

# Skin Absorption of (volatile) Liquids: A skin-PBPK Model

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W. ten Berge (wtberge@planet.nl), D. Huizer and F. Jongeneelen  
Industox, Nijmegen, The Netherlands

### Starting points of SkinPerm

A guesstimate of systemic absorption from dermal exposure to substances by using simple retrievable information:

- molecular weight
- water solubility (mg/litre)
- vapour pressure (Pascal)
- log(octanol/water) at pH 5.5 (skin pH)
- density (mg/cm<sup>3</sup>)

### Estimate 1st step:

- Aqueous skin permeation coefficient  $K_{aq}$  (QSAR) from Log(Kow), Mw (ten Berge 2009)
- Skin/water partition coefficients  $P_{sw}$  (QSAR) from Log(Kow), (ten Berge 2009)
- Skin permeation coefficient neat substance  $K_{aq}/P_{sw}$
- Maximum available volume for absorption in SC is 0.4 ml
- Estimate maximum mass in SC in equilibrium with a saturated aqueous solution (=  $M_{aq}$ )
- Actual mass in stratum corneum is  $M_{sc}$
- Postulate that,  
⇒the systemic absorption rate is related to  $M_{sc}/M_{aq}$   
⇒the systemic absorption rate is maximum at  $M_{sc} \geq M_{aq}$

### Estimate 2nd step:

- Evaporation from liquid substance layer on the skin according to REACH Guidance App R14.1
- Evaporation rate from stratum corneum using the Henry coefficient and aqueous permeation coefficient  $K_{aq}$
- Postulate that:  
⇒the evaporation rate is related to  $M_{sc}/M_{aq}$   
⇒the evaporation rate is maximum at  $M_{sc} \geq M_{aq}$

### Output:

Parameters as function of the time after the start of exposure:

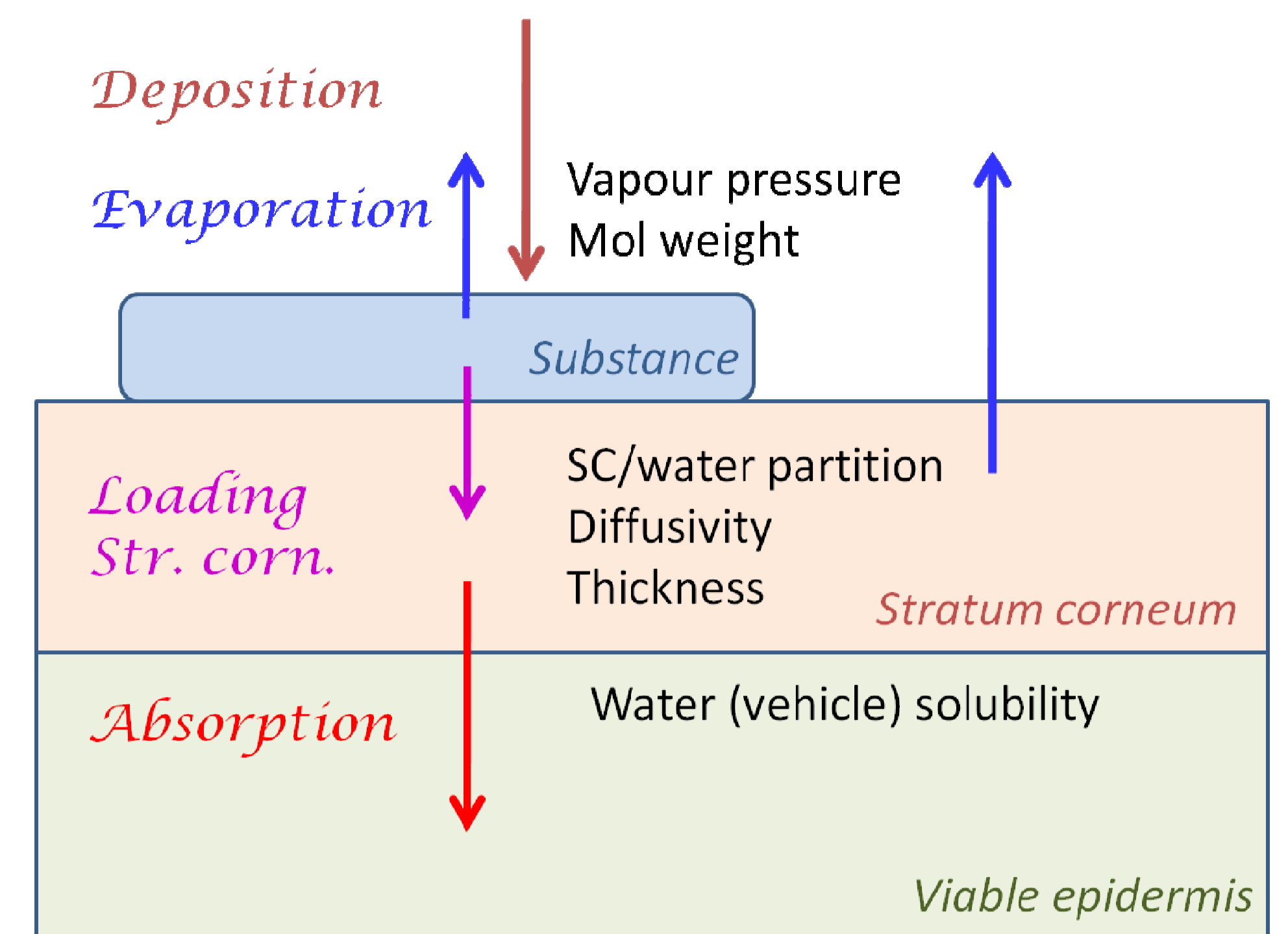
- the mass of the substance upon the skin
- the mass of the substance in the stratum corneum
- the mass of the substance evaporated
- the mass of the substance absorbed

### Conclusions:

- Simulation of evaporation from, metabolism in and permeation through the skin was done on the basis of QSARs and physical behaviour
- Simulations were in line with experimentally observed evaporation and absorption for a number of studies (see references)
- This method is to be used for risk assessment of dermal absorption of industrial chemicals (REACH)
- This method might be helpful to improve the design of experimental dermal absorption studies

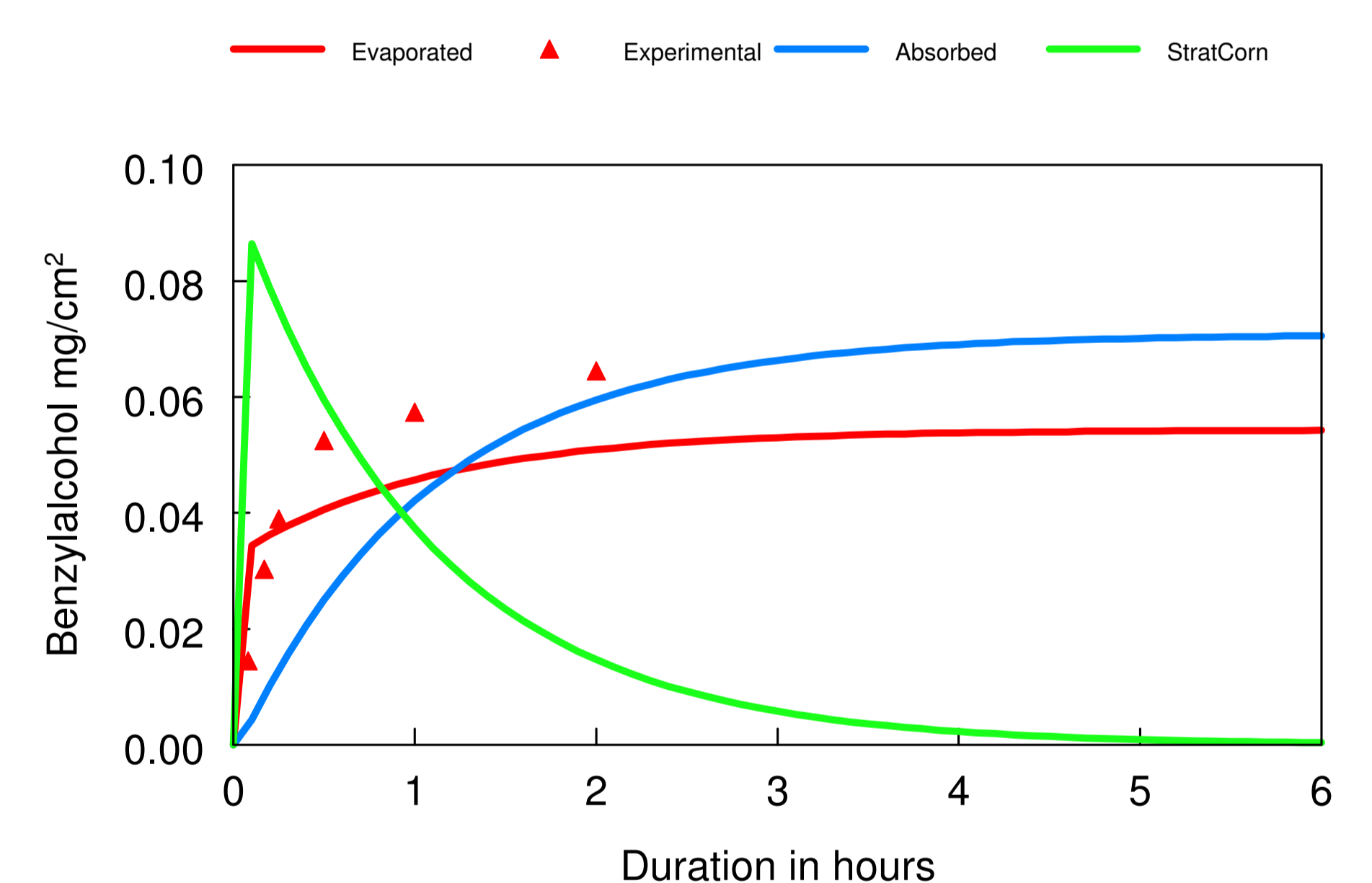
### References

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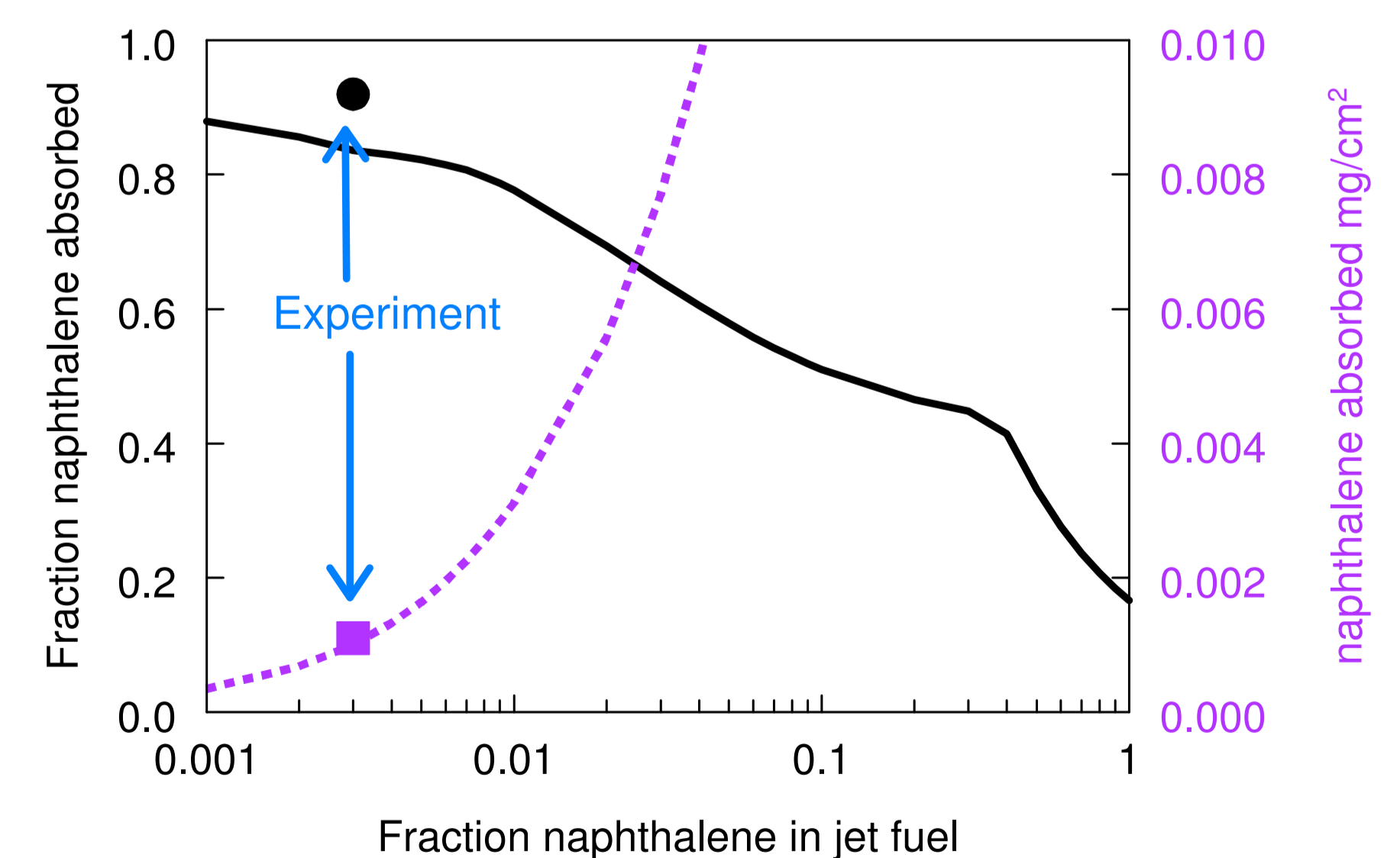


Substance	Absorption Observ. %	Absorption Estim. %
Benzene	0.2	0.4
Benzylalcohol	48.0	57.0
Linalool	42.5	22.9
Dihydromyrcenol	34.2	38.9
10-Undecanal	54.7	47.5
Citronellol	58.8	57.3
2-Phenylethanol	83.4	56.0
(E)-Cinnamic alcohol	96.3	59.1
Alpha-Damascene	43.0	45.5
Cis-7-p-Menthanol	53.1	66.4
2,2,2-Trichlorophenyl-ethylacetate	59.5	50.7
MPCC	76.3	84.4
(E)-2-Benzylidene-Octanal	95.7	88.8
15-Pentadecanolide	93.4	96.2

Dermal absorption of 0.125 mg/cm<sup>2</sup> benzylalcohol



Naphthalene absorbed in 24 hours dependent on fraction naphthalene in jet fuel (single dose 0.4 mg/cm<sup>2</sup>)



Application of 7.8 mg/cm<sup>2</sup> fluroxypyrmeptyl on human skin (hydrolysis rate 0.01/hr)  
Result after 48 hours

Type of sample	% radiolable measured	% radiolable estimated
Receptor fluid	0.438	0.274
Skin residue	2.3	7.31
Mass on skin	97.3	92.4