Spectrum on skin

Jonathan Hadgraft
&
Majella Lane

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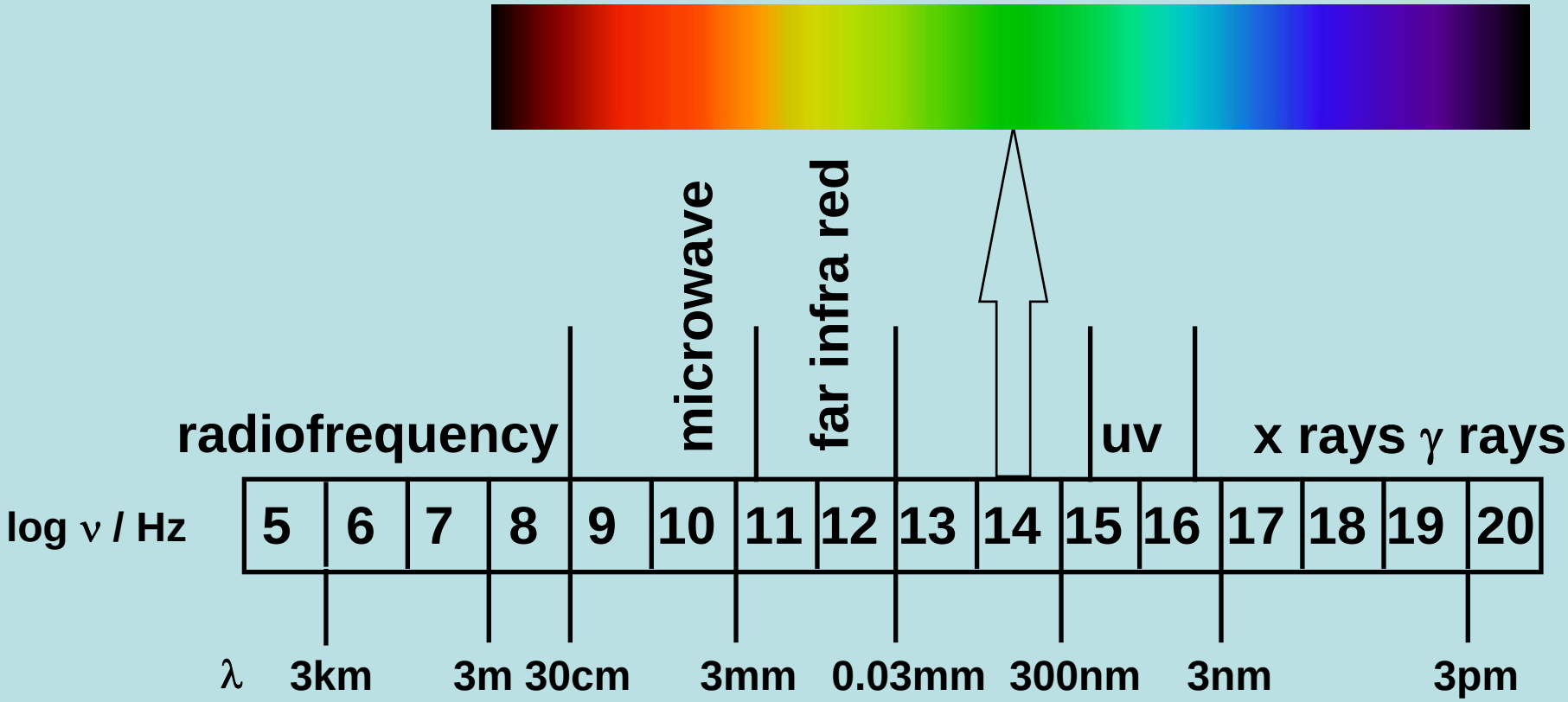
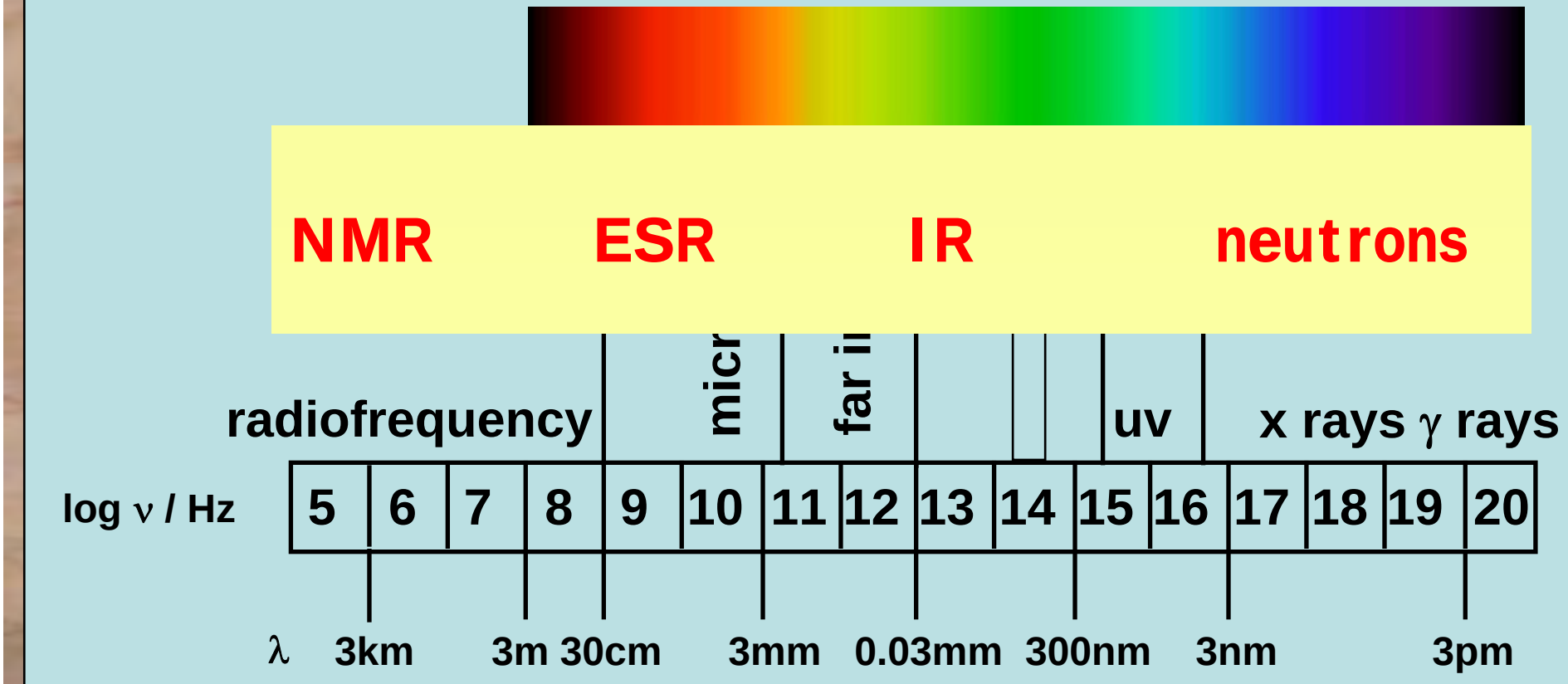

radiofrequency
microwave
far infra red
uv
x rays γ rays
log ν / Hz
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
λ 3km 3m 30cm 3mm 0.03mm 300nm 3nm 3pm


NMR
ESR
IR
neutrons
radiofrequency
micr
far ir
uv
x rays γ rays
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3km
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0.03mm
300nm
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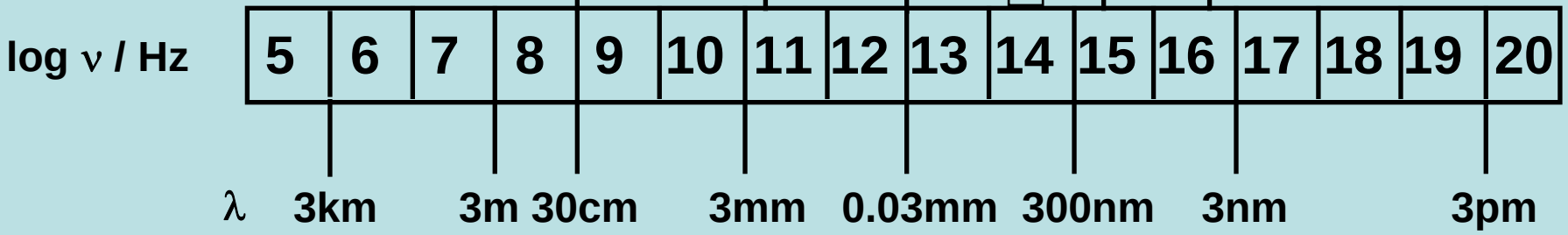
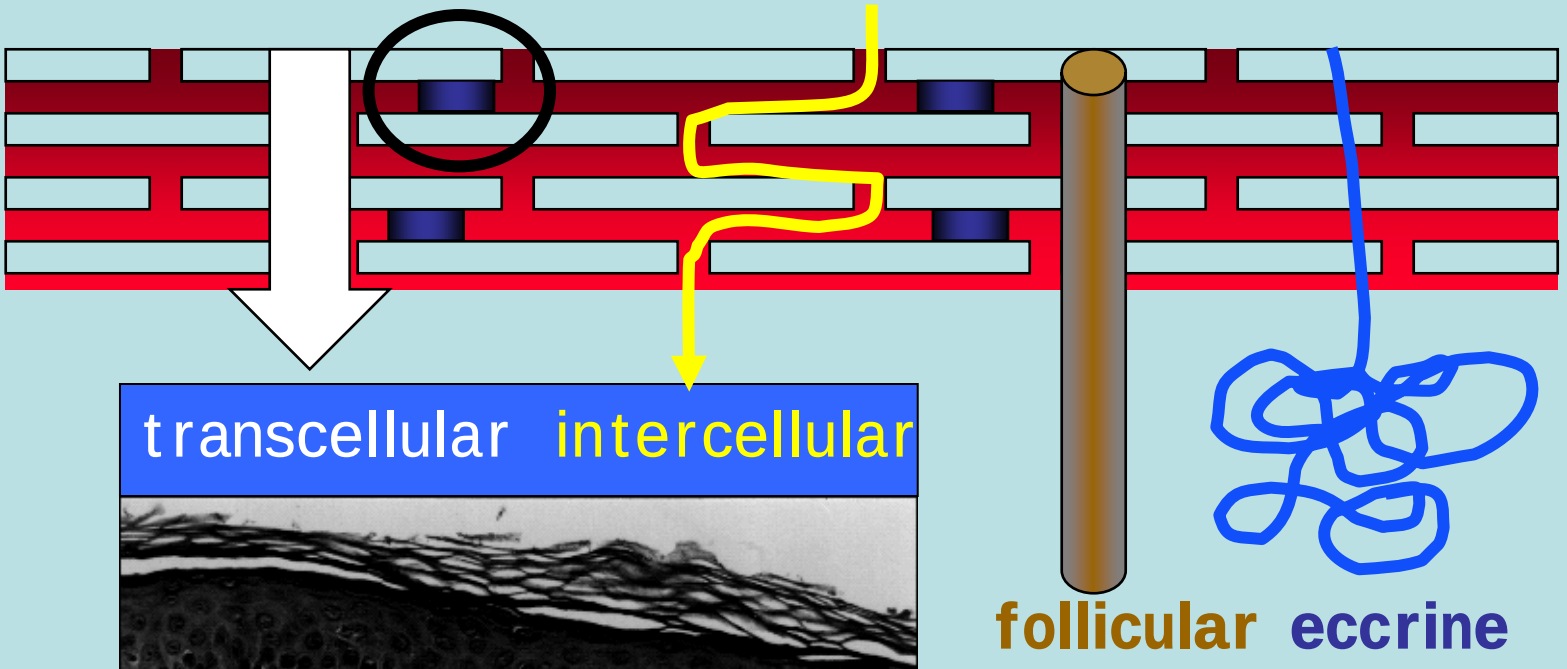
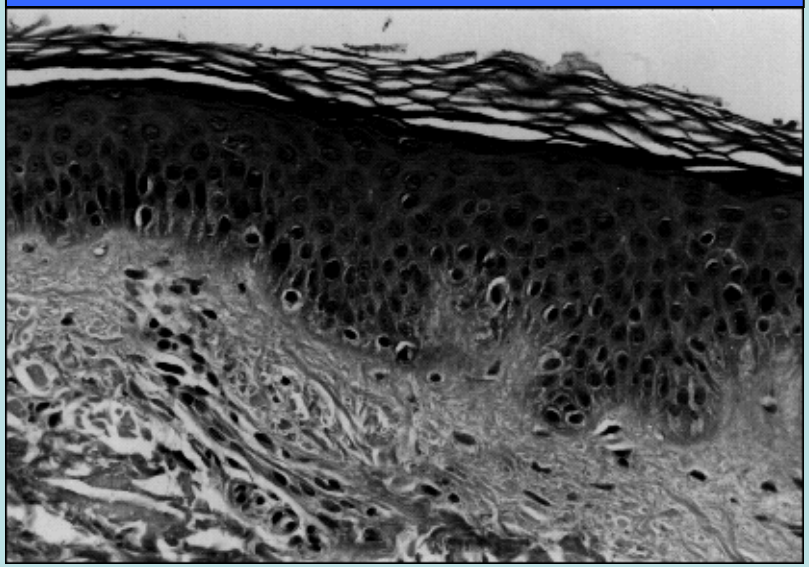

radiofrequency
microwave
far infra red
uv
x rays γ rays
log ν / Hz
5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
λ
3km
3m
30cm
3mm
0.03mm
300nm
3nm
3pm

Skin structure

Major barrier is in stratum corneum (15 µm thick)



transcellular intercellular

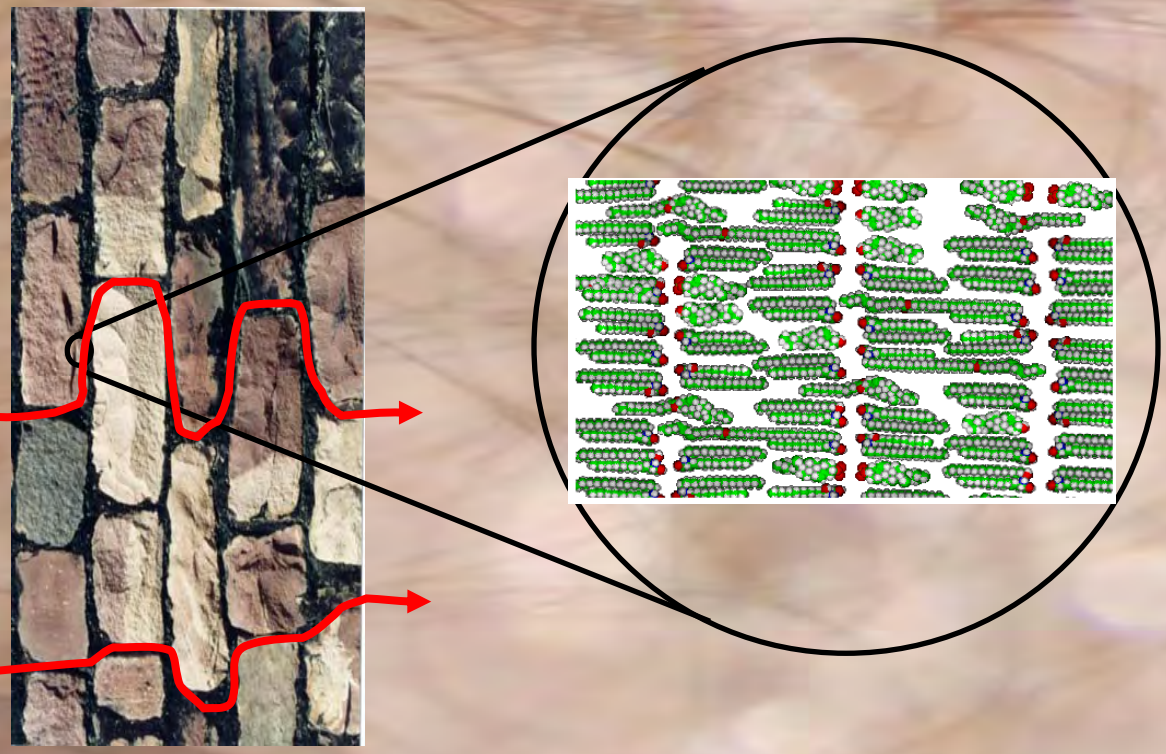


follicular eccrine

Role of lipids

Corneodesmosomes

Composition & structure of intercellular channels

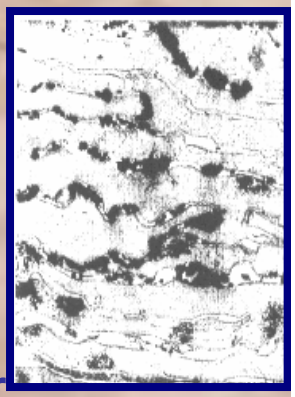


Michaels et al.
1975

Albery
& Hadgraft

Elias

Boddé



Potts
& Francoeur

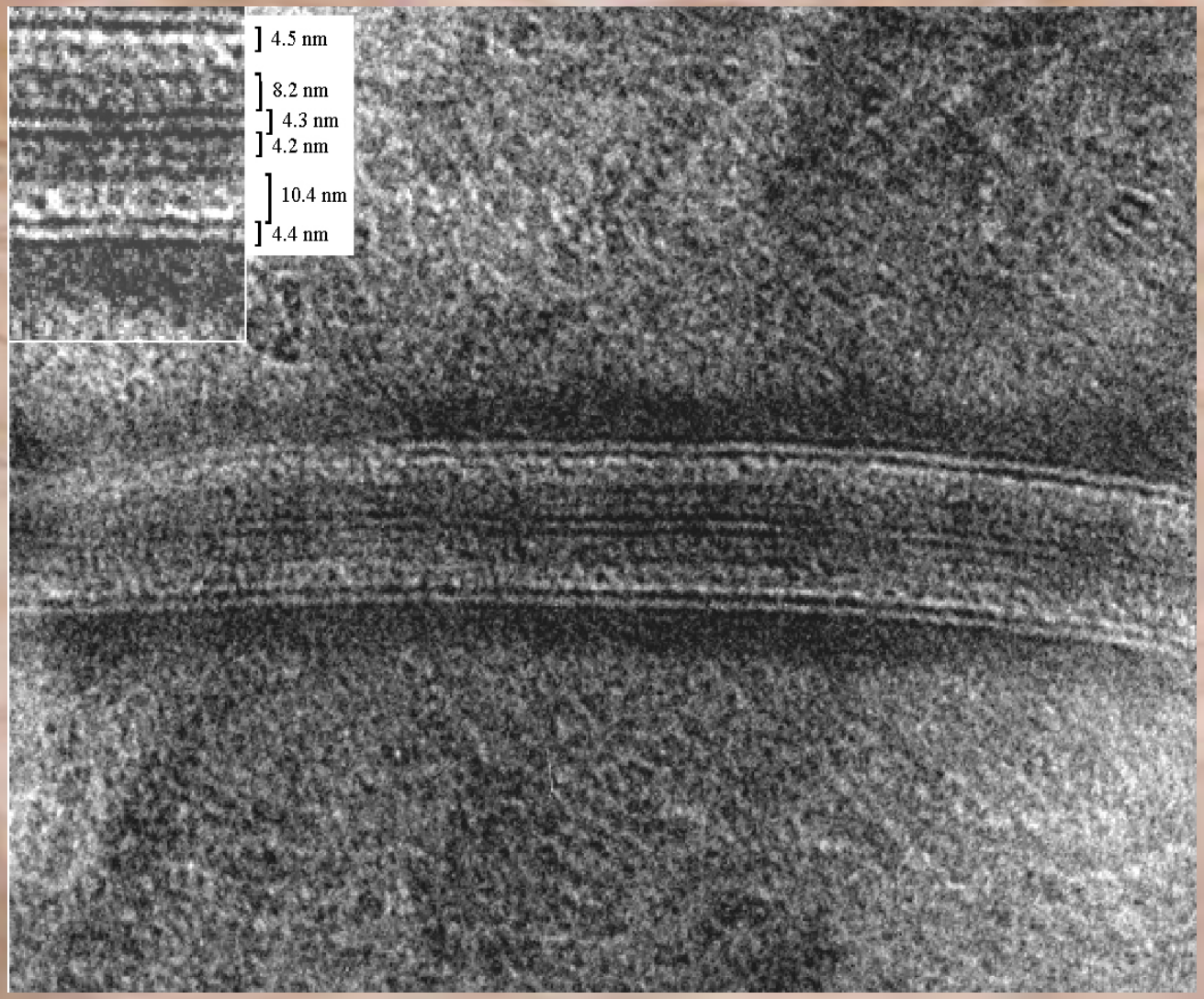
Talreja et al.

ceramides (50%)
cholesterol (25%)

cholesteryl sulphate (5%)
free fatty acids (15%)

Boddé H. et al Int. J. Pharm. 53 (1989) 13-24

Cryo-sectioning and cryo-TEM



Freezing 20 ms

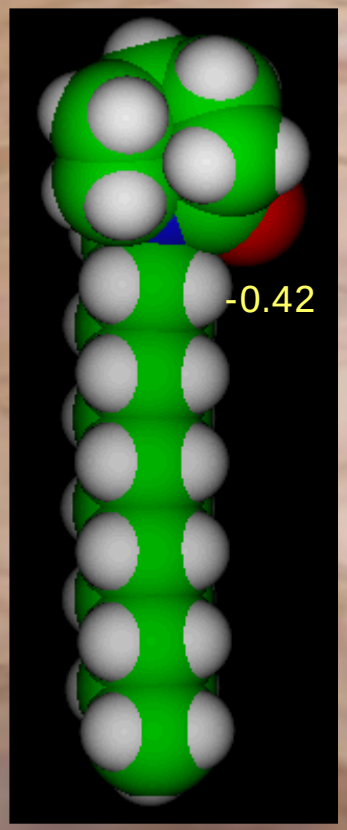
-180C

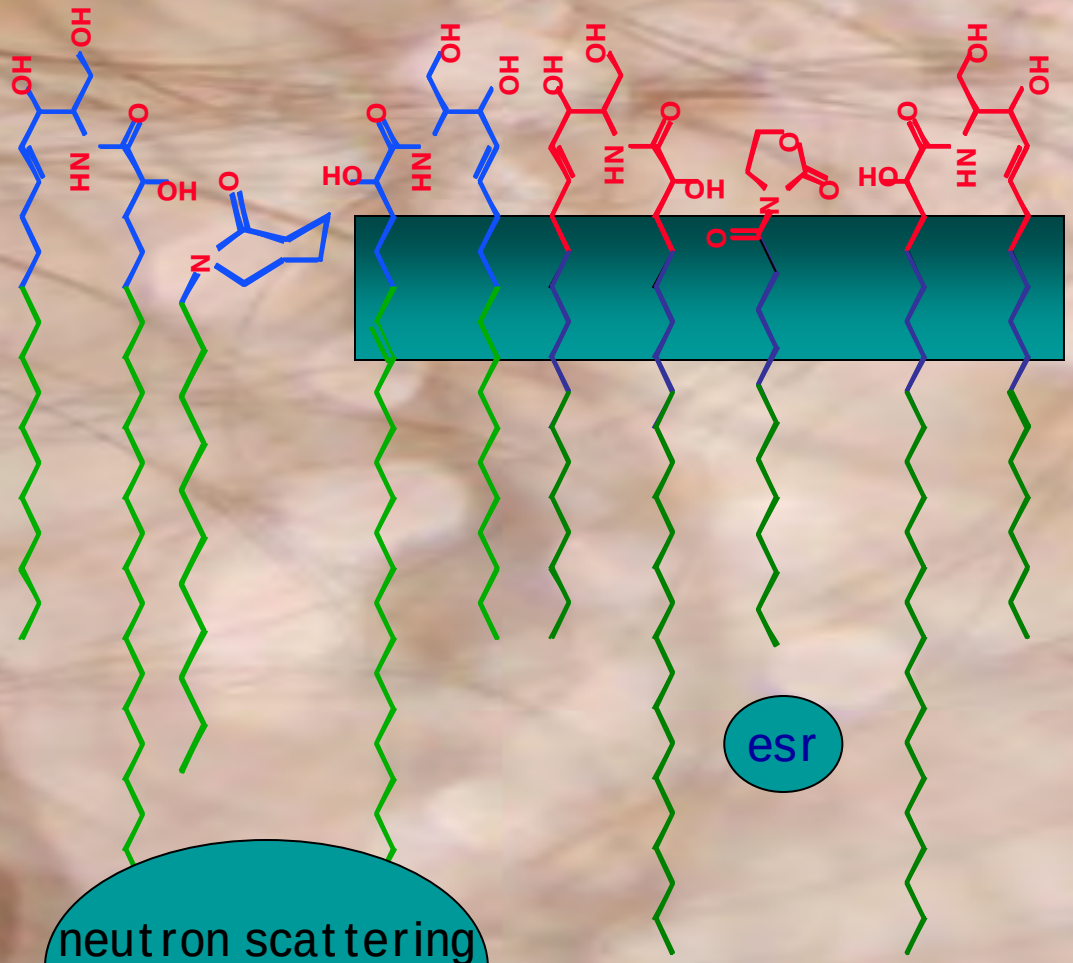
50 – 100 nm thick vitreous section

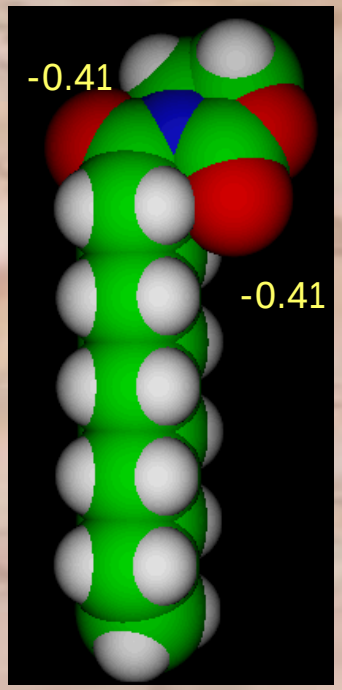
No cryo protectants

Lars Norlen

Hydrogen bonding with ceramides







neutron scattering & monolayers

Hadgraft, J. et al. Int. J. Pharm. (1997) 141, 17-25

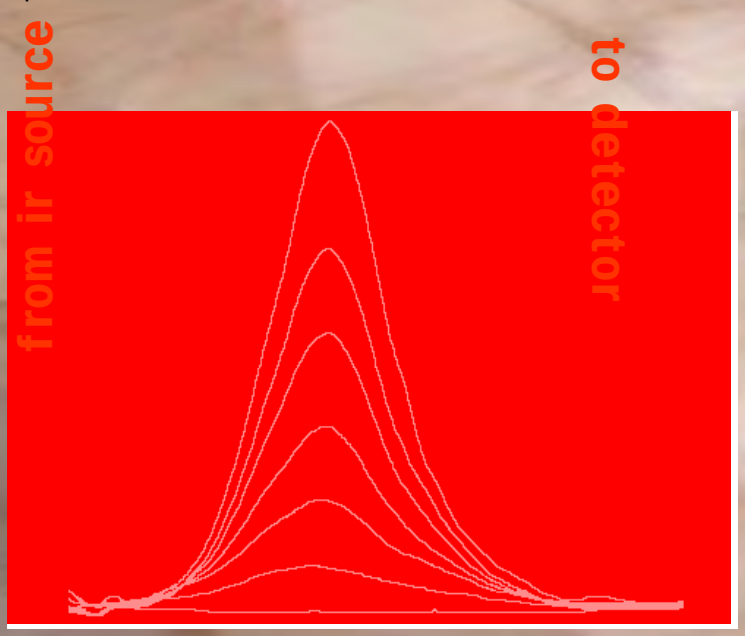
Gay, C.L. et al. (1989) Int J. Pharm. 49, 39-45

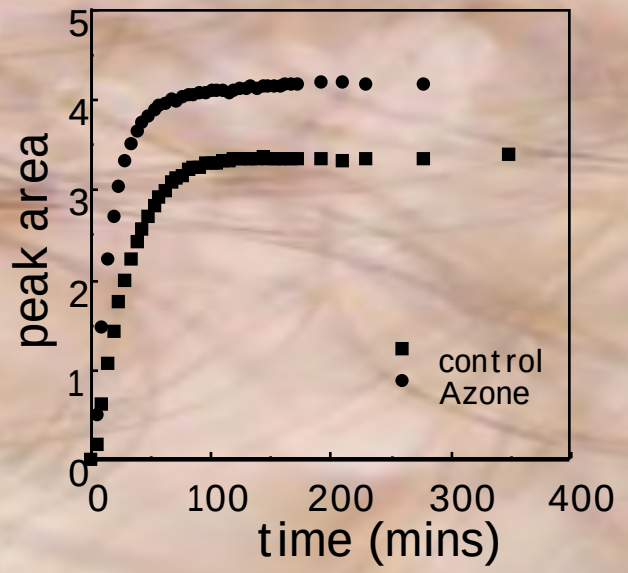
Biophysical techniques

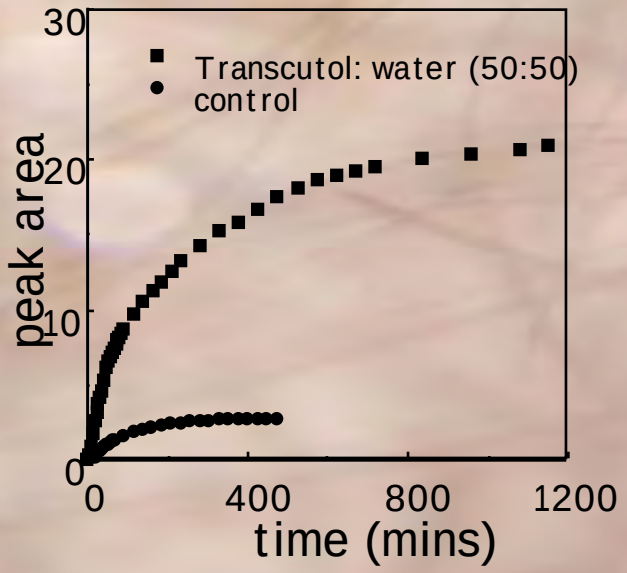
- Infra red
  - Diffusion studies
  - Imaging
  - Diagnosis
- NMR
- OTTER
- TEWL
- MS

Fourier Transform Infra Red

Diffusion studies



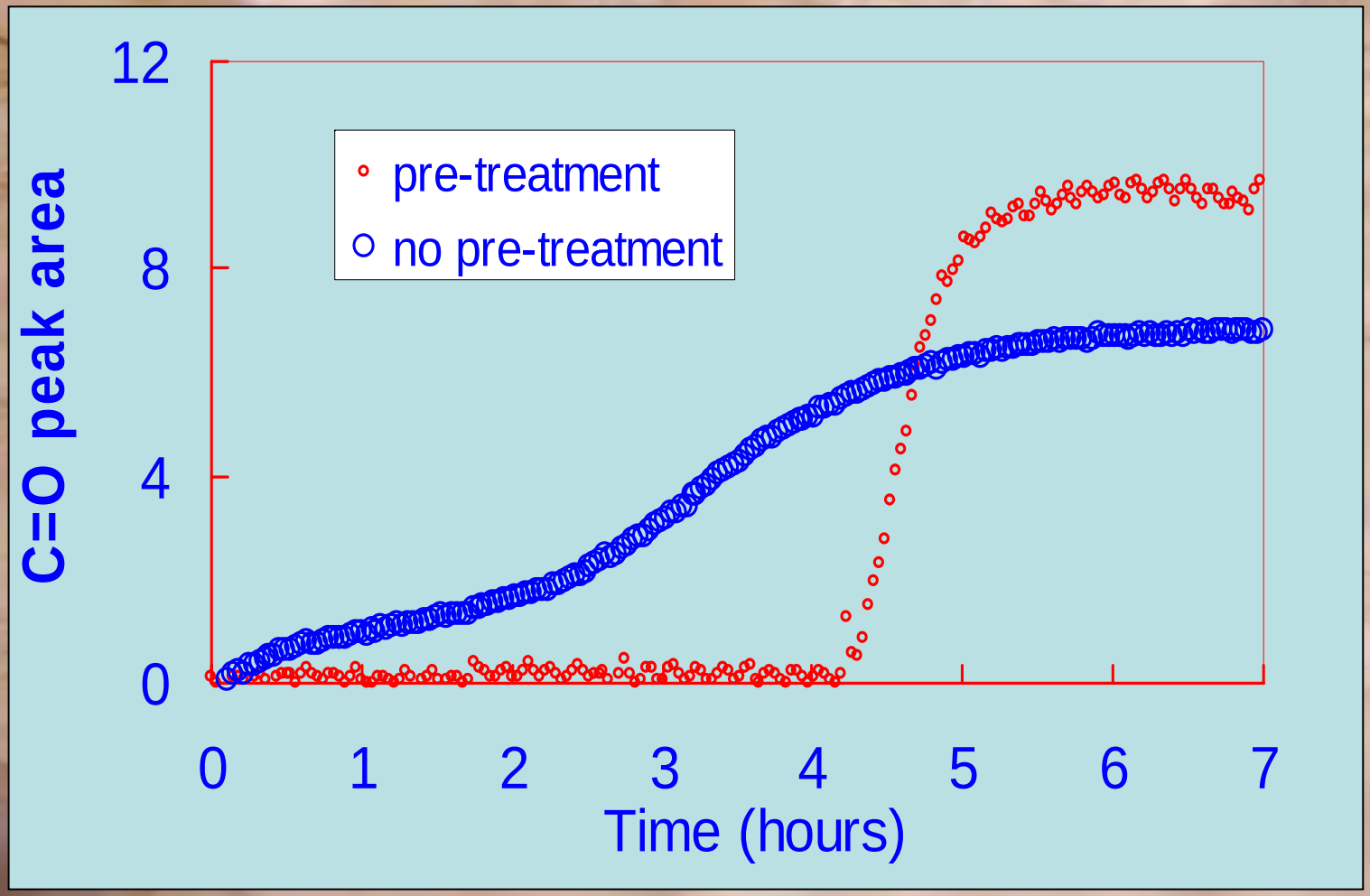




Harrison, J. et al. Pharm. Res. (1996) 13, 542-546

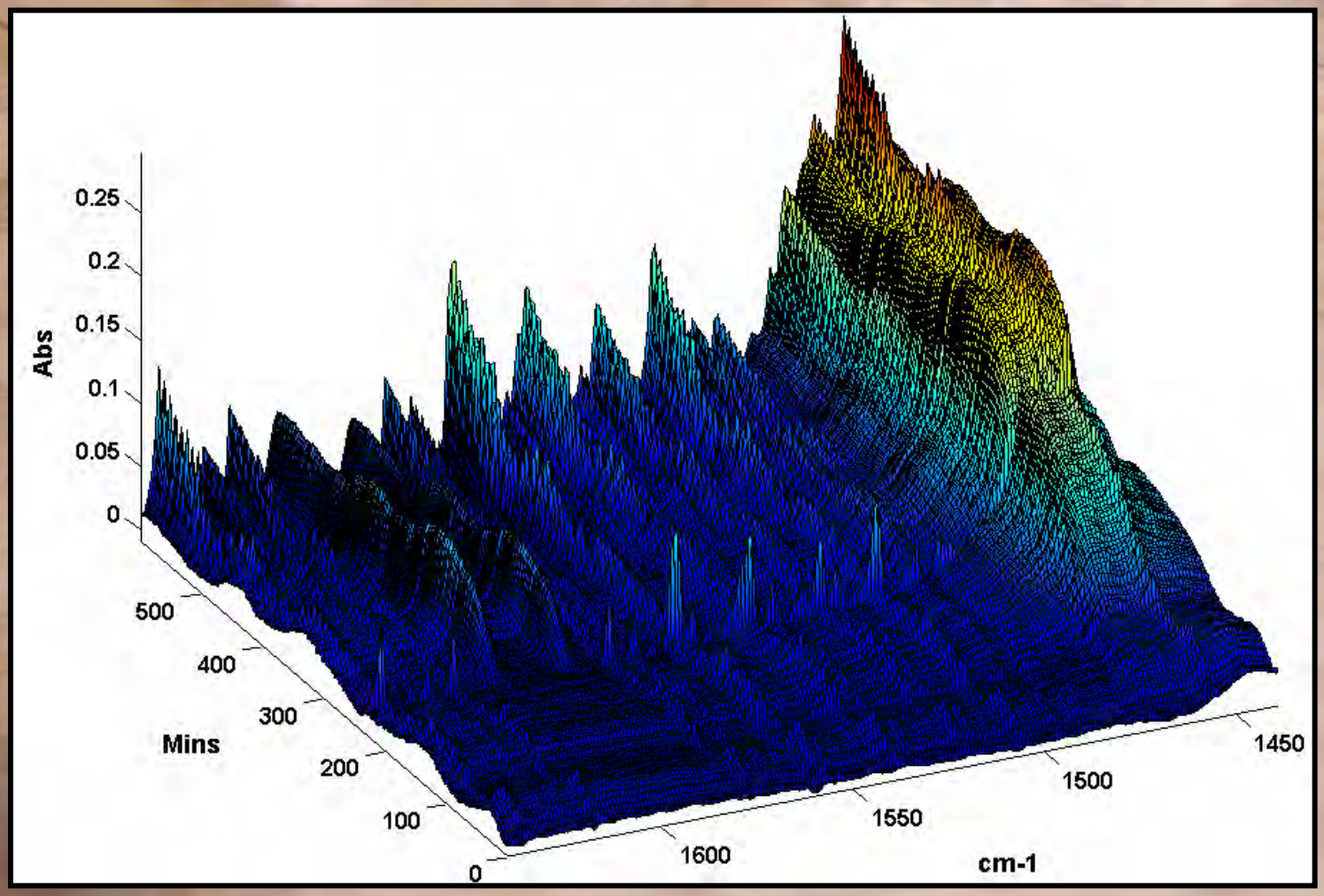
ATR FTIR benzoic acid – octanol:

silicone membrane

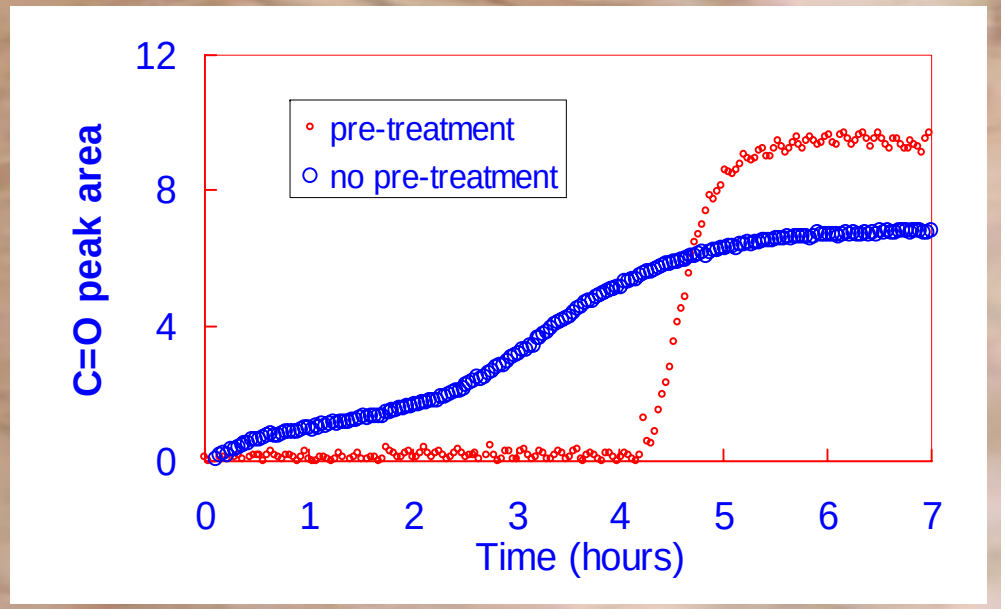


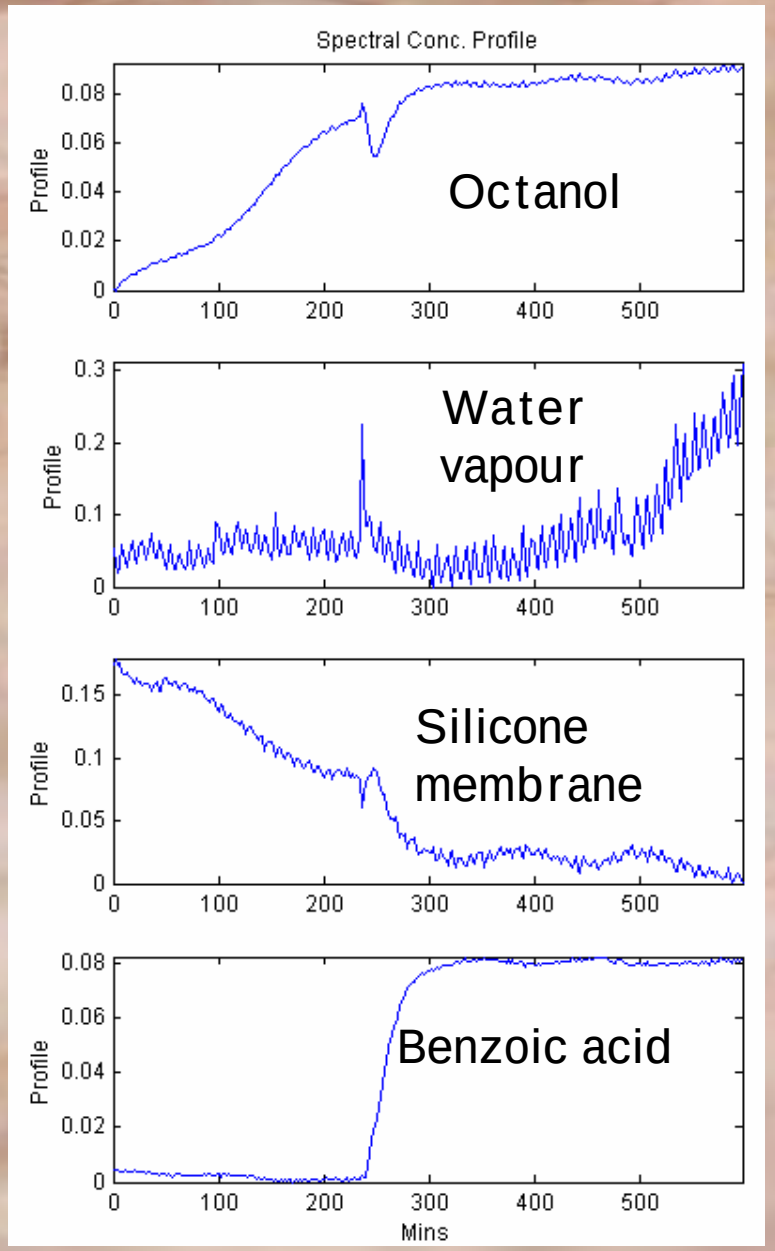
Dias, Hadgraft, Raghavan & Tetteh. J. Pharm. Sci. 93 (2004) 186-196

Something for nothing: chemometrics



InSight

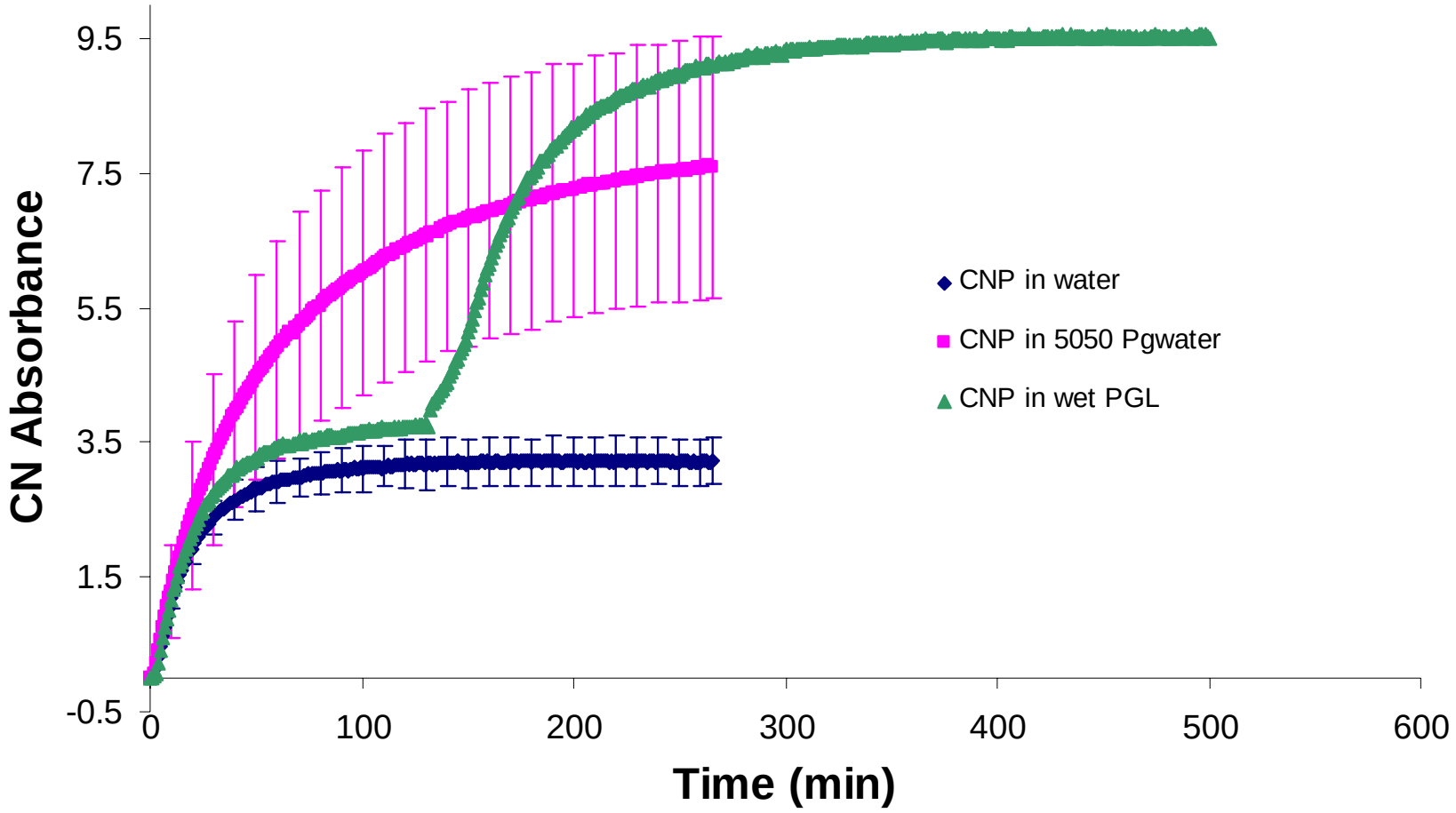




Software enables separation of methyl and ethyl paraben

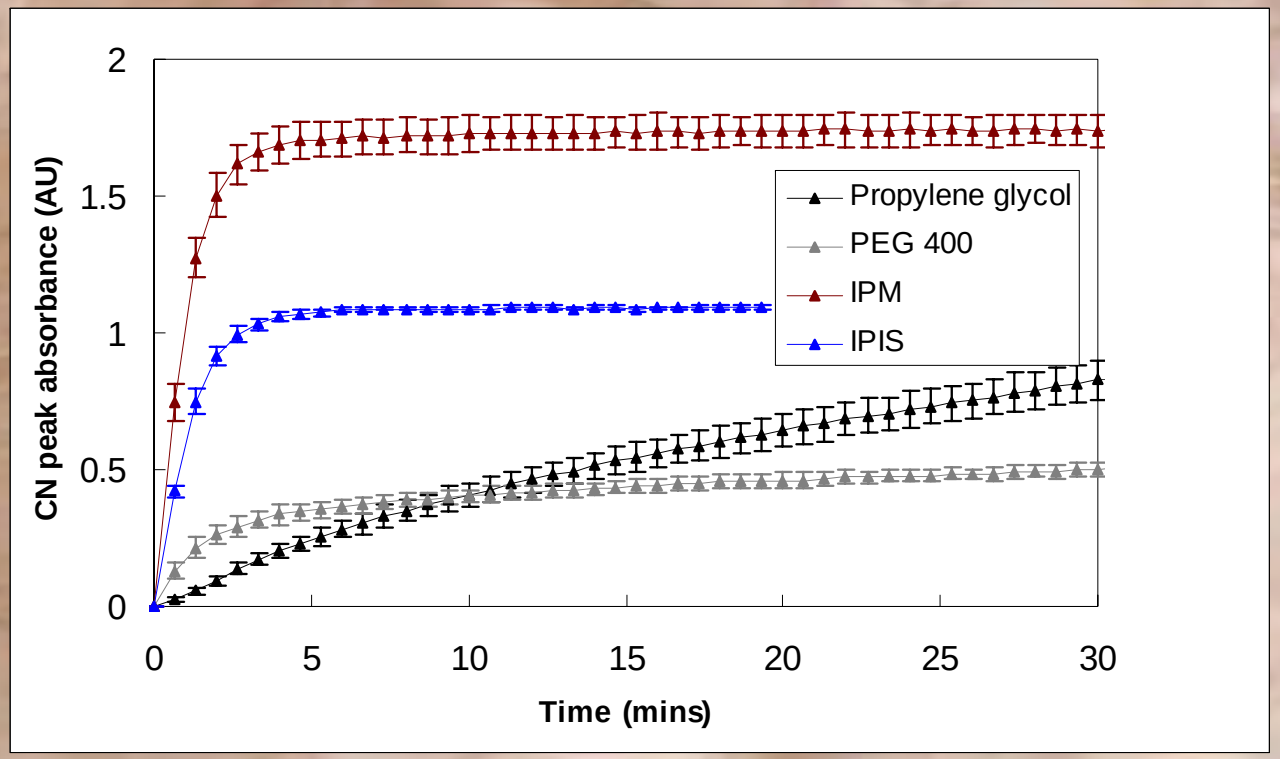
Dias, Hadgraft, Raghavan & Tetteh. J. Pharm. Sci. 93 (2004) 186-196

Russeau

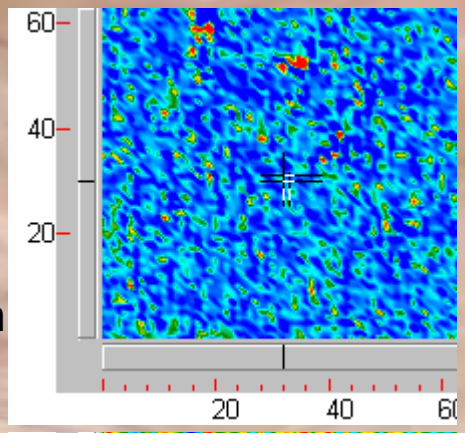


McAuley, Lane

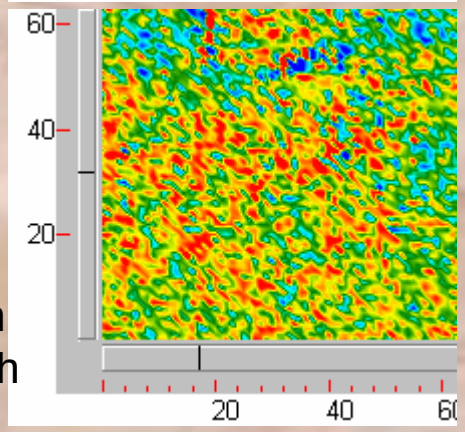
Silicone membrane: pools?



ipm

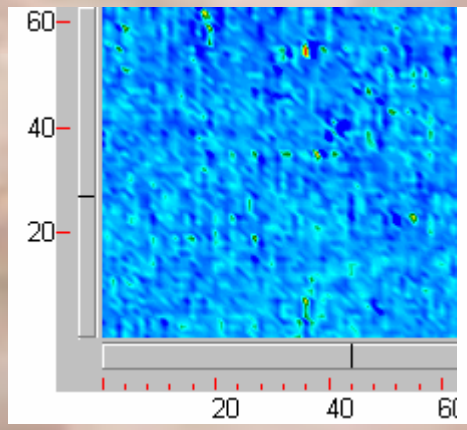


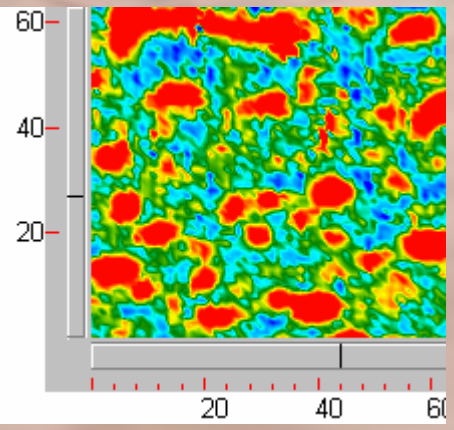
ipm
21 h



Profiles analysed using Scientist and solutions to Fick's Laws, modelling

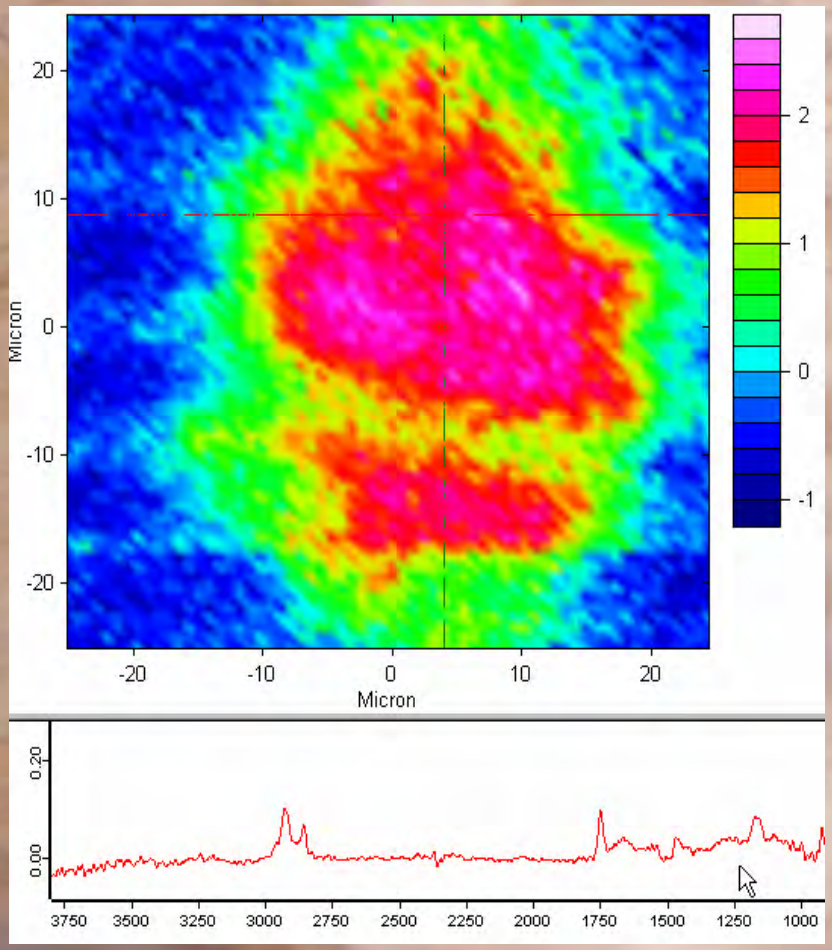
pg

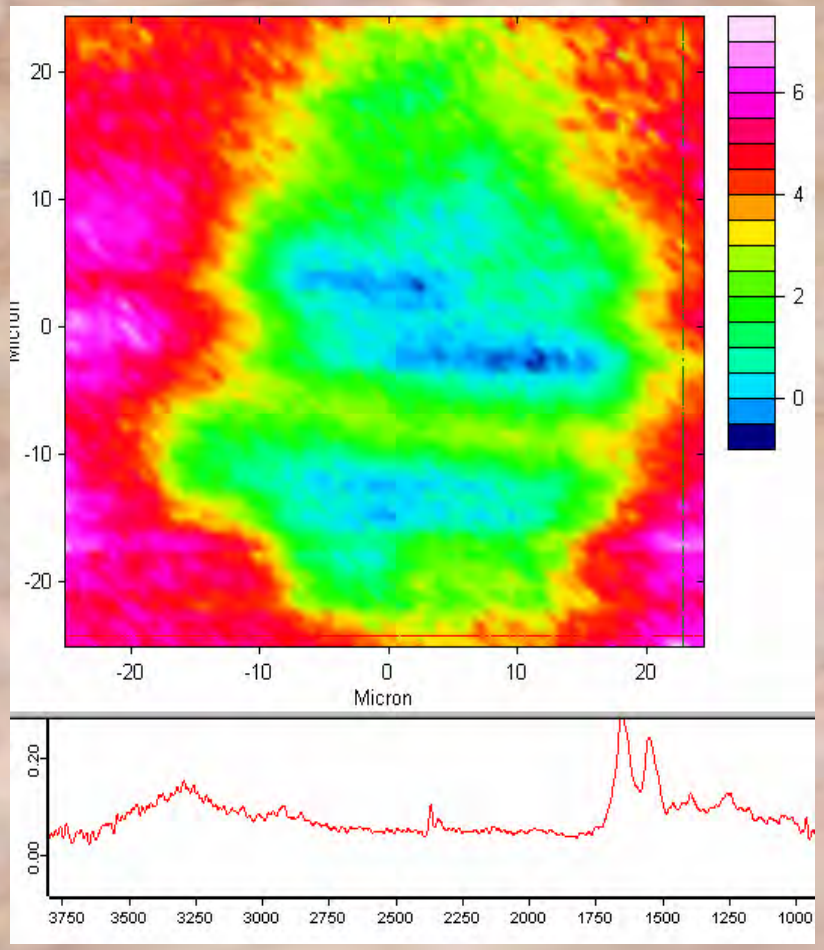




Kazarian, McAuley, Lad, Lane

Infra red imaging: chemometrics



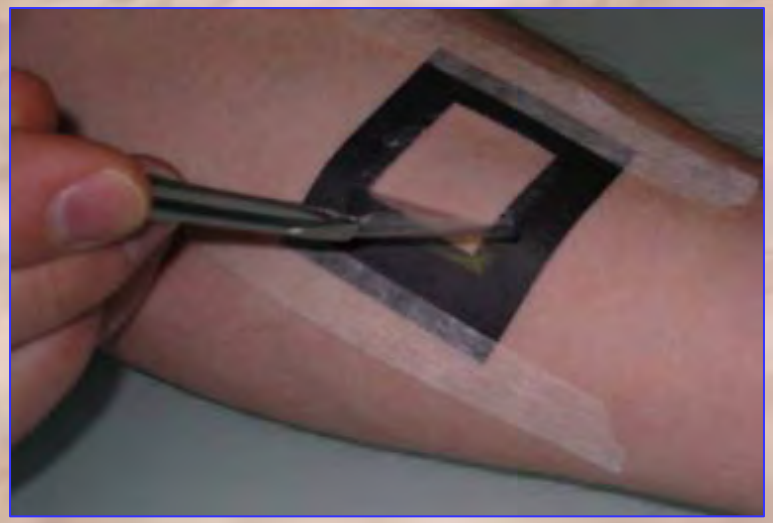


50 x 50 µm

Kazarian

Sampling the skin: tape stripping

Determination of drug concentration in the stratum corneum (SC) by sequential removal of thin layers of SC at the same site with adhesive tape.

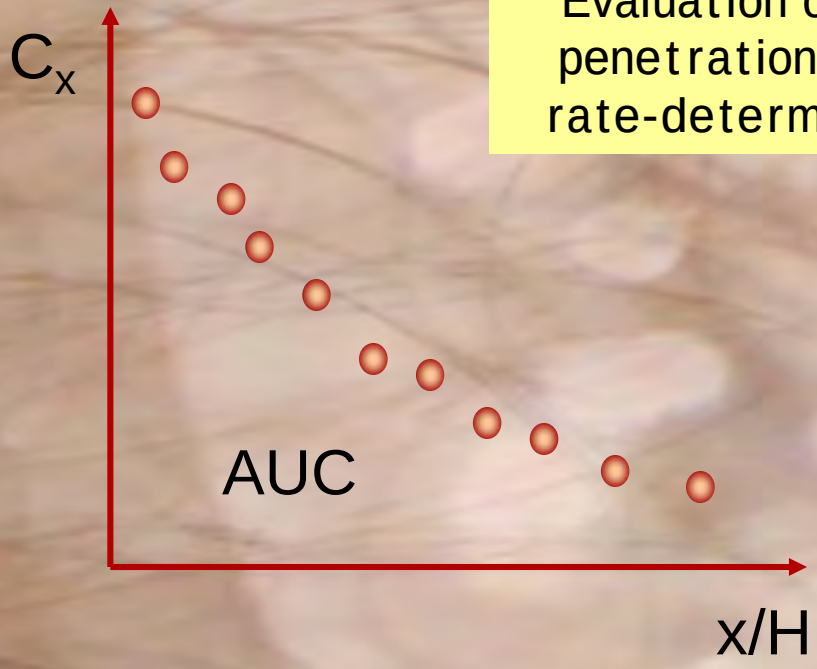


Industrial – University collaboration

Guy et al.

Distribution profile of active across the stratum corneum (SC)

Evaluation of the rate and extent of active penetration into the *stratum corneum* - the rate-determining barrier to skin permeation.



Measure drug concentration profile as a function of position in the SC

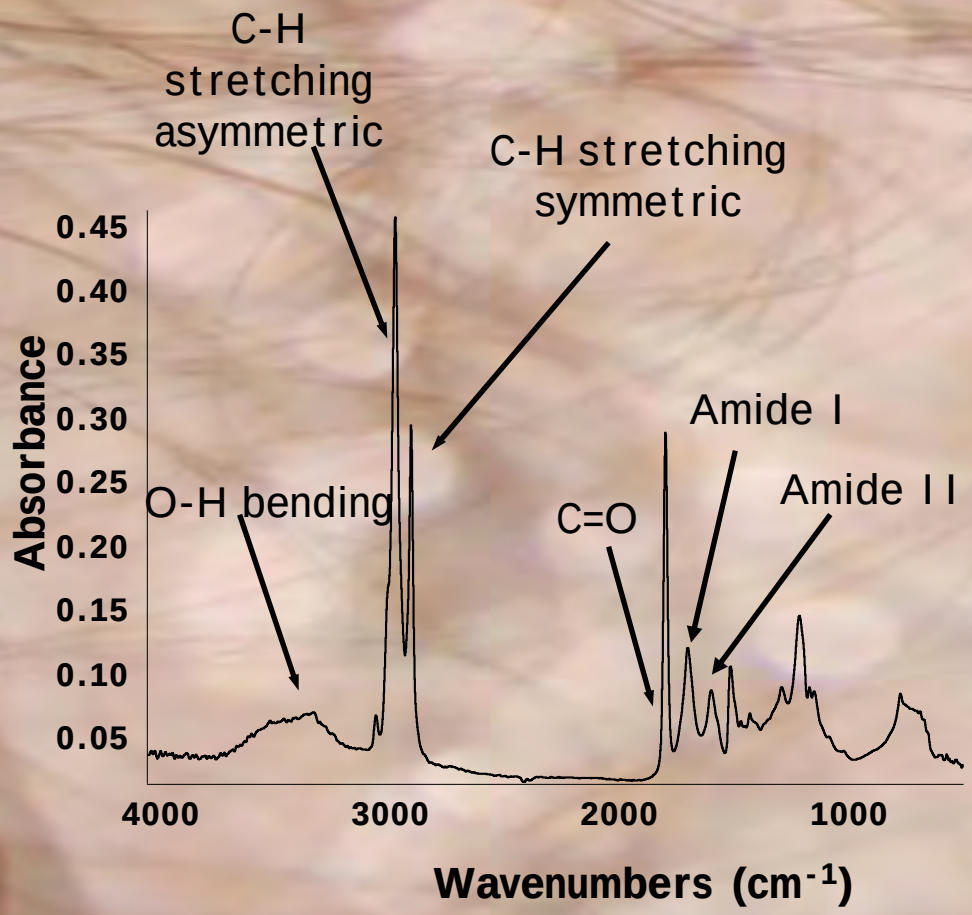
Required: (i) amount on each strip, (ii) penetration depth into SC

Guy et al.

Lipid extraction – lipid disorder

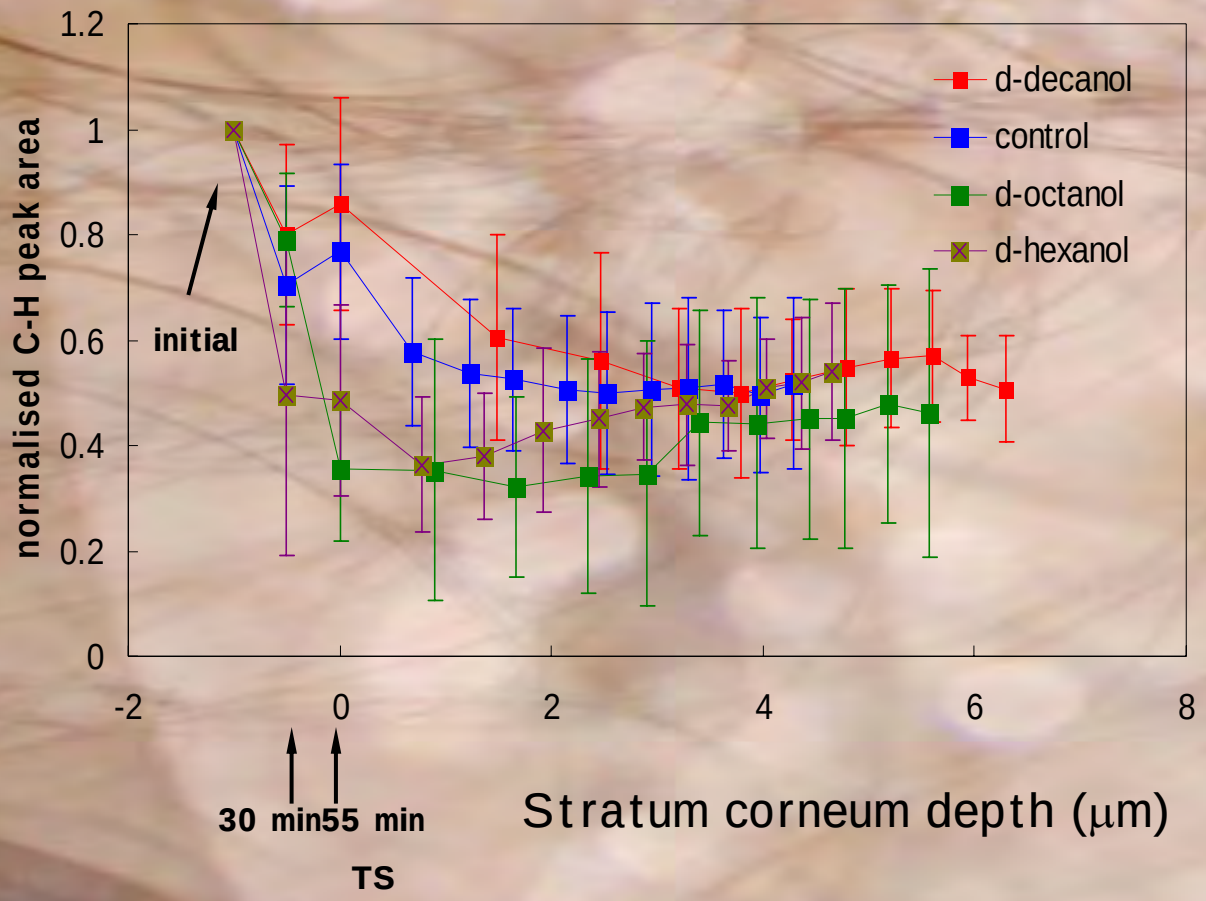
Peak height (area)

Peak shift



Dias, Guy, Hadgraft. Lane

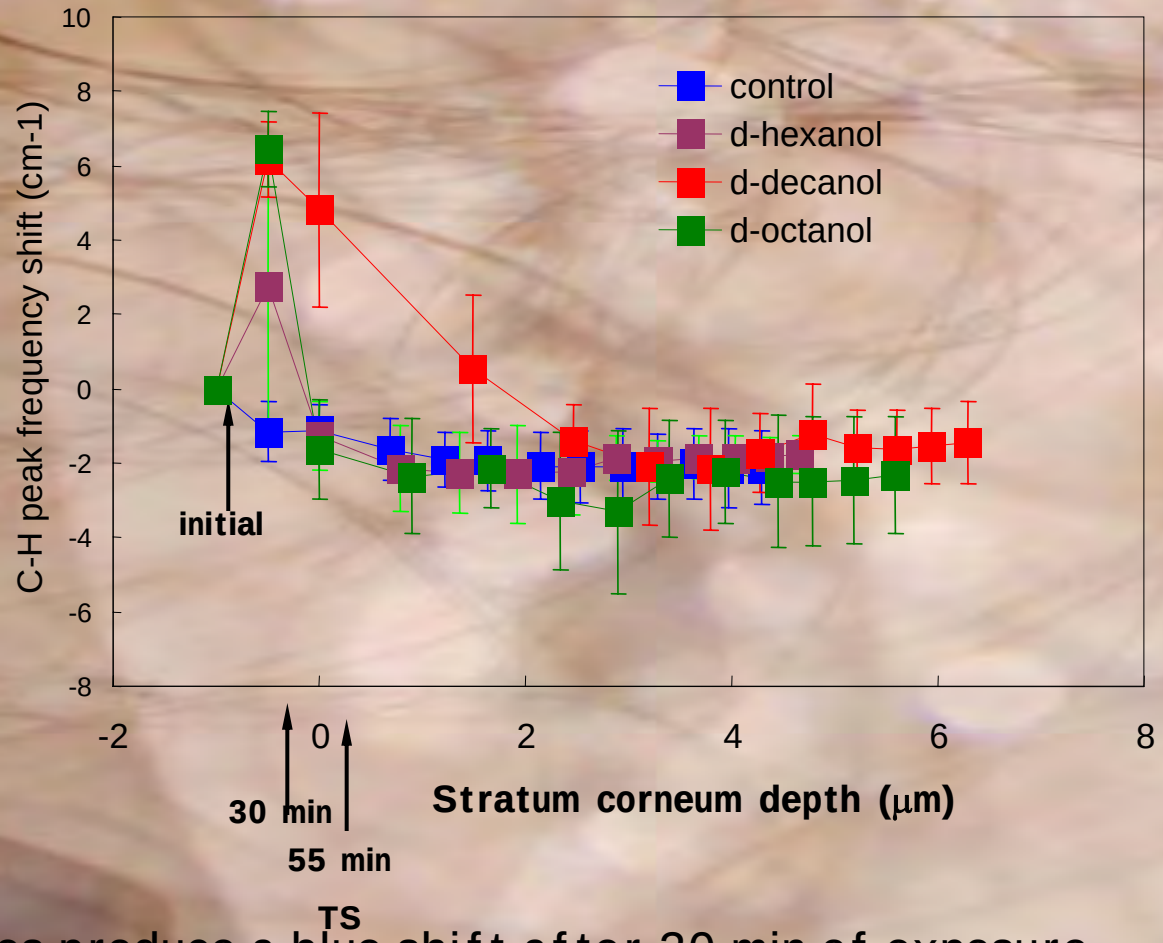
Lipid extraction (peak area)



- Both D-octanol and D-hexanol extract the lipids after 55 min of exposure
- D-decanol does not extract the SC lipids

Dias, Guy, Hadgraft. Lane

Lipid disorder (peak shift)

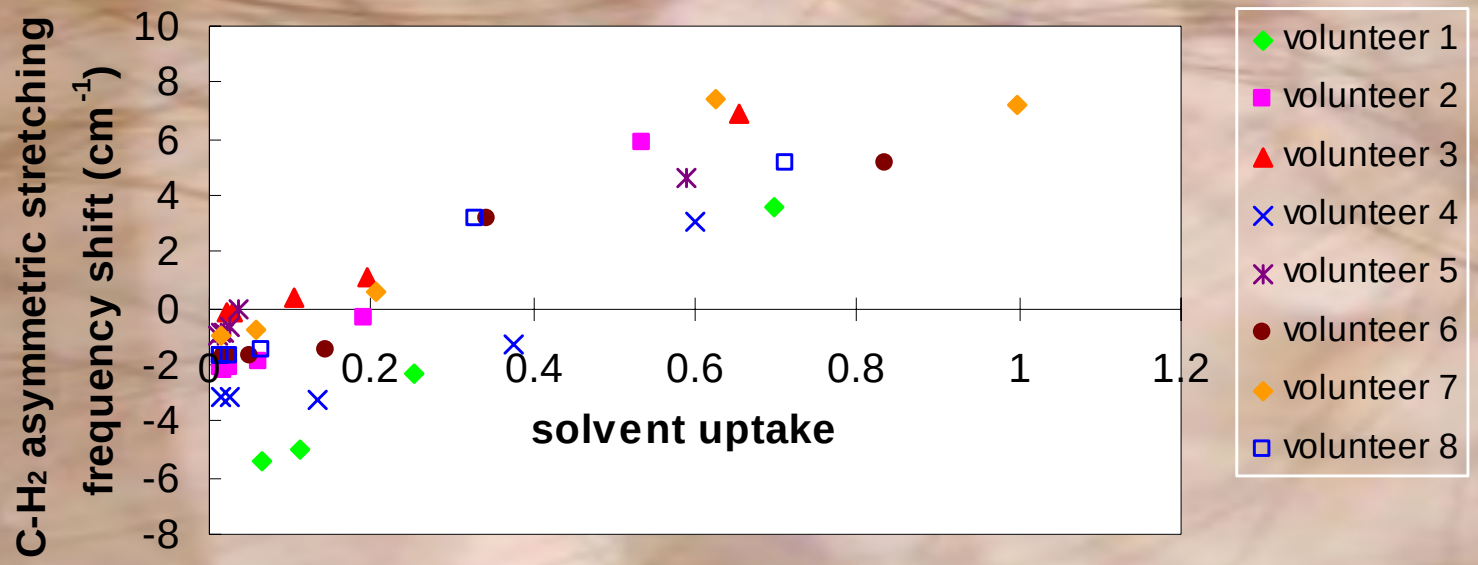


All vehicles produce a blue shift after 30 min of exposure

D-decanol disordering effect is maintained for 55 min and in ~2 μm of the SC.

Dias, Guy, Hadgraft. Lane

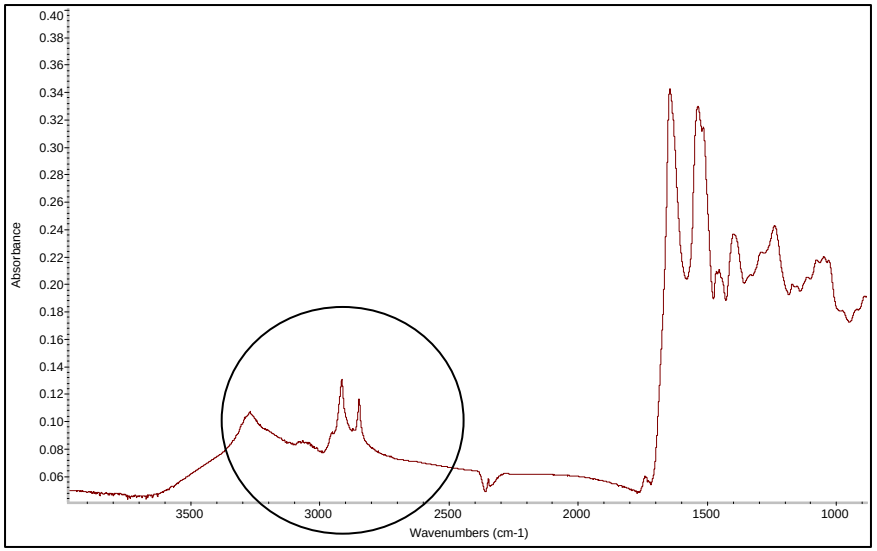
Solvent uptake (peak area) and lipid disorder (peak shift)

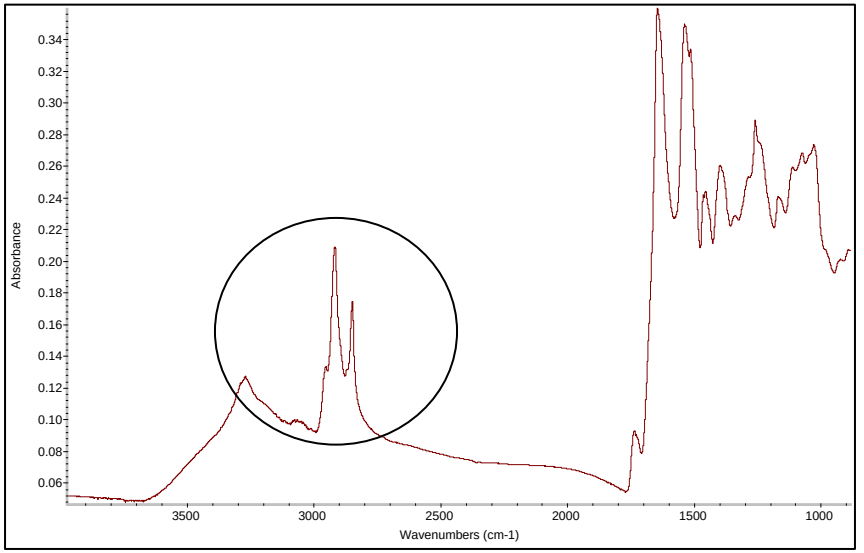


Relationship between the solvent uptake (normalised C-D peak area) and the frequency shift for each volunteer, after exposure to D-decanol for 30 min, 55 min and tape stripping.

Dias, Guy, Hadgraft. Lane

Diagnostics?
Psoriasis UVA treatment





Pre-treatment
Peak areas

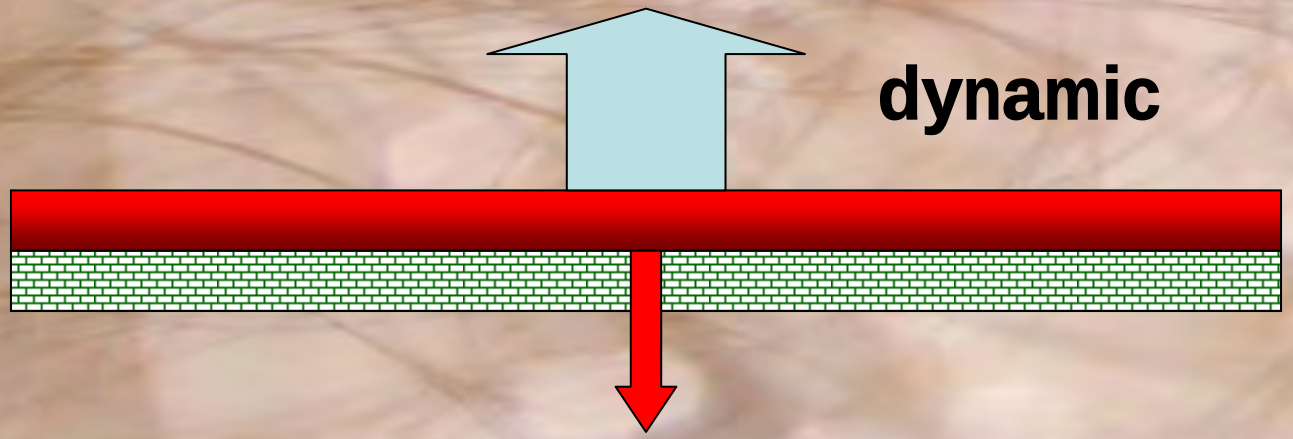
- C-H asymmetric = 0.07
- C-H symmetric = 0.03

Post-treatment
Peak areas

- C-H asymmetric = 0.18
- C-H symmetric = 0.07

Watkinson & Burgess 2002.

Clinical dosing: 2 mg/cm^2

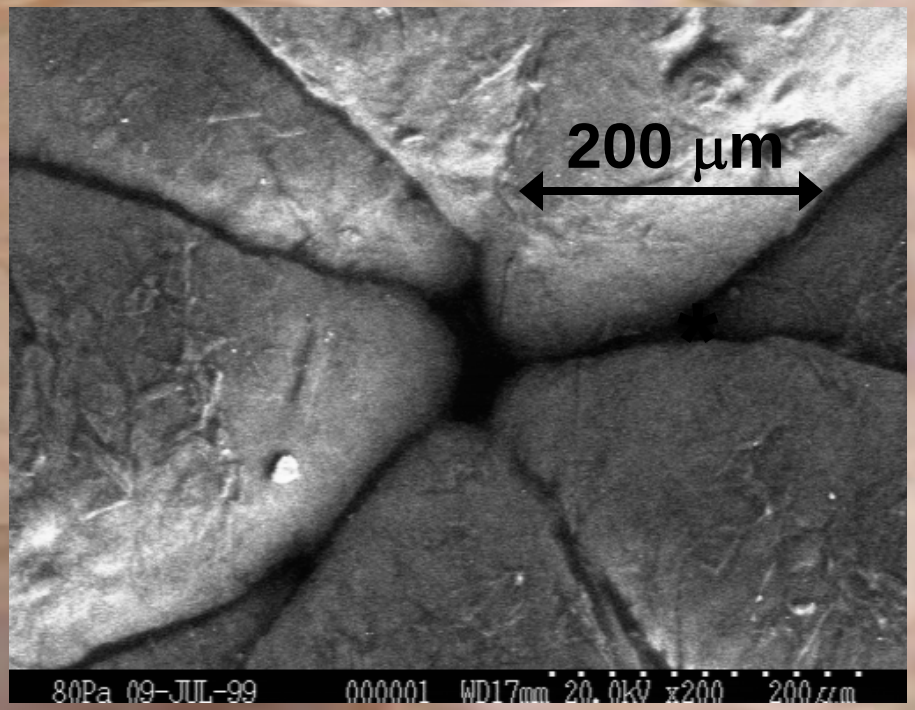


Skin lipids 20%
volume: limited
solubility capacity

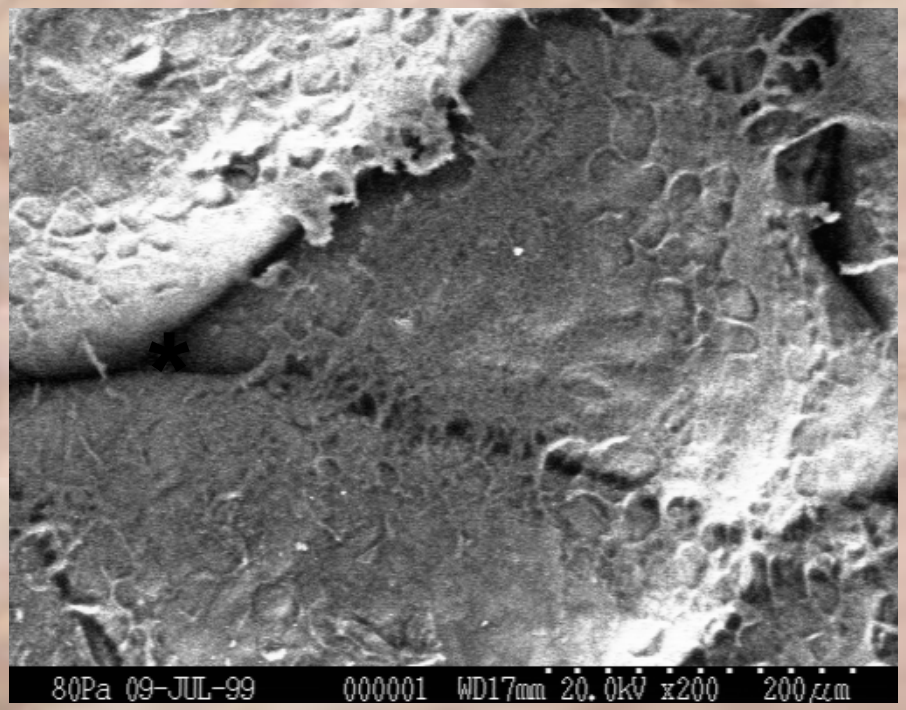
In vitro experiments difficult to mimic dose

What does solvent deposited solid chemical look like on skin surface?

Environmental Scanning Electron Micrographs (ESEM)



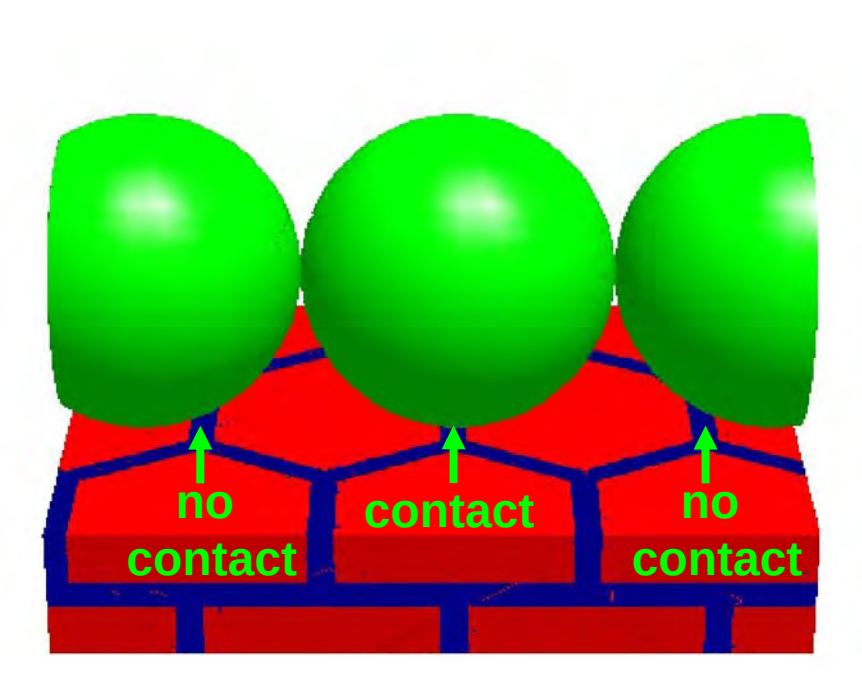
No deposited chemical



10 μg/cm^2 4-cyanophenol in acetone

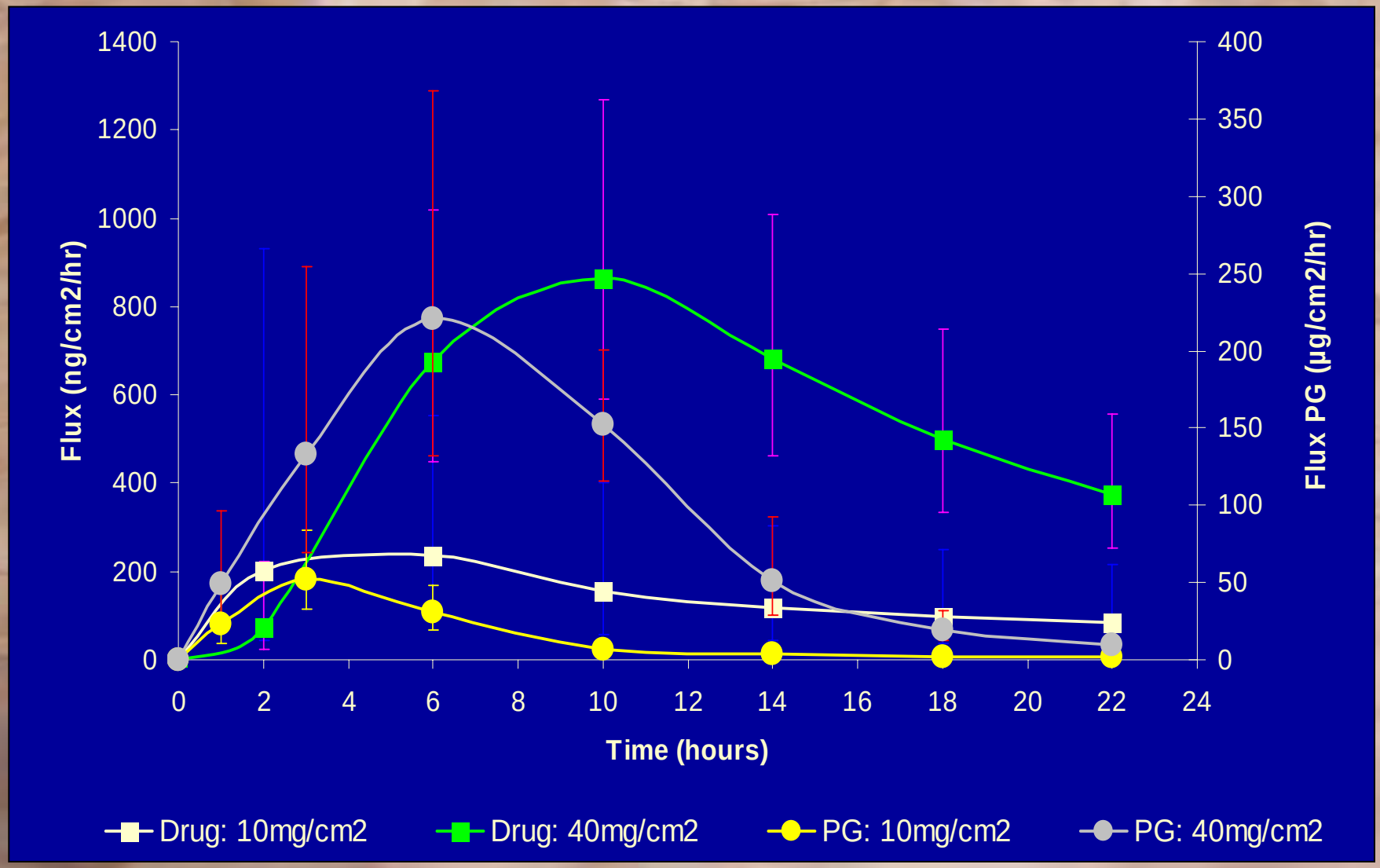
Bunge

Particle size and contact with intercellular channels



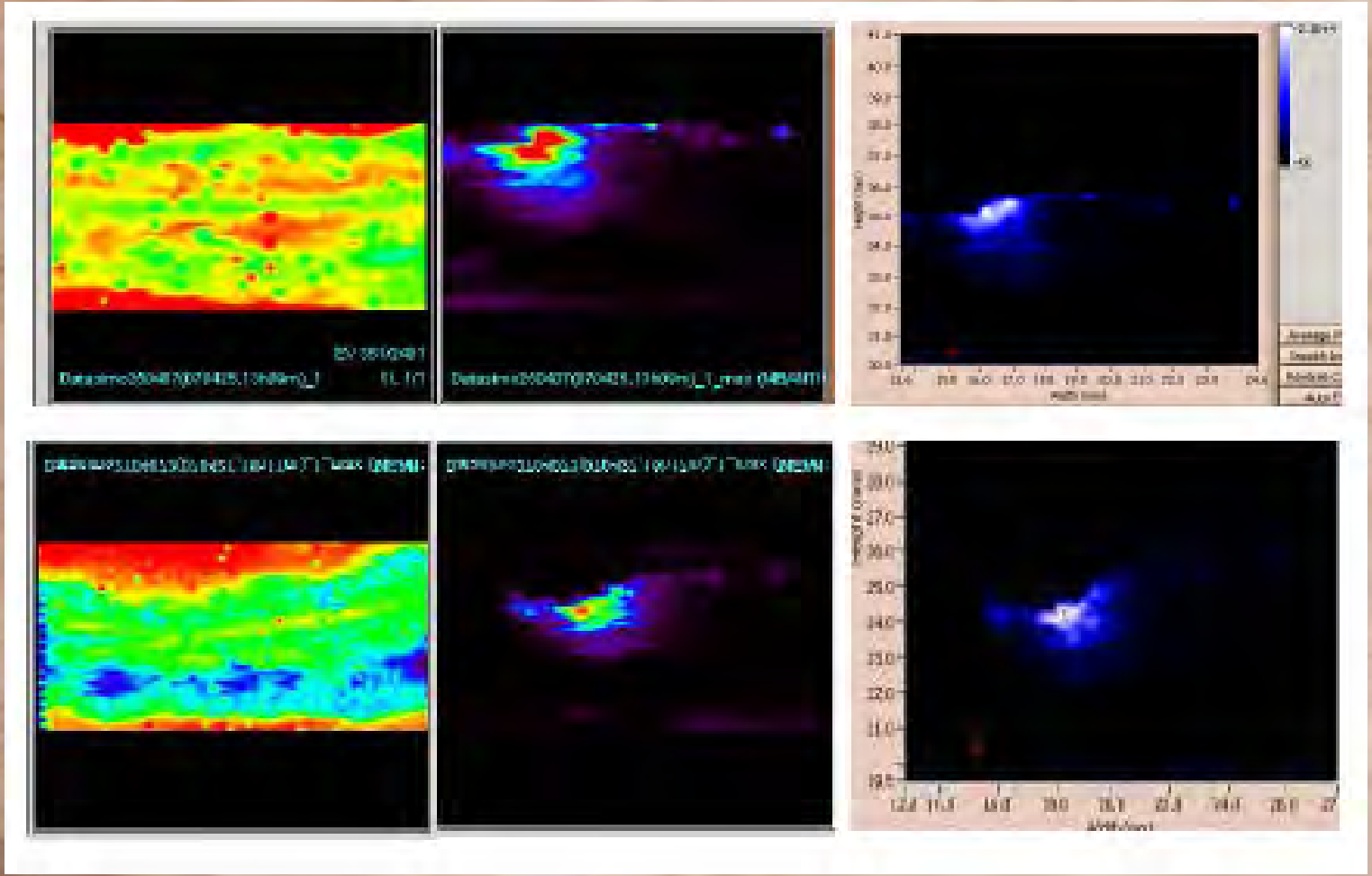
Bunge

Permeation of propylene glycol and drug: effect of the amount of gel applied



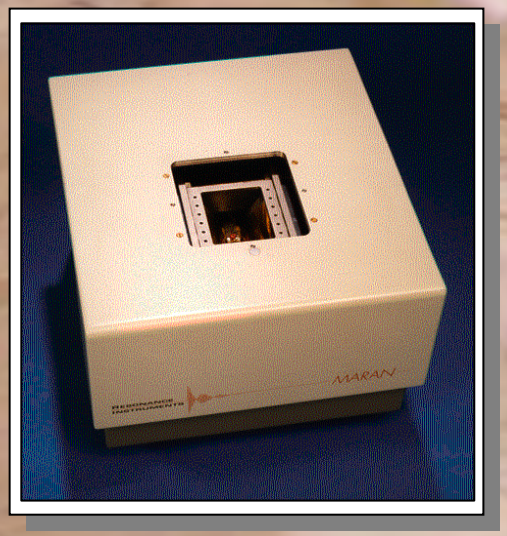
Trottet et al. Int. J. Pharm. 274 (2004) 213-219

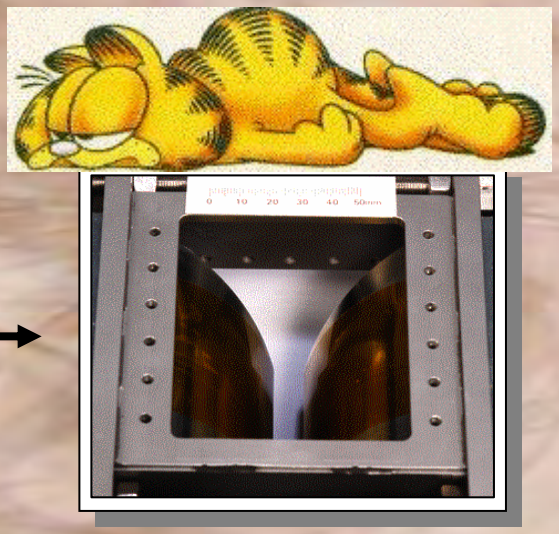
Mass spectroscopy



Royal Society fellow Dr Simona Francese
Malcolm Clench SHU

GARField - a magnet for planar samples



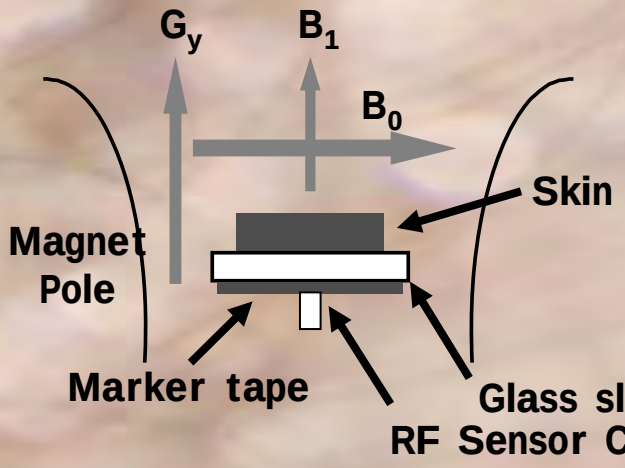


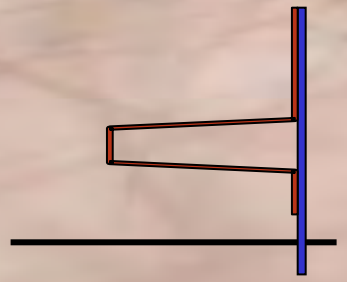
Fourier Transform gives 1D projection

B_o **: Magnetic field (0.7 T)**

G_y **: Field Gradient (17 T/m)**

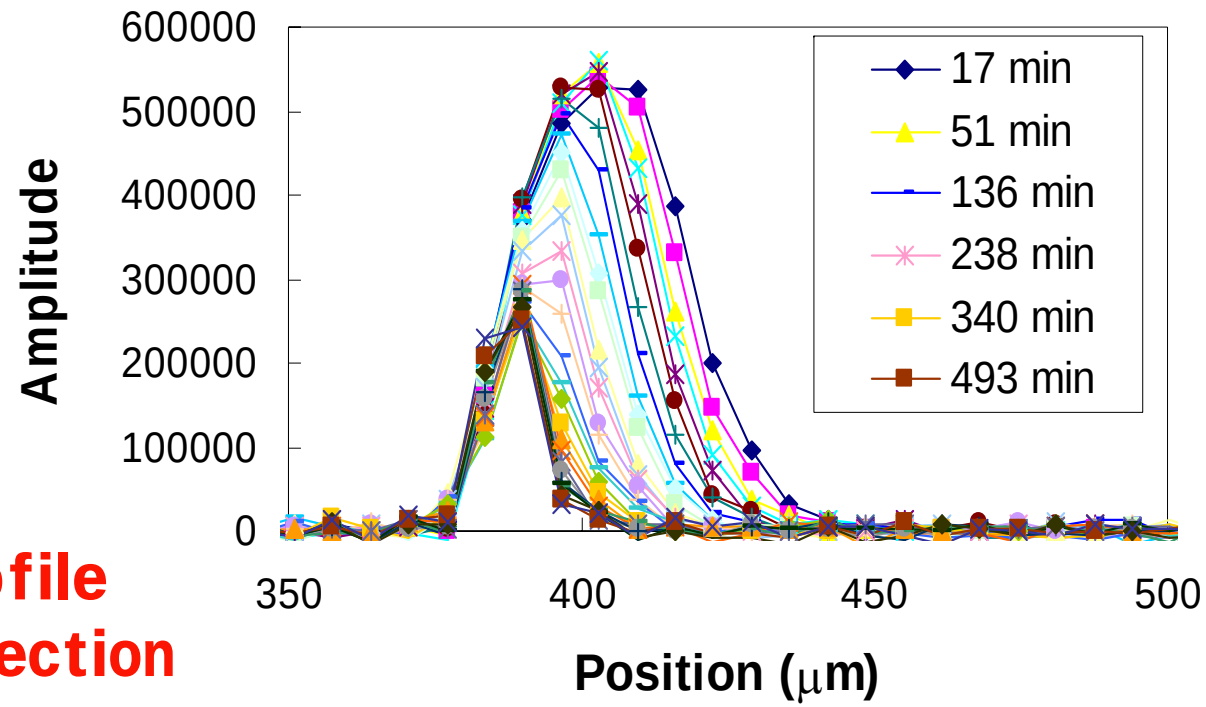
B_1 **: Radio Frequency field**

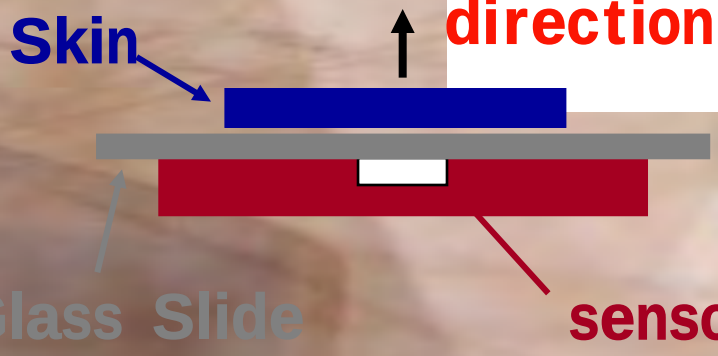




P. M. Glover, P. S. Aptaker, J. R. Bowler, E. Ciampi, P. J. McDonald J. Magn. Reson. (1996) **139**, 90.

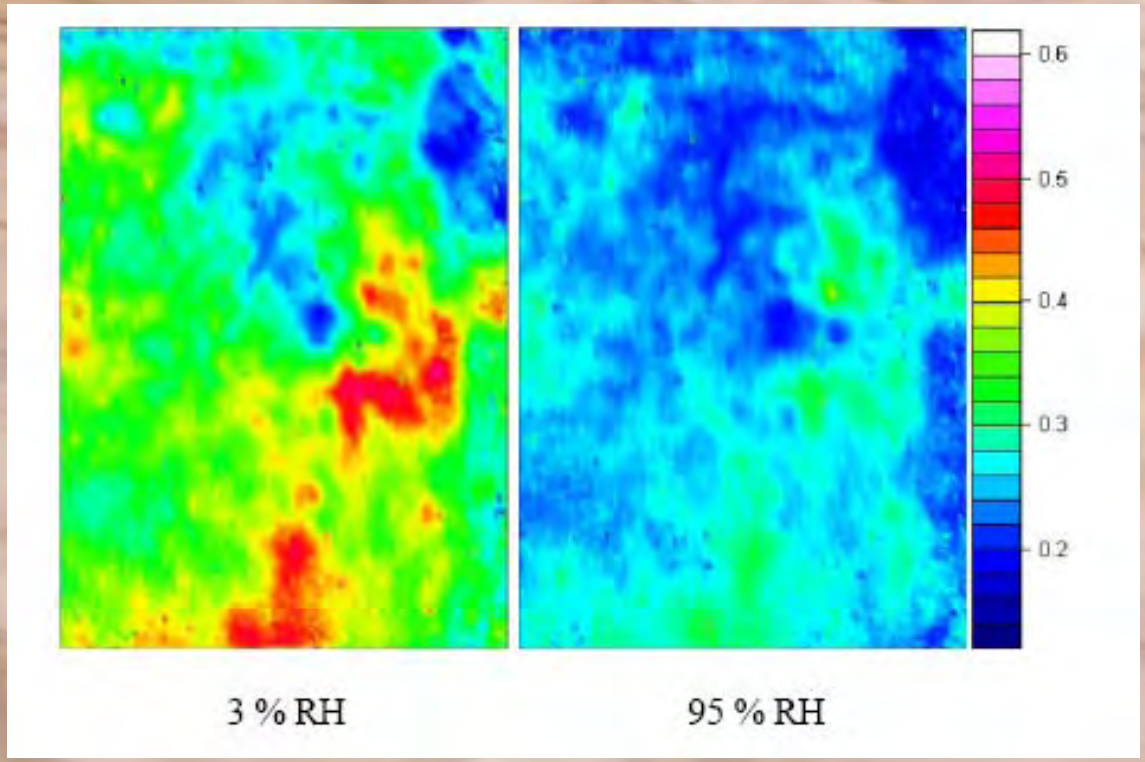
Skin dehydration – in vitro





M Dias, J Hadgraft, P M Glover and P J McDonald, J. Phys. D: Appl. Phys. (2003) **36** 364

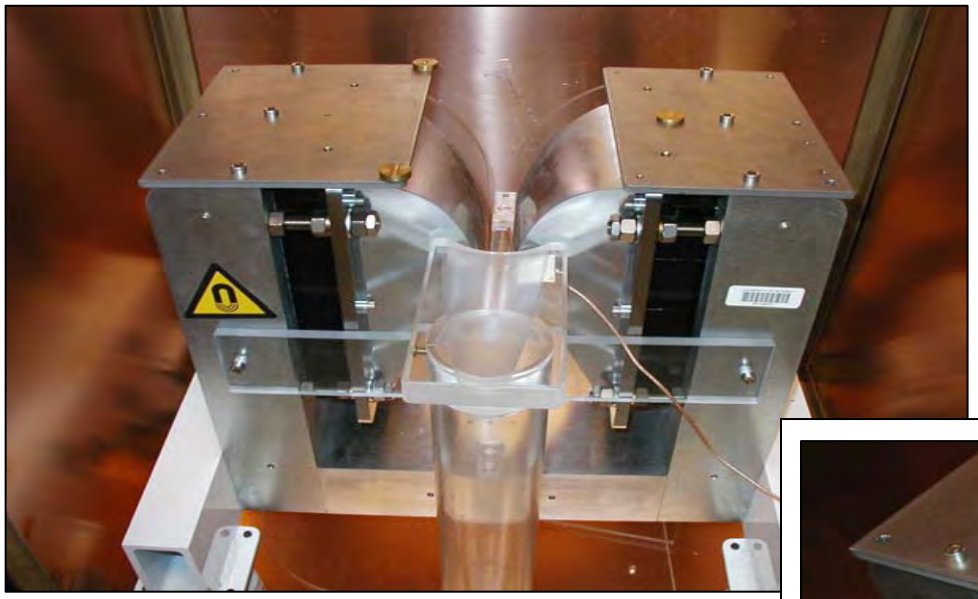
Comparison with imaging studies

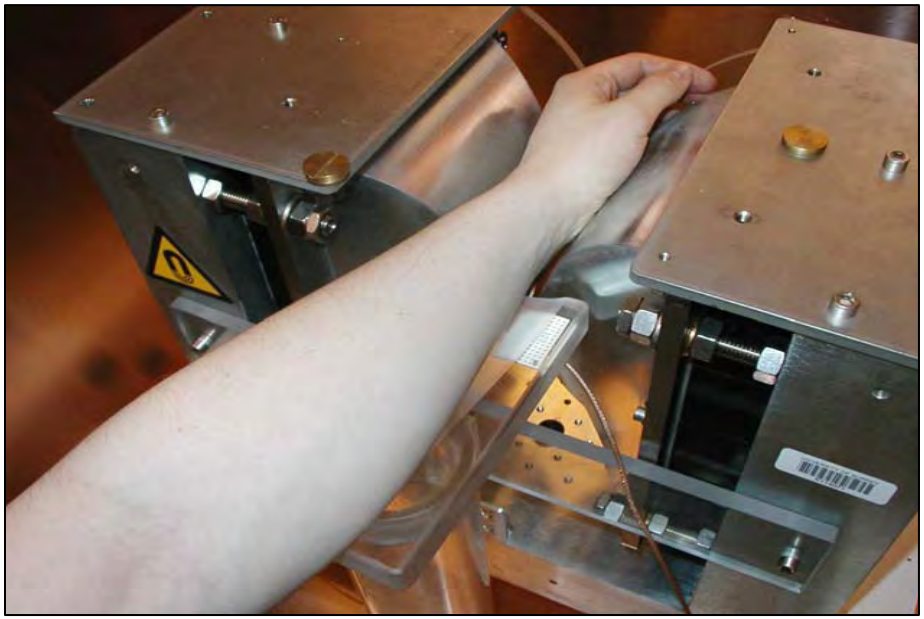


Time course of kinetics similar

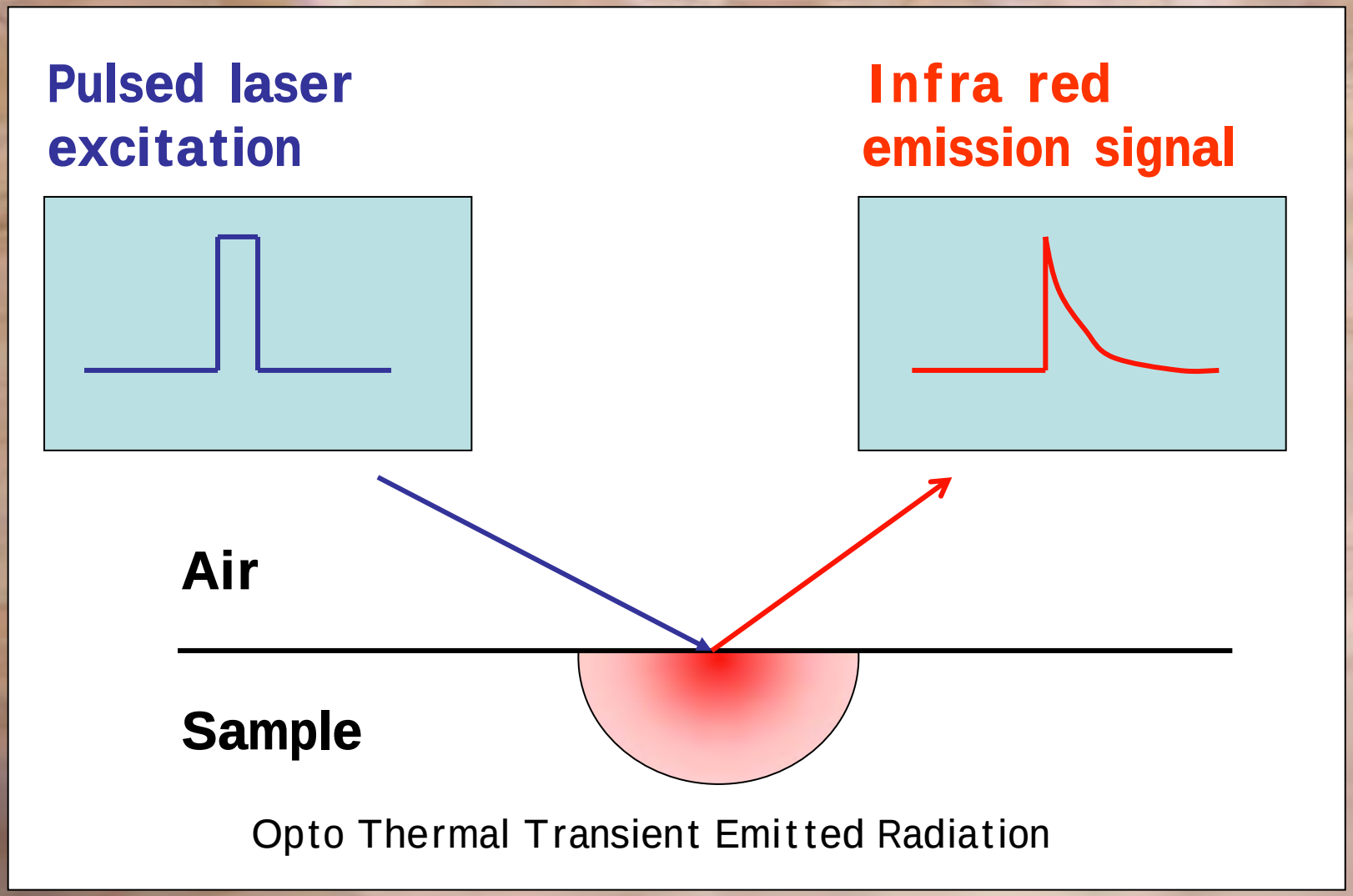
Chan & Kazarian

In vivo – lower arm & hand

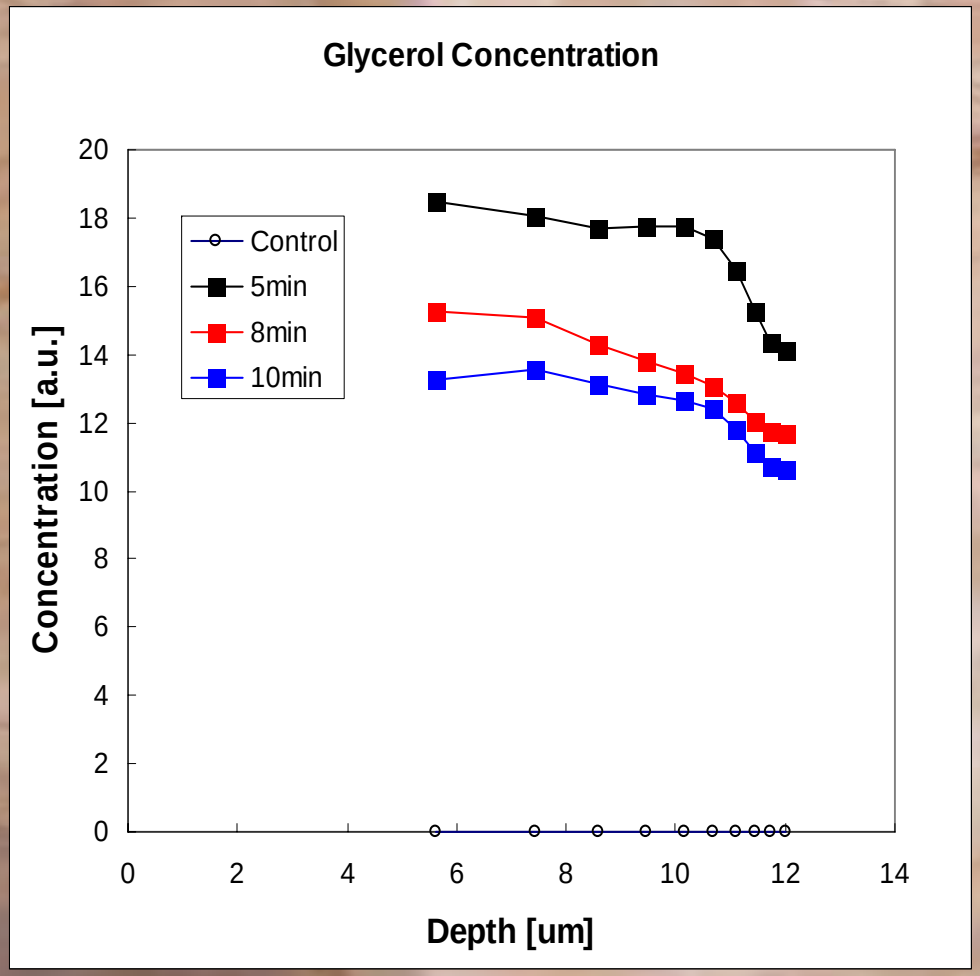


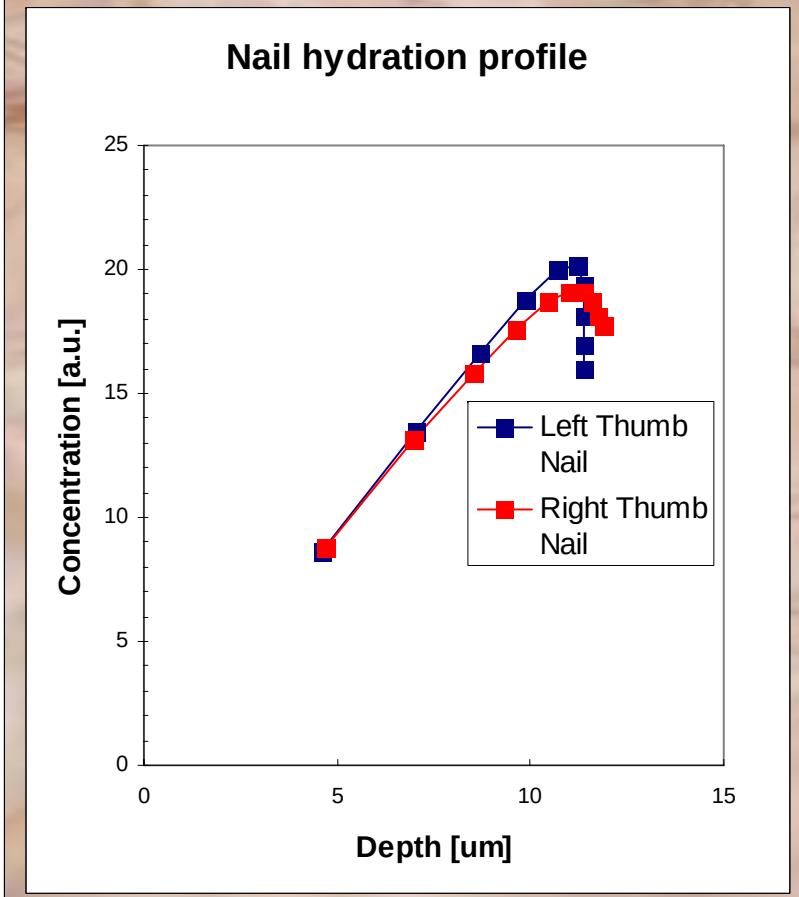


OTTER


Pulsed laser excitation
Infra red emission signal
Air
Sample
Opto Thermal Transient Emitted Radiation

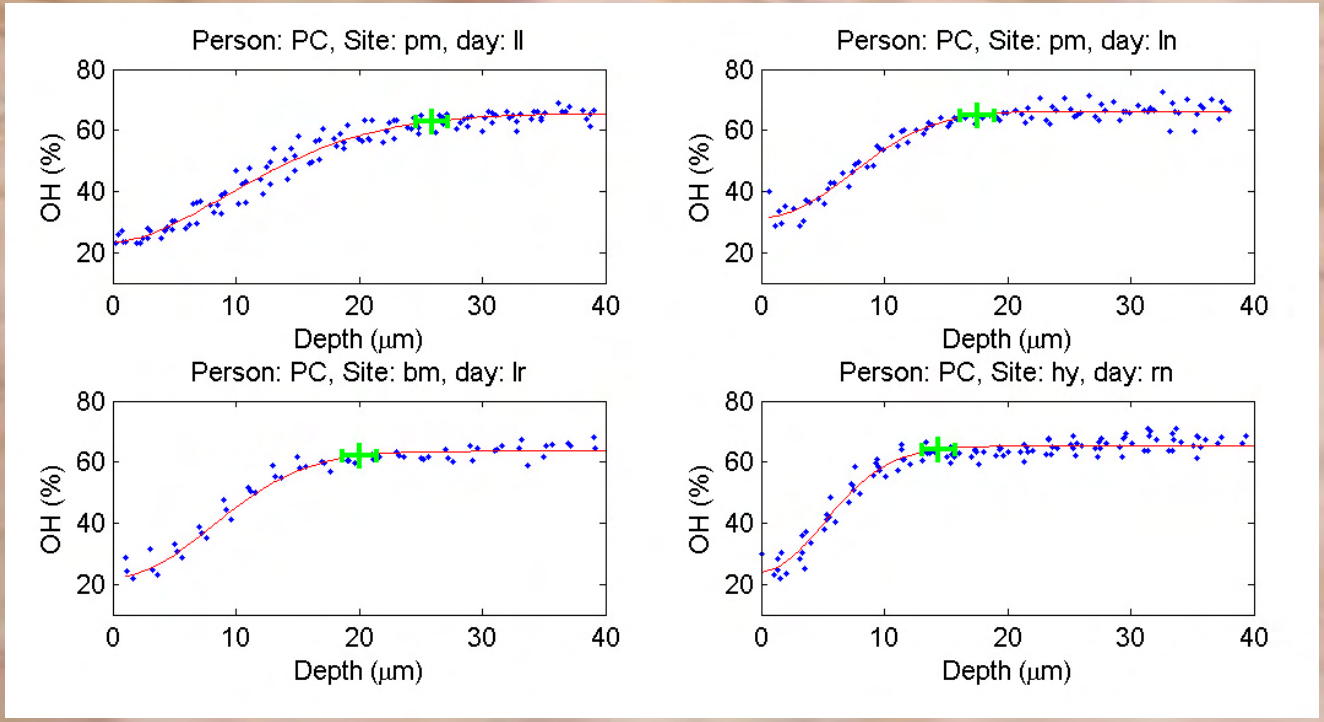
Permeation into nails in vivo





Hirata, Imhof, Xiao, Zheng, McAuley, Lane

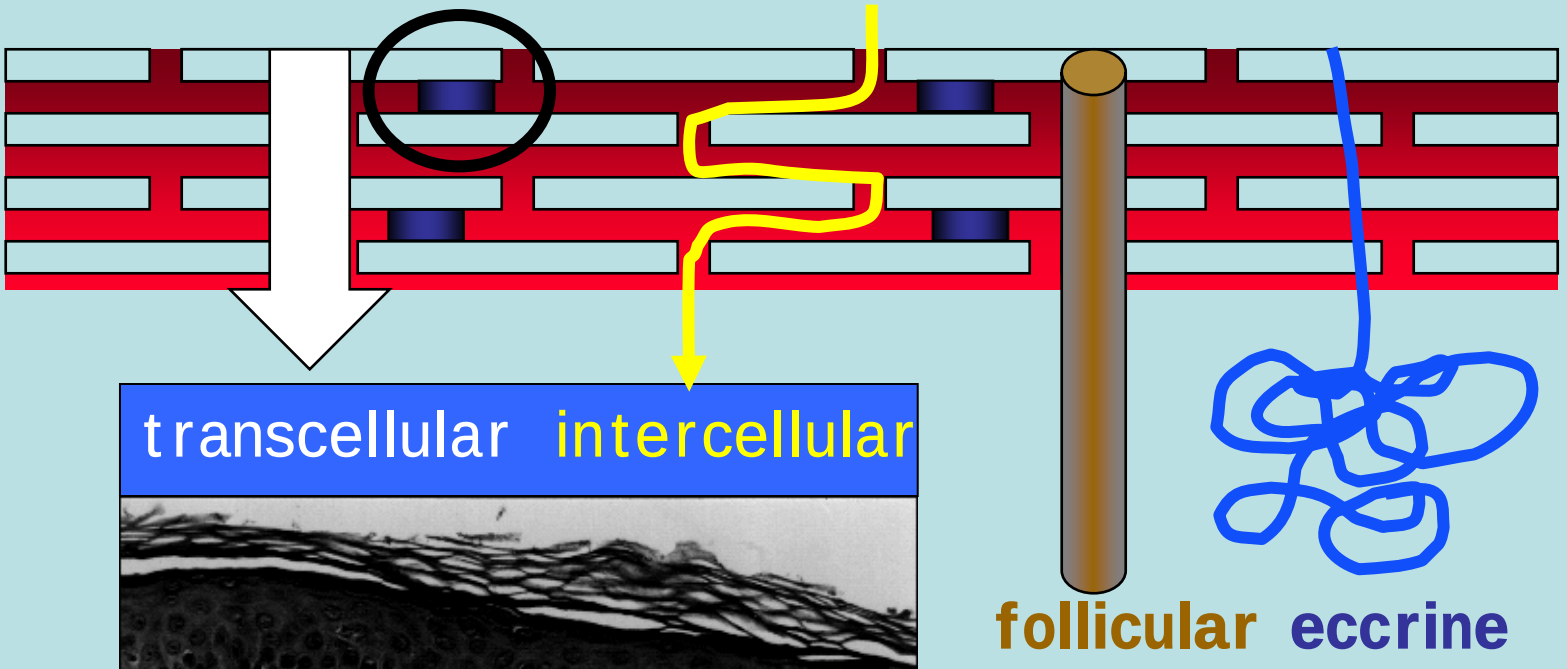
Hydration profiles in vivo laser confocal Raman



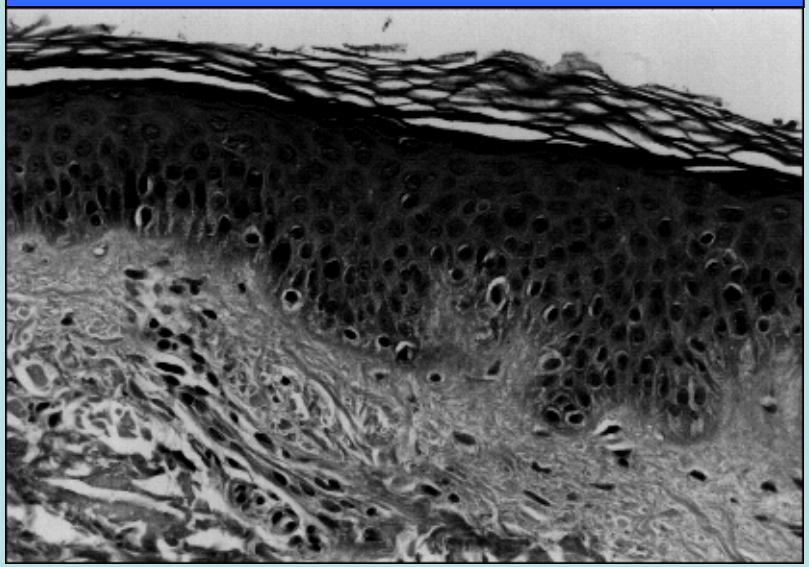
Cork, Matts et al.

Skin structure

Major barrier is in stratum corneum (15 µm thick)



transcellular intercellular



follicular eccrine

Role of lipids

Corneodesmosomes