Investigating human skin volatile emissions using HS-SPME-GC-MS
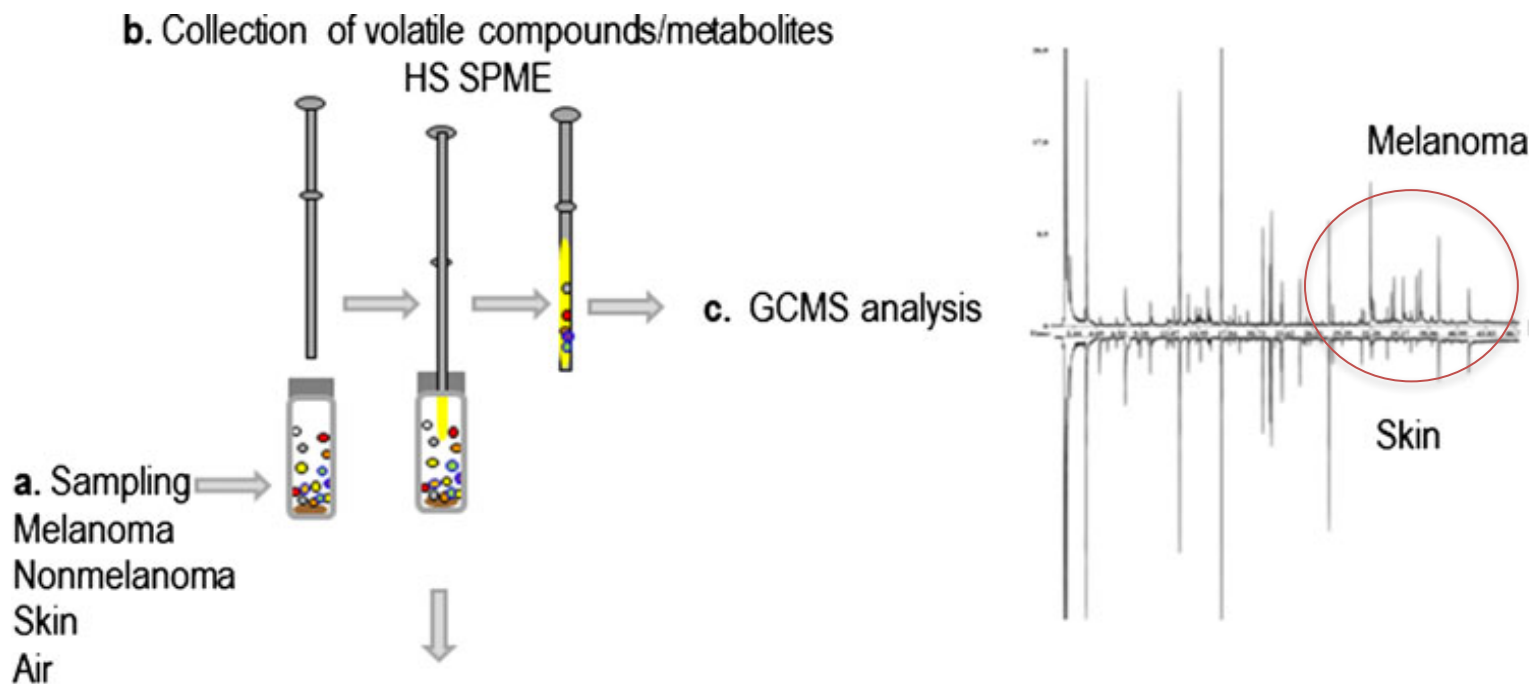
Dr Emer Duffy

Volatiles & human health

- Humans emit hundreds of volatile organic compounds (VOCs)

- Many of these VOCs can reflect internal biochemical pathways, and their chemical pattern may be used as a non-invasive route towards diagnosing disease & monitoring therapy

- Monitoring breath VOCs has attracted significant interest for non-invasive diagnostic applications

http://www.theverge.com/2015/4/14/8410317

The Breathometer Mint™

https://www.breathometer.com/mint/

Skin emits volatile metabolites which can also be linked to health status

Data on clinically relevant biomarker VOCs from skin is emerging (e.g. cancer, diabetes, hepatic disease)

- Skin biopsy emits unique volatile fingerprint that varies in normal vs. melanoma skin
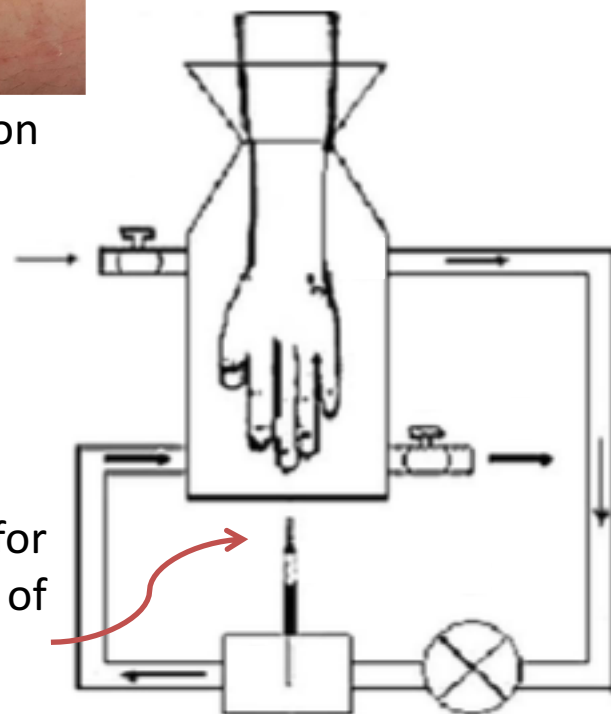

b. Collection of volatile compounds/metabolites
HS SPME

c. GCMS analysis

Melanoma

Skin

a. Sampling
Melanoma
Nonmelanoma
Skin
Air

..However this approach is still invasive to a patient

T. Abaffy, *et. al. Metabolomics*, 9 (2013) 998.

Due to the analytical sensitivity required for detection of skin volatiles, a pre-concentration step is typically employed

- Pre-concentration methods have included bag sampling, contact-mode methods e.g. gauze, glass beads, and solid-phase microextraction (SPME)
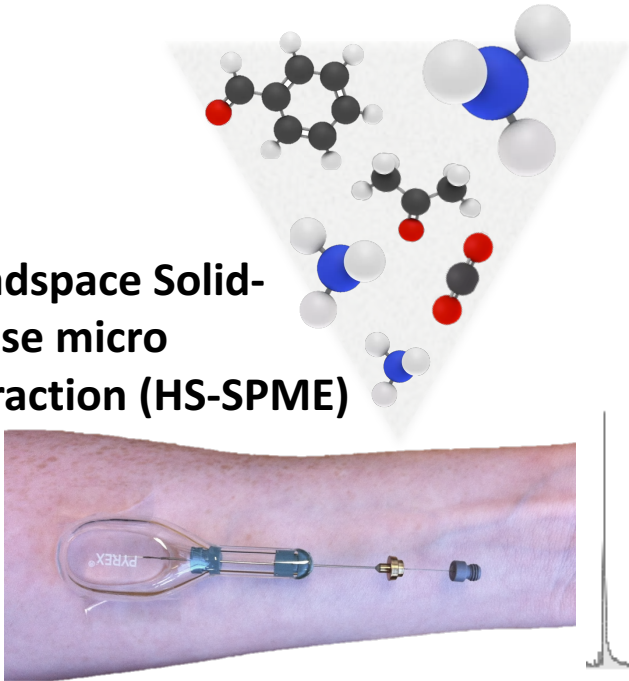

Thin film microextraction (wearable patch)

SPME Fibre for concentration of volatiles

A. Agapiou, A. Amann, P. Mochalski *et. al. TrAC* 66 (2015) 158.

Z. Zhang, J. Cai, G. Ruan, G. Li, *J. Chromatogr. B,* 822 (2005) 244.

Wearable platform for concentration of skin volatiles

Headspace Solid-phase micro extraction (HS-SPME)

GC-MS

Chemometrics

E. Duffy, M. Jacobs, B. Kirby, A. Morrin, *Experimental Dermatology*, 26 (2017) 919.
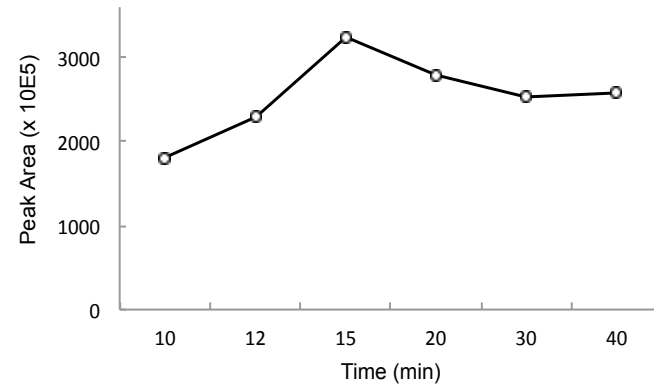
4
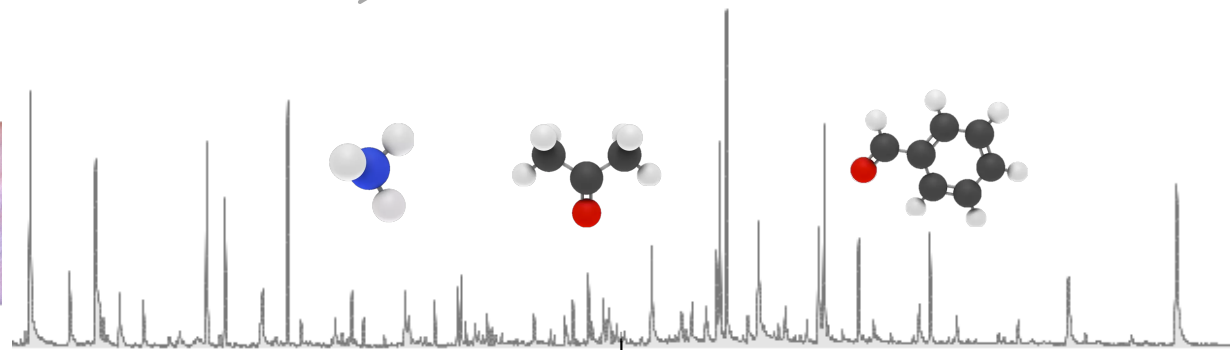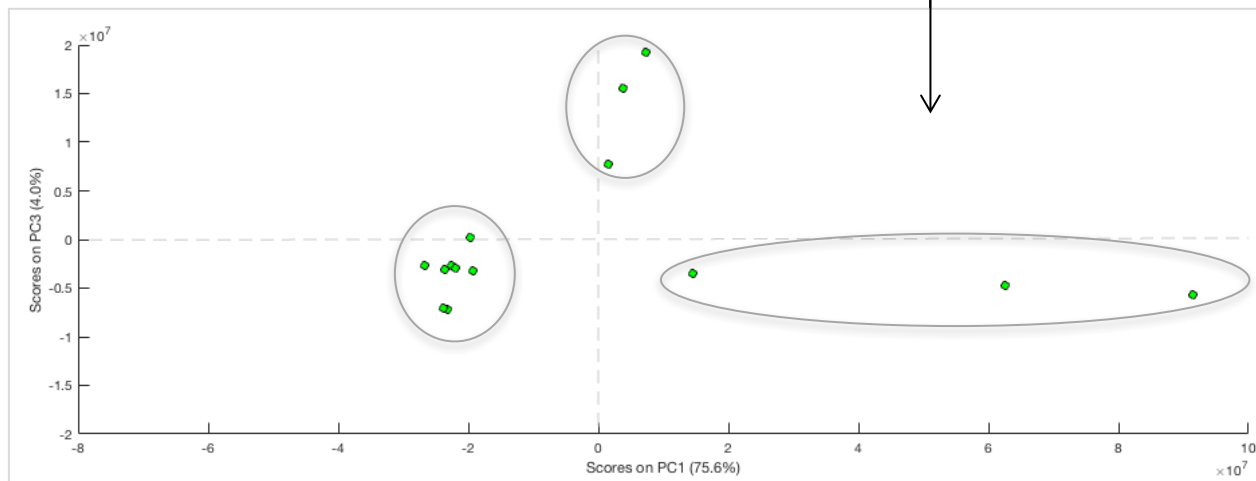
Developing a sampling protocol

Solid-phase microextraction (SPME)

No direct contact with skin needed, sample can be analysed directly with no other sample preparation steps needed

Example of an extraction time-profile curve for skin volatiles

Different SPME fibres were compared for extraction of skin volatiles. Polydimethylsiloxane divinylbenzene/carboxen fibre (PDMS-DVB/CAR) was selected for further work on concentration of skin volatiles based on compound recoveries, manufacturer recommendations and previous literature reports on sampling volatile skin emissions
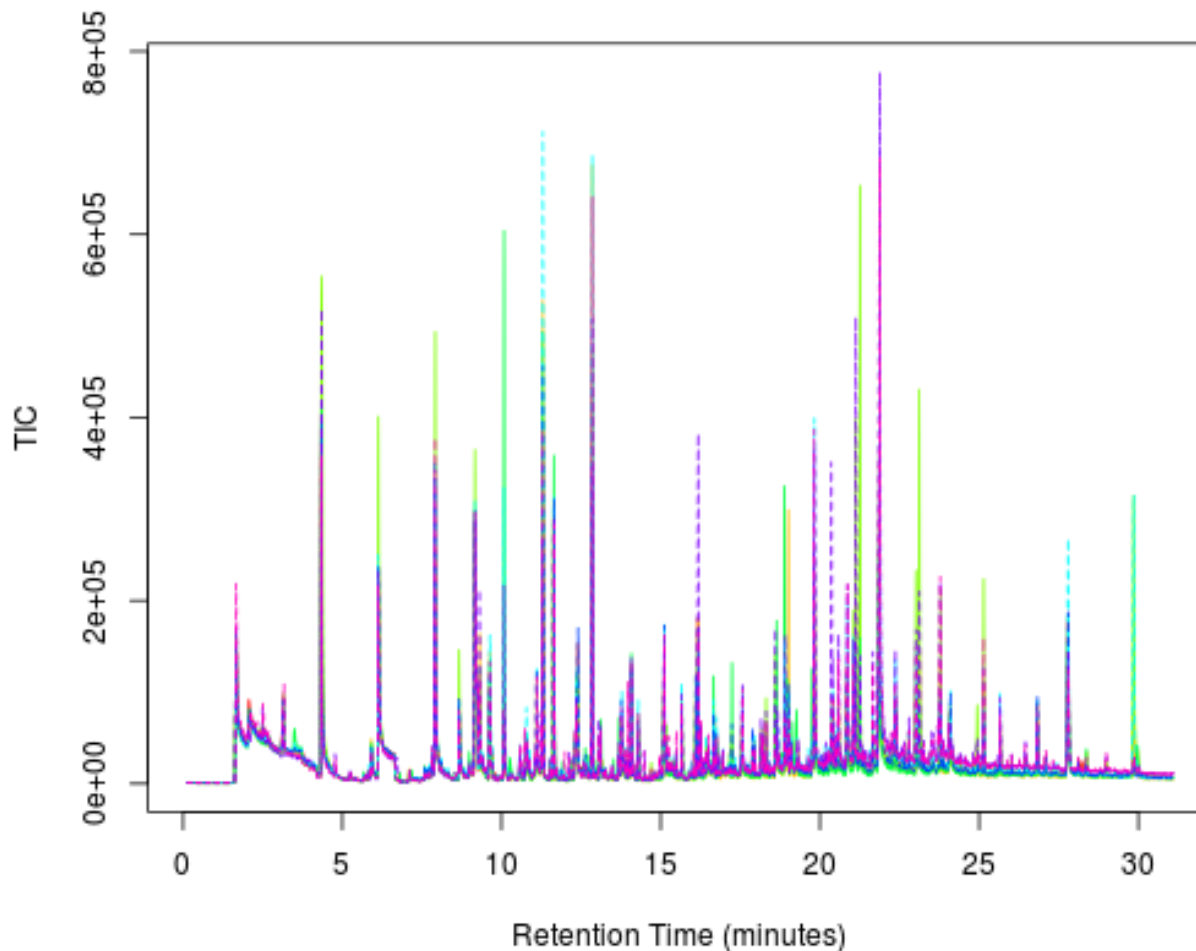
Analysis by GC-MS

Agilent 6890 GC-MSD, carrier gas: He, 1 mL/min; Splitless injection @ 250 °C
Column: SLB-5ms (30 m x 0.25 mm x 0.25 µm)
Oven: 30 °C hold 5 min, 10 °C /min 270 °C, hold 5 min
MS scan range: 30-400 *m/z*, ion source: 230 °C, ionising energy: 70 eV

Data processing

- Feature detection & chromatogram alignment (XCMS)
- Mass spectral database matching – compound IDs (National Institute of Standards & Technology)
- Retention index matching - using a standard mix of saturated alkanes (C_7-C_{30})
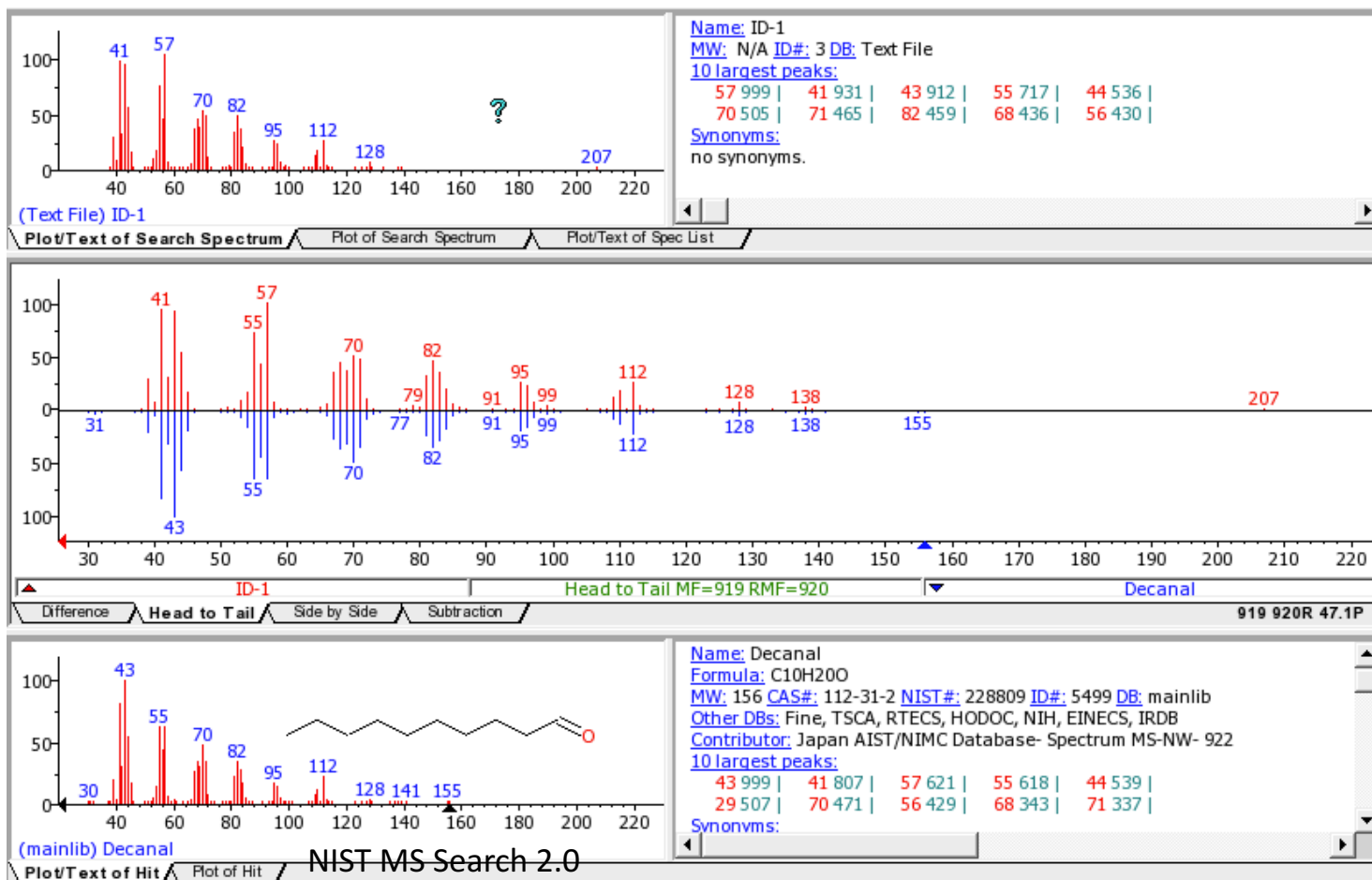
Skin volatiles typically contain a variety of aldehydes, acids, ketones, alkanes, alkenes & esters derived from both endogenous and exogenous sources
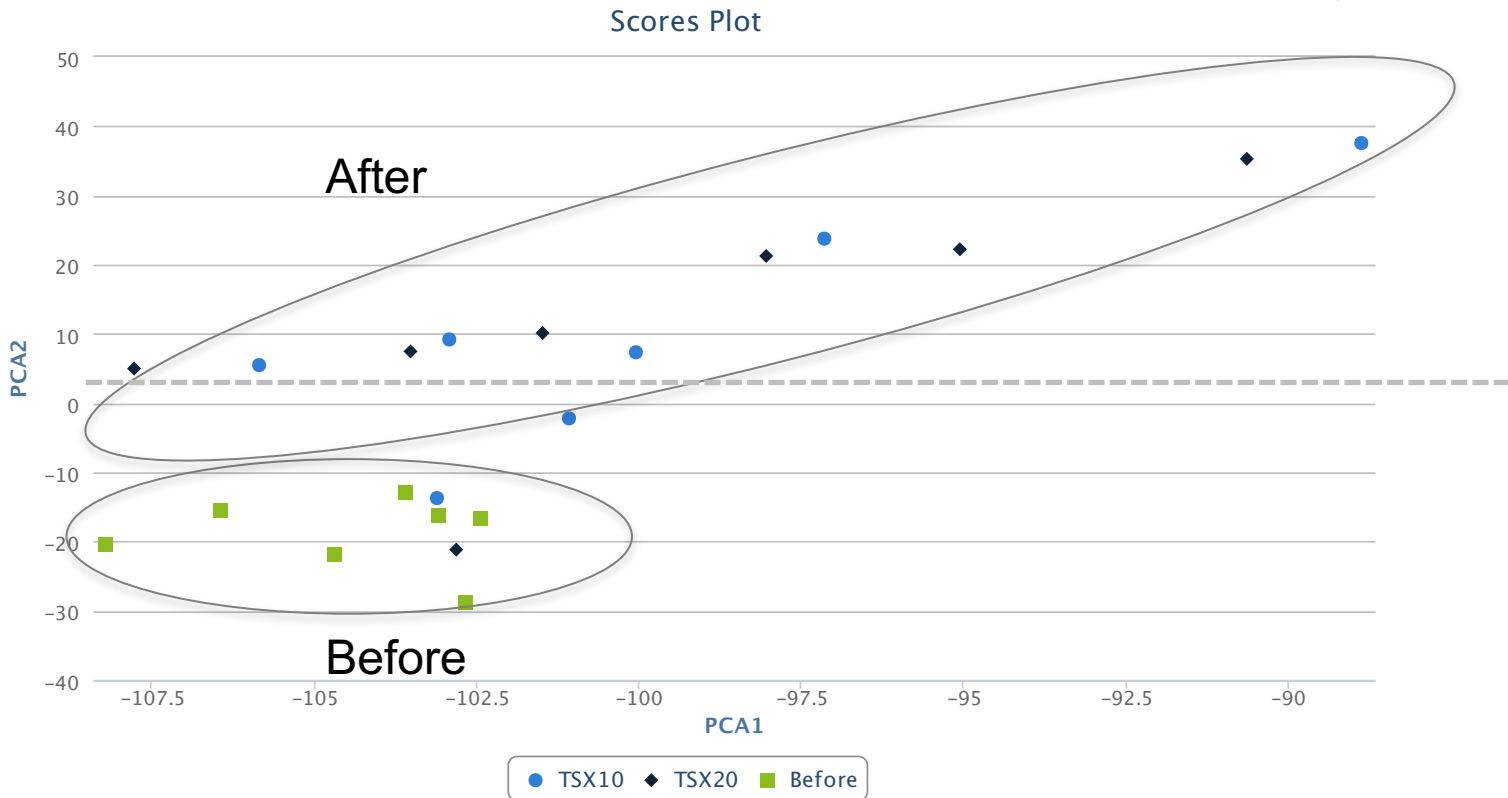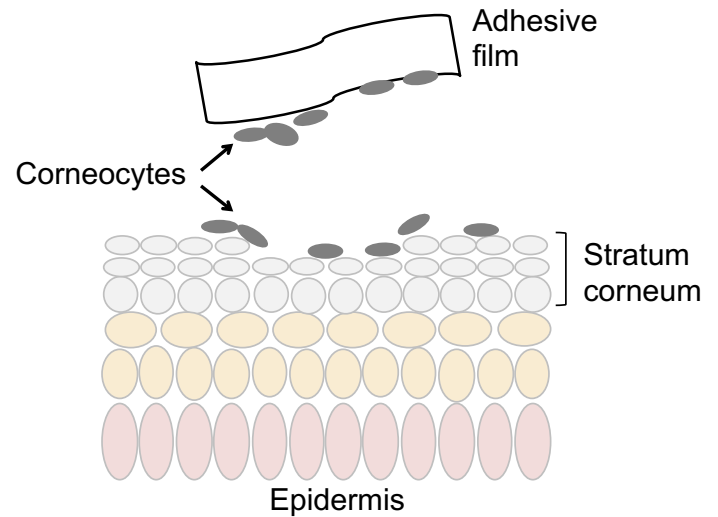
Compound distribution profiles
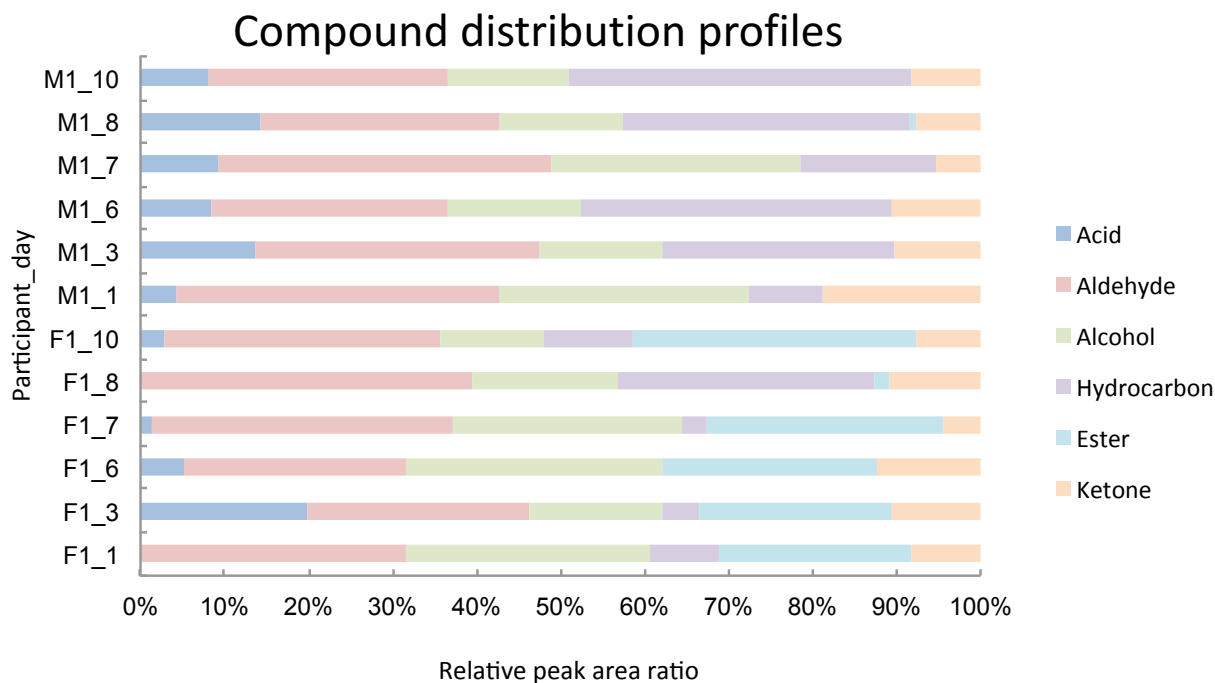
Their composition can vary temporally and also depends on sampling site and numerous environmental factors
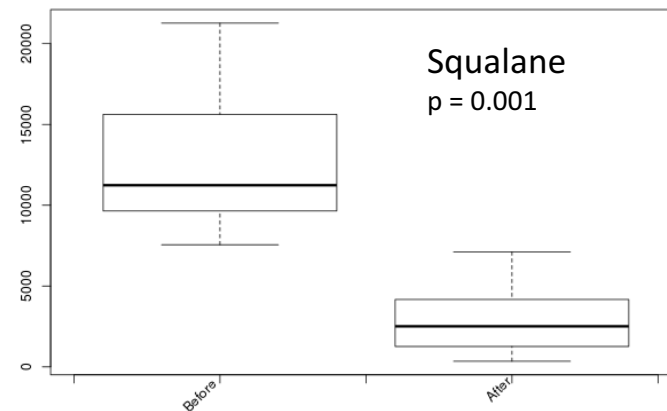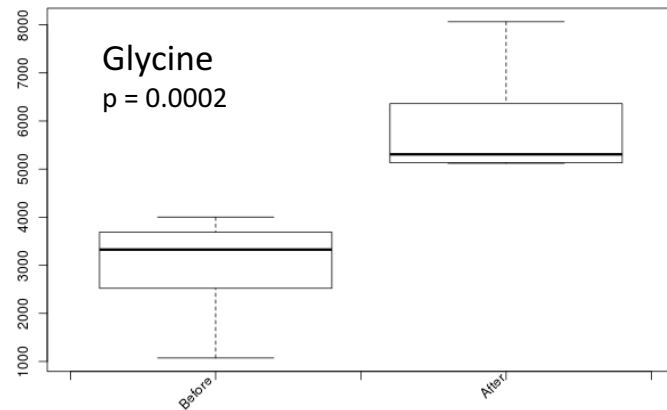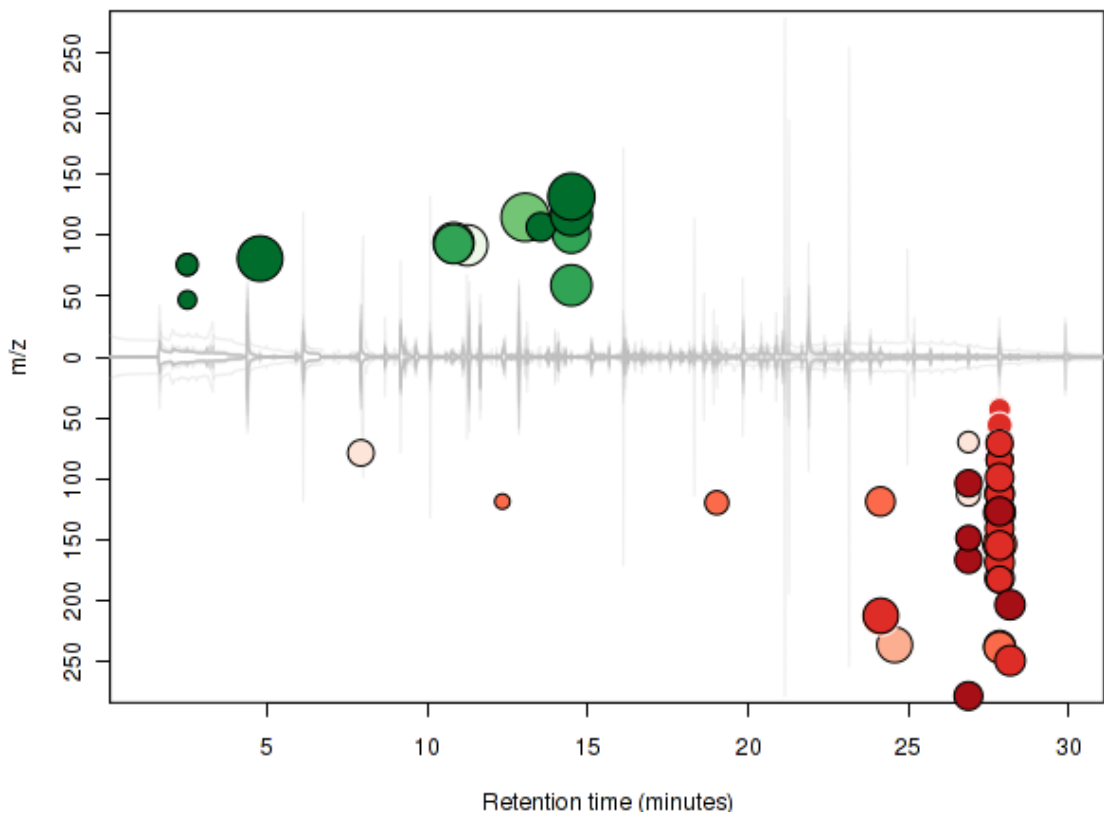
Control samples were collected to understand exogenous contributions (*e.g.* SPME fibre blanks, background air, materials used in the study etc.)
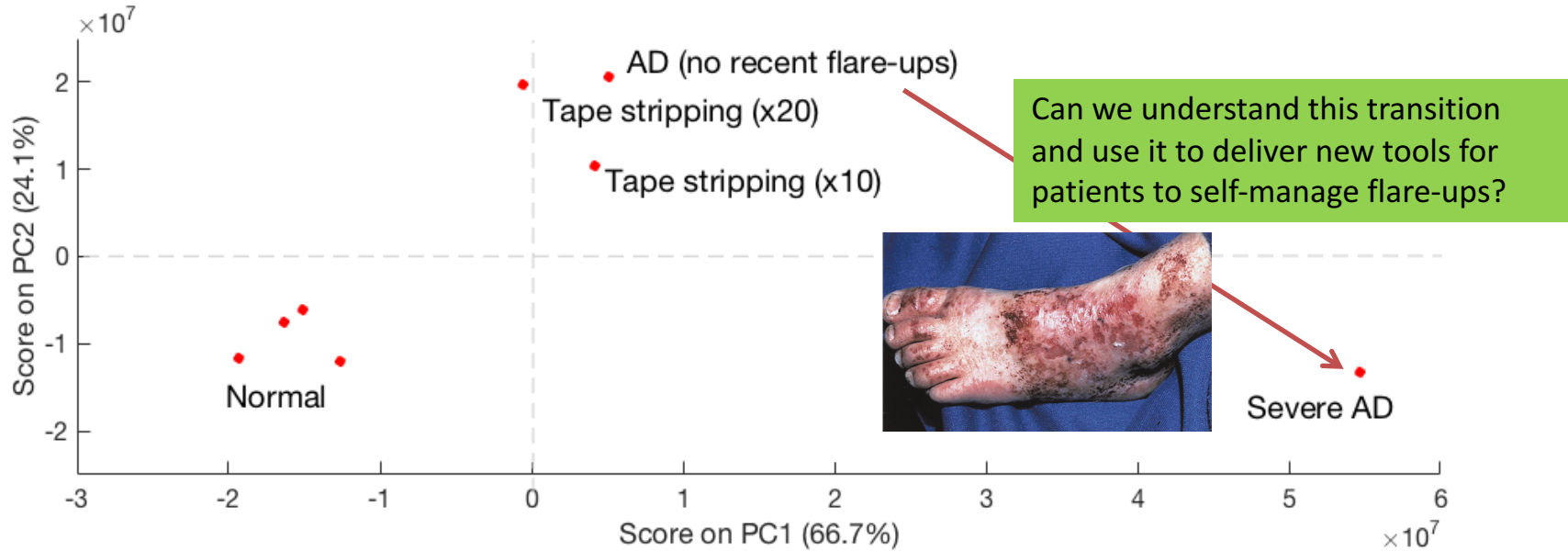
Compound	RT (min)	CAS	F1	F2	F3	F4	M1	M2	M3
Glycine	2.52	56-40-6	×			×		×	
Acetic acid	3.11	64-19-7	×	×	×	×	×	×	
Hexanal	5.92	66-25-1	×	×	×	×	×	×	×
Heptanal	7.80	111-71-7	×	×		×	×	×	×
6-Methyl-5-hepten-2-one	9.31	110-93-0	×	×	×	×	×	×	
Octanal	9.63	124-13-0	×	×	×	×	×	×	×
2-Ethyl-1-hexanol	10.08	104-76-7	×	×	×	×	×	×	×
1-Octanol	10.78	111-87-5						×	
Nonanal	11.30	124-19-6	×	×	×	×	×	×	×
Decanal	12.85	112-31-2	×	×	×	×	×	×	×
2-Decenal	13.69	3913-81-3	×			×	×	×	
Nonanoic acid	13.77	112-05-0	×	×	×	×	×	×	×
1-Tridecene	13.89	2437-56-1		×			×	×	
Undecanal	14.30	112-44-7	×	×	×	×	×	×	×
Decanoic acid	15.12	334-48-5	×	×	×	×	×	×	×
Tetradecane	15.47	629-59-4		×	×		×	×	
Dodecanal	15.49	112-54-9		×	×		×	×	×
Geranyl acetone	15.66	3796-70-1	×	×	×	×	×	×	×
Undecanoic acid	16.17	112-37-8					×	×	
1-Tridecanol	16.35	112-70-9	×			×	×	×	
Pentadecene	16.67	13360-61-7						×	×
Pentadecane	16.76	629-62-9	×		×	×	×	×	
Tridecanal	16.95	10486-19-8		×				×	×
Lilial	17.23	80-54-6	×	×		×	×		
Dodecanoic acid	17.57	143-07-7	×	×	×	×	×	×	×
Tetradecanal	18.15	124-25-4	×	×	×	×	×		×
Tetradecanoic acid	19.83	544-63-8	×	×	×	×	×	×	×
Pentadecanoic acid	20.86	1002-84-2	×	×	×	×	×	×	×
1-Hexadecanol	20.87	36653-82-4	×	×	×	×	×	×	
n-Hexadecanoic acid	21.83	57-10-3	×	×	×	×	×	×	×
Isopropyl palmitate	22.24	142-91-6	×	×	×	×	×	×	
Squalane	27.79	111-01-3	×	×	×	×	×	×	×
Squalene	29.86	111-02-4	×	×		×		×	

E. Duffy, M. Jacobs, B. Kirby, A. Morrin, *Experimental Dermatology*, 26 (2017) 919.

Discriminating volatile emissions before and after acute barrier disruption

Adhesive film

Corneocytes

Stratum corneum

Epidermis

Scores Plot

After

Before

TSX10   TSX20   Before

PCA1

PCA2

E. Duffy, M. Jacobs, B. Kirby, A. Morrin, *Experimental Dermatology*, 26 (2017) 919.

Dysregulation of features after barrier disruption

E. Duffy, M. Jacobs, B. Kirby, A. Morrin, *Experimental Dermatology*, 26 (2017) 919.

Can we understand this transition and use it to deliver new tools for patients to self-manage flare-ups?
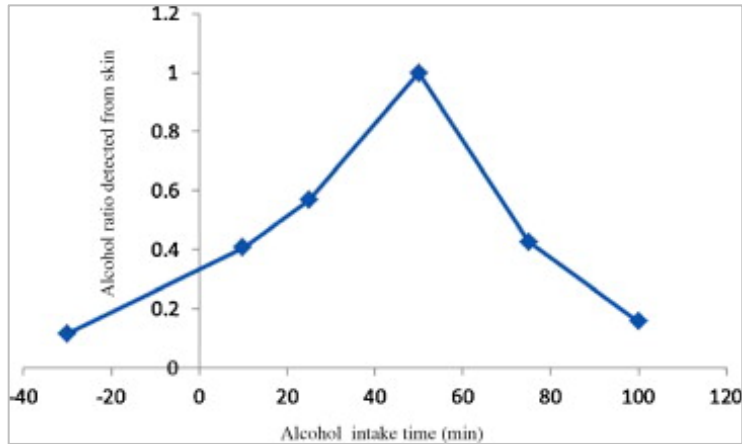
Ongoing clinical study at SVUH:
Understanding skin volatiles in chronic skin conditions & moles towards development of new non-invasive analytical tools

Naevus   Melanoma

www.cancer.gov
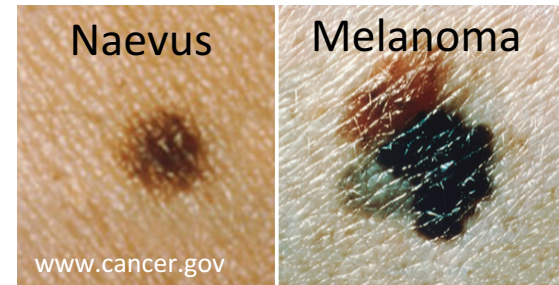
Some other research on skin volatiles
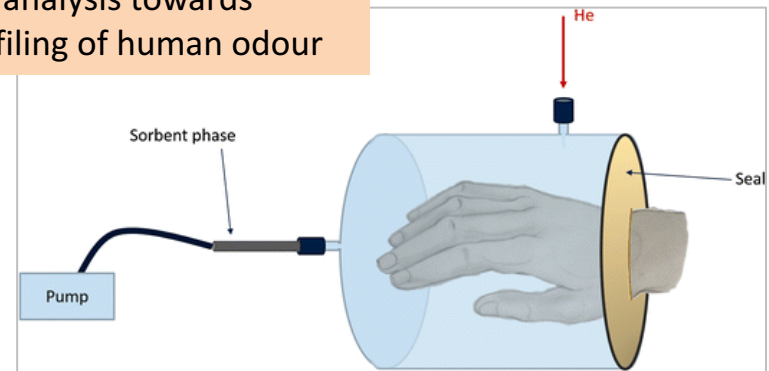
Detection of alcohol from the skin

R. Jiang, E. Cudjoe, B. Bojko *et al. Anal. Chim. Acta.* 804 (2013) 111.
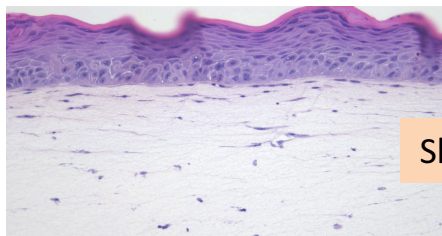
Understanding host-finding cues for mosquitoes

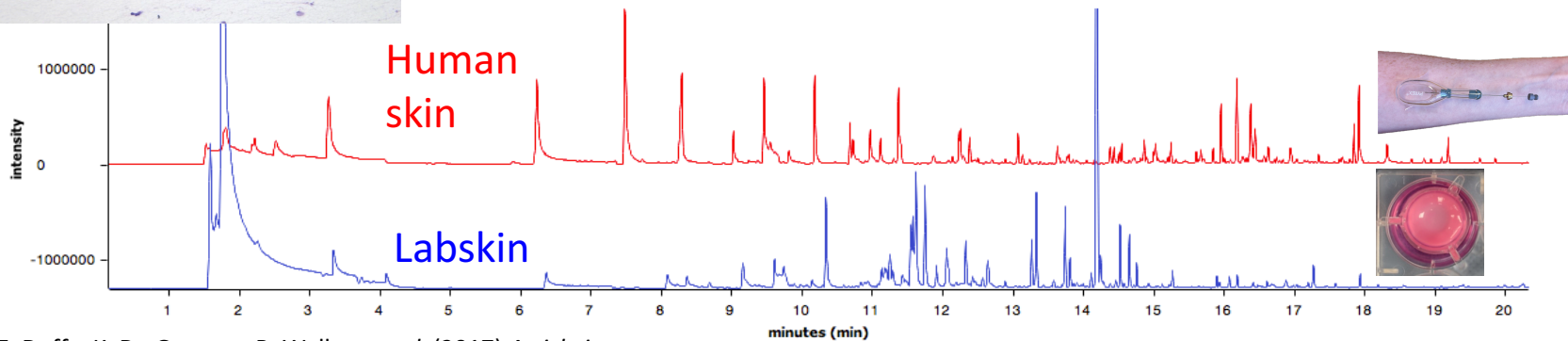N.O. Verhulst, B.T Weldegergis, D. Menger, W. Takken, *Sci. Rep.* 6 (2016) 27141.

Hand odour analysis towards forensic profiling of human odour

V. Cuzuel, E. Portas, G. Cognon *et al. Anal. Bioanal. Chem.* 409 (2017) 5113.

Skin barrier research

Human skin

Labskin

E. Duffy, K. De Guzman, R. Wallace *et al.* (2017) *Article in press*

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Thank you!

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