Mathematical Model for the Stratum Corneum Water Loss Barrier

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Introduction

Aim

To aid interpretation of TEWL & related measurements.
Introduction

Skin

Skin is complicated & some simplifying assumptions are necessary!

Introduction
The simplified model

![Diagram showing liquid water and water vapour transfer through the skin and to the air.]

**Liquid Water**
**Water Vapour**

LE = Water Source
SC = Barrier Membrane
Air = Water Sink
Introduction

Main simplifying assumptions

1. Macro-scale model. No bricks. No mortar.
2. One-dimensional diffusion.
3. Steady-state only. Fick’s 1st law.
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Model Component 1: Water

Water & water vapour

Water is represented in this model by its concentration or density (kgm\(^{-3}\)).

Assume that water is condensed within the skin & evaporates from the SC surface.

\[
\begin{align*}
\text{Density of water} & = 1000 \text{ km}^{-3} \\
\text{Density of water vapour} & \sim 0.01 \text{ km}^{-3}
\end{align*}
\]

Evaporation causes a dilution by a factor \(\sim 10^{-5}\)!

Despite the low density, the water vapour interacts strongly with the SC (see later).
Model Component 2: Skin

A simplified model for the outer skin layers

Living Epidermis (LE):
- High water mobility
- High hydration

Stratum Corneum (SC):
- Low water mobility
- High hydration at the base
- Low hydration at the surface
- Linear hydration profile (for now)
- No swelling (for now)

Confocal Raman Spectroscopy
In-vivo hydration profiles confirm these basic assumptions as a reasonable starting point.

Figure adapted from:
Model Component 2: Skin

Hydration gradient and diffusion: Fick’s 1st Law

The hydration gradient in the SC implies diffusion. For steady-state conditions, use Fick’s first law (in one dimension):

\[ J = -D_{SC} \frac{dc}{dz} \]

Where
- \( J \) = Flux density [kgm\(^{-2}\)s\(^{-1}\)]
- \( D_{SC} \) = Mean diffusion coefficient [m\(^2\)s\(^{-1}\)]
- \( c \) = Concentration [kgm\(^{-3}\)]

For a linear hydration profile, this simplifies to:

\[ J = D_{SC} \frac{c_1 - c_2}{L_{SC}} \]
Model Component 2:- Skin

Diffusion coefficient for water in the SC

Reasonable values for normal volar forearm SC might be:-

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$J$</td>
<td>10 gm$^2$h$^{-1}$</td>
</tr>
<tr>
<td>$c_1$</td>
<td>700 kgm$^{-3}$</td>
</tr>
<tr>
<td>$c_2$</td>
<td>100 kgm$^{-3}$</td>
</tr>
<tr>
<td>$L_{SC}$</td>
<td>15 µm</td>
</tr>
</tbody>
</table>

$J = D_{SC} \frac{c_1 - c_2}{L_{SC}}$

These data are enough to give a rough estimate of $D_{SC} \approx 7 \times 10^{-14}$ m$^2$s$^{-1}$

and $\tau \approx \frac{L_{SC}^2}{D_{SC}} \approx$ 1 hour.

(For comparison, @30ºC, water $D_{WW} \approx 2.7 \times 10^{-9}$ m$^2$s$^{-1}$ [1] & $\tau \approx$ 80ms).

Model Component 3:- Air

Microclimate of uncovered skin

The microclimate next to in-vivo skin depends mainly on:-

- Air movement
- Air temperature
- Air humidity

For uncovered skin, air movements dominate, because moving air is MUCH more effective than diffusion for transporting heat and water vapour.
Model Component 3:- Air

Diffusion boundary layer concept

Physical Description:-
The air in contact with the skin is stationary because of viscous friction. Air velocity increases with distance from the skin surface.

Fluid Dynamics Model:-
2-layer approximation of Still Air + Moving Air. The still air layer is the diffusion boundary layer [1].

Skin Literature:-
The still air is Nilsson’s zone of diffusion next to uncovered skin [2].

Model Component 3:- Air

Boundary layer thickness

The properties of the air next to uncovered skin depend on air movements.

Typical calculations for a horizontal cylinder of 10 cm diameter [1].

**Model Component 3: Air**

Model for water vapour transport in air

The air next to the SC is modelled as a **diffusion boundary layer** of fixed thickness $L_A$.

The moving air beyond is modelled as a **vapour sink**, where ambient conditions of RH & temperature are maintained irrespective of vapour flux.

Note that the humidity at the SC surface increases with water vapour flux, whereas the humidity at the vapour sink is unaffected.
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Overview

Skin & Air
Heat exchange: SC surface is cooler than the body interior
Heat exchange: Air adjacent to the SC is warmer than ambient air
Evaporation of water from the SC surface
Continuity of flux density across the SC/air interface
Hygroscopic interaction between the SC surface and humid air (SC surface boundary condition)

Skin & Water
SC base is hydrated by contact with the LE (SC base boundary condition)
Water diffuses through the SC (TEWL)
Water affects SC properties (diffusion coefficient, swelling)
Component Interactions

Sorption/desorption in hygroscopic materials

The water content of hygroscopic materials depends on the humidity of the adjacent air. Measurements such as those below [1] establish a relationship between moisture content and relative humidity, known as the sorption isotherm.

Note the hysteresis – the moisture content also depends on the history of exposure to humid air. Hysteresis is ignored in the model at present.

Component Interactions

SC surface boundary condition

SC surface hydration is assumed to be determined by the hygroscopic interaction with the adjacent moist air [1]. The model uses a parameterization (- - -) of the sorption isotherm data of [2].

The SC surface is assumed to adapt rapidly to humidity changes, because only its top layer is exposed to air.

The bulk of the SC takes longer to adapt, because of the low mobility of water in the SC.

Note that skin surface RH is lower than ambient RH, because skin is warmer than ambient air.

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Example of parameters used in the calculations:

The parameter values in black are assumed constants. $D_{SC}$ is the unknown. It is determined by iteration. The aim of the iteration is to satisfy the sorption relationship between $c_2$ and $RH_2$ at the SC surface.

For a given $J_W$, $c_2$ increases as $D_{SC}$ increases.

For a given $J_V (=J_W)$, $RH_2$ depends on the air-side parameters $\theta_2$, $L_A$, $D_{VA}$, $\theta_3$ & $RH_3$.

Once determined, you can hold $D_{SC}$ constant & explore changes of $J$ with $\theta_2$, $L_A$, $RH_3$, etc.
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Example Calculations 1:- Intact Skin
Baseline TEWL vs SC surface temperature

Caused by the temperature-dependence of SC surface RH, via the sorption isotherm.
This is not a good test of the theory, because the Halkier-Sorensen effect has medical origin.

Example Calculations 1:-- Intact Skin

Baseline TEWL vs RH

The calculated trend of decreasing TEWL with increasing RH is contradicted by the experimental evidence of [1], for example. This is a well known problem with models using a constant diffusion coefficient.

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Example Calculations 2:- Skin Stripping

Tape stripping method

Tape stripping is a minimally invasive technique where adhesive tape is used to remove successive layers of SC, as illustrated on the left. The photo below shows what a tape looks like after a strip.

For each strip you can measure:-
The quantity of SC removed → Mean thickness of SC removed
The concentration of actives → Penetration
Transepidermal water loss (TEWL) → Barrier property
Etc.
Example Calculations 2:- Skin Stripping

Example measurements of TEWL changes during stripping

TEWL increases as more SC layers are removed.

The reciprocal ($1/\text{TEWL}$) is often found to decrease ~linearly with the cumulative thickness of SC removed. The intercept with the horizontal axis gives the thickness of the intact SC [2].

Non-linear ($1/\text{TEWL}$) plots are sometimes observed.


Example Calculations 2:- Skin Stripping

Current model: Kalia, Pirot & Guy

The model of Kalia, Pirot & Guy [1] uses the hydration profile illustrated top left. Stripping is described by including the thickness of SC removed ($\Lambda$) in Fick’s first law, i.e.

$$J = \frac{TEWL}{D \cdot K \cdot \Delta c} \cdot \frac{L - \Lambda}{(L - \Lambda)}$$

This analysis gives a linear ($1/TEWL$) plot, with a $z$-axis intercept equal to the thickness $L$ of the intact SC.

Our hydration profile is shown bottom left. No partition at the LE/SC interface, but including a hygroscopic interaction at the SC/Air interface.

Example Calculations 2: Skin Stripping

Model applied to the stripping process

An exaggerated strip thickness of 2µm is assumed here, to illustrate the stripping process.

Point 1: Before stripping
Steady-state surface hydration, hydration gradient & TEWL.

Point 2: Immediately after stripping
The surface hydration is elevated, therefore the vapour flux has increased. However, the SC hydration gradient is unchanged, therefore the TEWL is unchanged.

Point 3: After a new steady-state is reached
Surface hydration has decreased but remains above Point 1. The SC hydration gradient is now steeper than before, therefore the TEWL has increased. Vapour flux and TEWL are now equal again.
Example Calculations 2:- Skin Stripping

Steady-state hydration profiles

This shows steady-state hydration profiles with 0, 2, 4, ... microns of SC removed. Note the increase of steady-state surface hydration (the end-points of the blue lines) as more layers are removed.
Example Calculations 2:- Skin Stripping

Transient & steady-state SC surface hydration

This shows calculated transient & steady-state SC surface hydration with 0, 1, 2, ... microns of SC removed. The excess hydration immediately after a strip is subsequently lost by evaporation from the SC surface (=Skin Surface Water Loss, SSWL).
Example Calculations 2:– Skin Stripping

(1/TEWL) dependence on SC thickness removed

Notes:–
1. The values plotted are steady-state TEWL
2. The intercept gives intact SC thickness = 15.14 µm (true value = 15.0 µm).
3. The last point deviates slightly from the trend line
4. The agreement with the Kalia, Pirot & Guy model [1] is remarkable

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Additive swelling model

SC swelling is assumed to be additive, where the volume of hydrated SC is given by the sum of the volumes of dry SC and water of hydration. With this assumption, for isotropic swelling,

$$\frac{\Delta L}{L_{DRY}} = \frac{c}{3(\rho_w - c)}$$

where $\Delta L$ is the hydration-dependent swelling, $L_{DRY}$ is the thickness of dry SC, $\rho_w$ is the density of water and $c$ is the concentration of water in the SC.

Unidirectional swelling (in thickness only) is three times larger.

Swelling is easily incorporated into the model, by dividing the SC into a number of layers.
More Model Components:– Swelling & $D_{sc}(c)$

Skin hydration profile

Steady-state hydration depth profiles measured using confocal Raman spectroscopy give information about water mobility in the SC and viable epidermis. Shown here are example profiles measured on untreated volar forearm skin in-vivo.

Hydration depth profiles relate to TEWL via Fick’s first law of diffusion. The slope at any point is inversely proportional to the diffusion coefficient, $D_{sc}$.

$$D_{sc} = \frac{-J}{dc/dz}$$

Figure adapted from:–
More Model Components: -  Swelling & $D_{SC}(c)$

Linear & exponential hydration profiles

1. A **linear profile** (ie constant $D_{SC}$).

2. An **exponential profile**

$$c(z) = c_{\text{max}} - \Delta c \cdot \exp\left(\frac{-z}{z_0}\right)$$

for which

$$D_{SC}(c) = \frac{k}{(c_{\text{max}} - c)}$$

These profiles are compared with a confocal Raman profile in the above figure. The deviation near the SC surface may be due to instrumental effects such as occlusion, spacial resolution or a non-planar SC surface.

Raman data provided by River Diagnostics BV, Rotterdam, The Netherlands.
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The calculated trend of decreasing TEWL with increasing ambient RH is contradicted by the experimental evidence of [1], for example. The inclusion of a hydration-dependent diffusion coefficient in the exponential model goes some way towards solving this problem, but currently not far enough.

Example Calculations 3
Swelling v ambient RH

The calculated thickness change with ambient RH looks plausible.
Example Calculations 3

Skin stripping: - Exponential model

These calculations use an intact in-vivo SC thickness of 15 µm with a baseline TEWL of 10 gm⁻² h⁻¹.

The reciprocal TEWL plots are ~linear for ~1st half of SC thickness removed. However, these initial gradients do not extrapolate to the correct SC thickness. In particular, with finite SC swelling, thickness removed depends on hydration.
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The work to develop a realistic model of the SC barrier is ongoing. Once the steady-state model performs satisfactorily, the next step is to calculate time-dependent properties, to enable questions about rates of change to be answered.

For the work to date, the main conclusions are:-

- Both linear & exponential models predict the wrong TEWL v ambient RH dependence.
- For the linear model, skin stripping 1/TEWL plots are nearly linear.
- For the exponential model, the initial slope of the 1/TEWL curve is ~linear. However, extrapolations from this initial slope lead to overestimates of SC thickness.
- Swelling causes a problem with SC thickness determination in skin stripping, because of differences between the in-vivo & in-vitro hydration of the removed SC.
- Work on a more realistic hydration depth profile & associated $D_{sc}(c)$ is in progress.