wrinkling of the skin. Understanding water uptake processes as related to lipid composition is highly relevant for skin related pharmaceutics and cosmetics, and also for understanding the toxicity of different compounds. Model membranes with different lipid compositions are often used in such studies.

APPROACH AND EXPERIMENTAL SETUP

In the work reviewed in this application note, a Q-Sense E4 instrument has been used and run in a well-controlled gas environment. Nitrogen gas was connected to the flow chambers and the humidity could be controlled with high precision using a moisture exchanger.

The model SC membranes consisted of ceramides, free fatty acids and cholesterol in different compositions. These were applied to the sensor surface (Au) using an airbrush, thereby forming tightly-packed and homogenous lipid membranes with thicknesses ranging from a few hundred nanometers up to several micrometers. By analyzing an uncoated sensor in dry nitrogen gas, a baseline could be established. Measurements under identical conditions were performed after an ex-situ coating of the membrane. From the relative changes in resonance frequency (mass uptake), Δf, and energy dissipation (viscoelasticity), ΔD, the membrane thickness could be determined using the Voigt viscoelastic model in QTools (Figure 1).

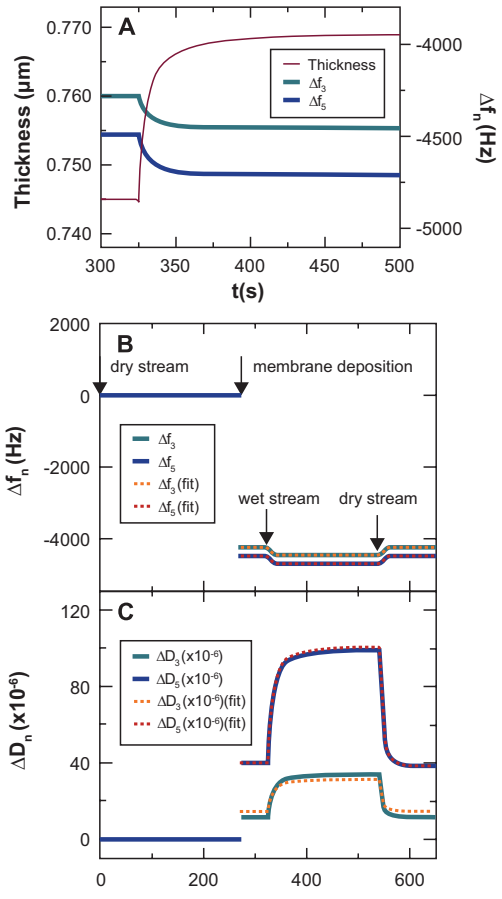

Figure 1. (A) The thicknesses of the membrane during increased humidity as calculated using the Voigt model in QTools. Displayed is also the Δf response relative to the uncoated sensor. (B) The frequency change Δf and (C) the dissipation change ΔD for the uncoated sensor and the sensor coated with a lipid membrane in a dry and a humid stream respectively. The 3rd and the 5th overtones are shown.

When the humidity over the lipid membrane is increased water vapor diffuses into the lipid molecules and causes swelling. This process results in a decrease in Δf (mass increase) and increase in ΔD (softer film). From the swelling characteristics it was possible to extract physical properties such as solubility, ***S***, and diffusivity, ***D***, of the water molecules in the membrane (Figure 1). The water permeability, ***P***, of the membrane, i.e. at which rate water molecules are able to permeate, is proportional to the product of ***S*** and ***D***.

RESULTS AND DISCUSSION

Different parameters were varied in order to determine their impact on ***S***, ***D*** and thereby ***P***. First the thickness of the SC membrane was varied, with a constant composition, as shown in Figure 2.

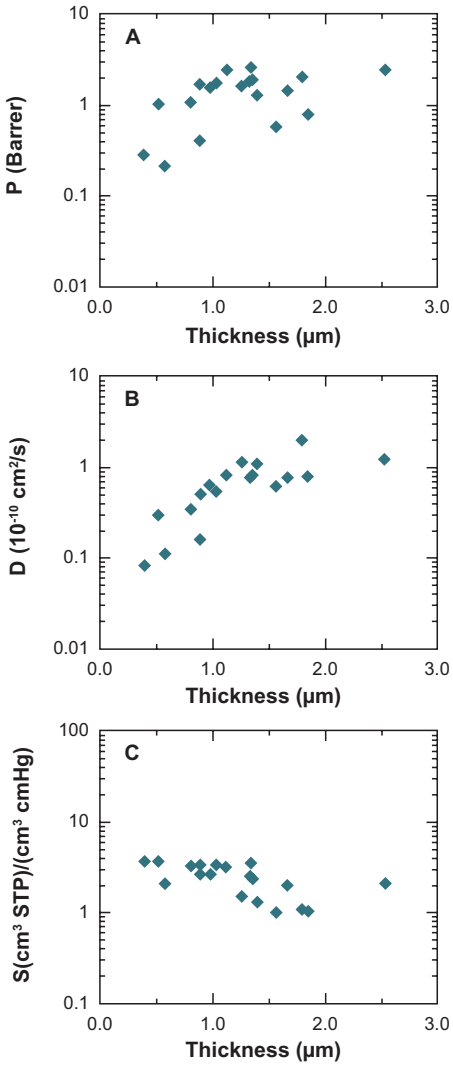

Figure 2. (A) The water permeability, *P*, (B) diffusivity, *D*, and solubility, *S*, for the model SC membrane plotted as a function of membrane thickness. All other parameters were kept constant.

D strongly increased with the membrane thickness whereas the effect on ***S*** was less pronounced. As an overall effect ***P*** increased with increased membrane thickness. This is to be expected since it is well known that the diffusion of water molecules normal to the membrane surface is the limiting factor, rather than the diffusion laterally in the membrane.

Additionally, the effect of the free fatty acid chain length was investigated. Due to a slight increase in hydrophobicity with increased chain length, a decrease in ***S*** could be observed. ***D***, on the other hand, increased with the chain length; as a result of these offsetting trends in ***S*** and ***D***, ***P*** remained constant. When comparing saturated and unsaturated free fatty acids it is clear that ***P*** in the former case is significantly lower (Figure 3). This is due to more order in the lipid membrane likely leading to a higher resistance against penetrating water molecules.

This effect is utilized in cosmetics and skin related pharmaceutics. The addition of unsaturated free fatty acids increases the water permeability of the skin and therefore benefits moisturizer performance. Model membranes can be customized on a molecular level in order to optimize factors affecting the membrane permeability on a very detailed level.

CONCLUSIONS

The effect of membrane composition on water permeability in SC was successfully studied using QCM-D. Based on the swelling characteristics, which were sampled through the changes in resonance frequency and energy dissipation, the diffusivity and solubility of water molecules in the membrane was calculated. The permeability is directly proportional to the product of these two factors.

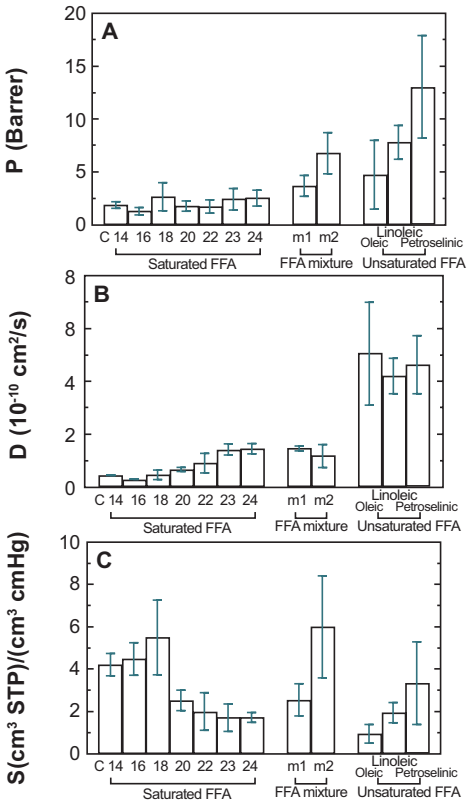

Figure 3. (A) The water permeability, *P*, (B) diffusivity, *D*, and solubility, *S*, for the model SC membrane with varying lipid chain length and saturation.

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REFERENCES

[1] Myung Han Lee, Bomyi Lim, Jin Woong Kim, Eun Jung An and Daeyeon Lee. *Effect of composition on water permeability of model stratum corneum lipid membranes*. Soft Matter, 2012, 8, 1539-1546.

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