Fluorescent ratiometric micro-tattoos for monitoring applications

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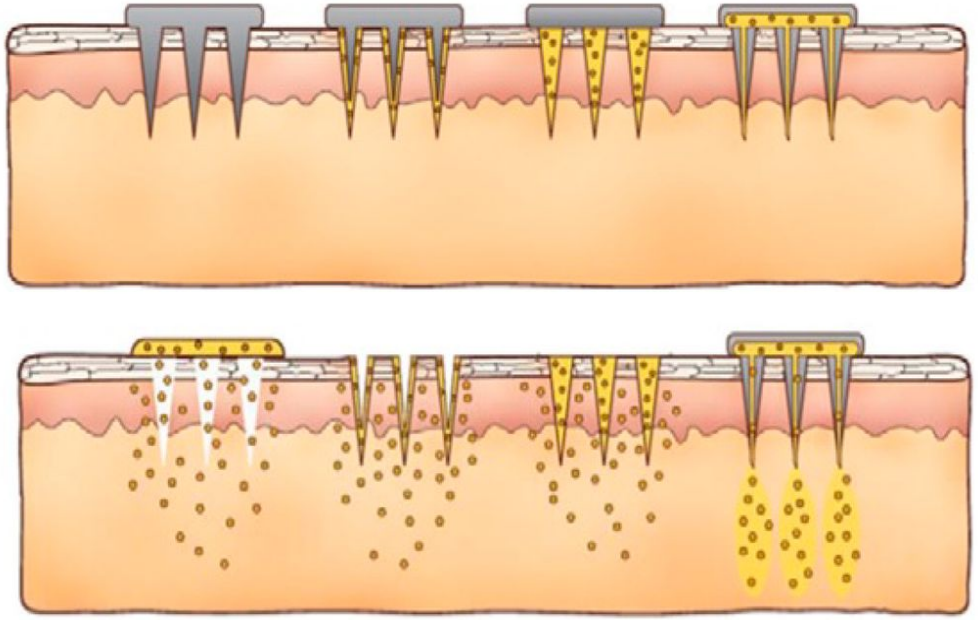
Advanced Delivery Science

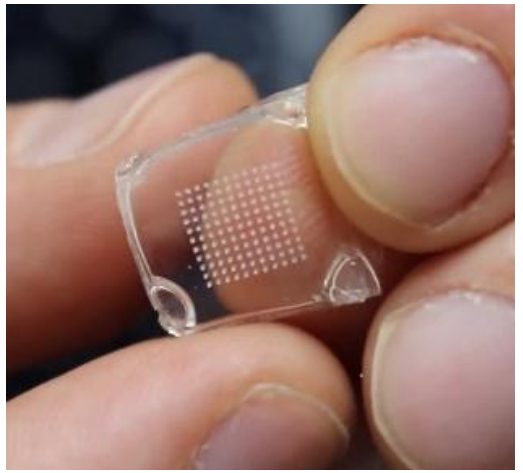
Microneedles

Miniaturized needles (hundreds of µm) at the midpoint between standard hypodermic needles and transdermal patches:
circumvent pain of hypodermic, allow the delivery of a considerably larger variety of molecules to the dermis compared to transdermal patches.



Main applications:

- Drug delivery
- Diagnostic/monitoring tools

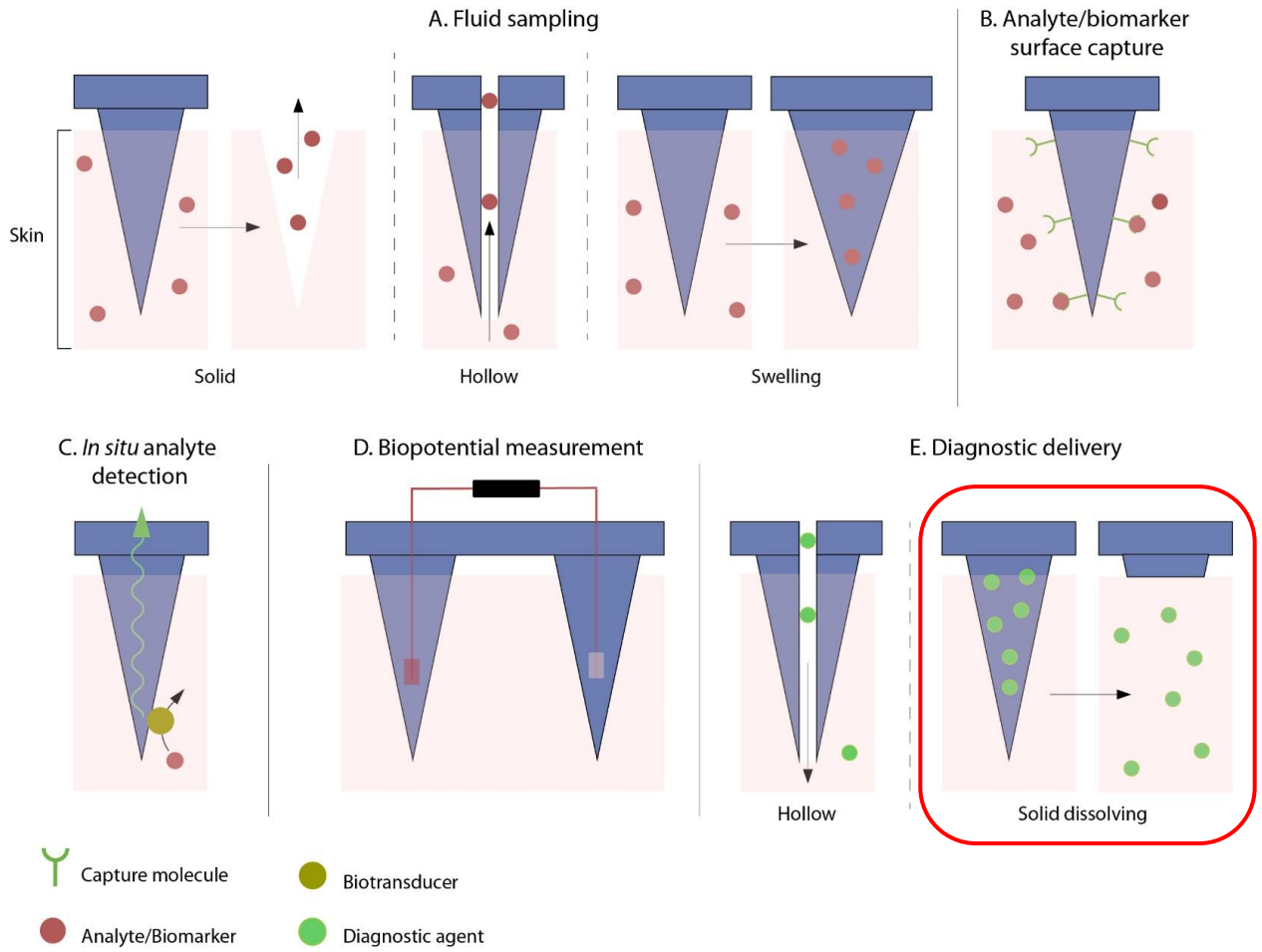


Kim YC *et al. Adv Drug Del Rev*, 2012

Diagnostic/monitoring applications of microneedles

Dermal ISF equilibrium with systemic circulation

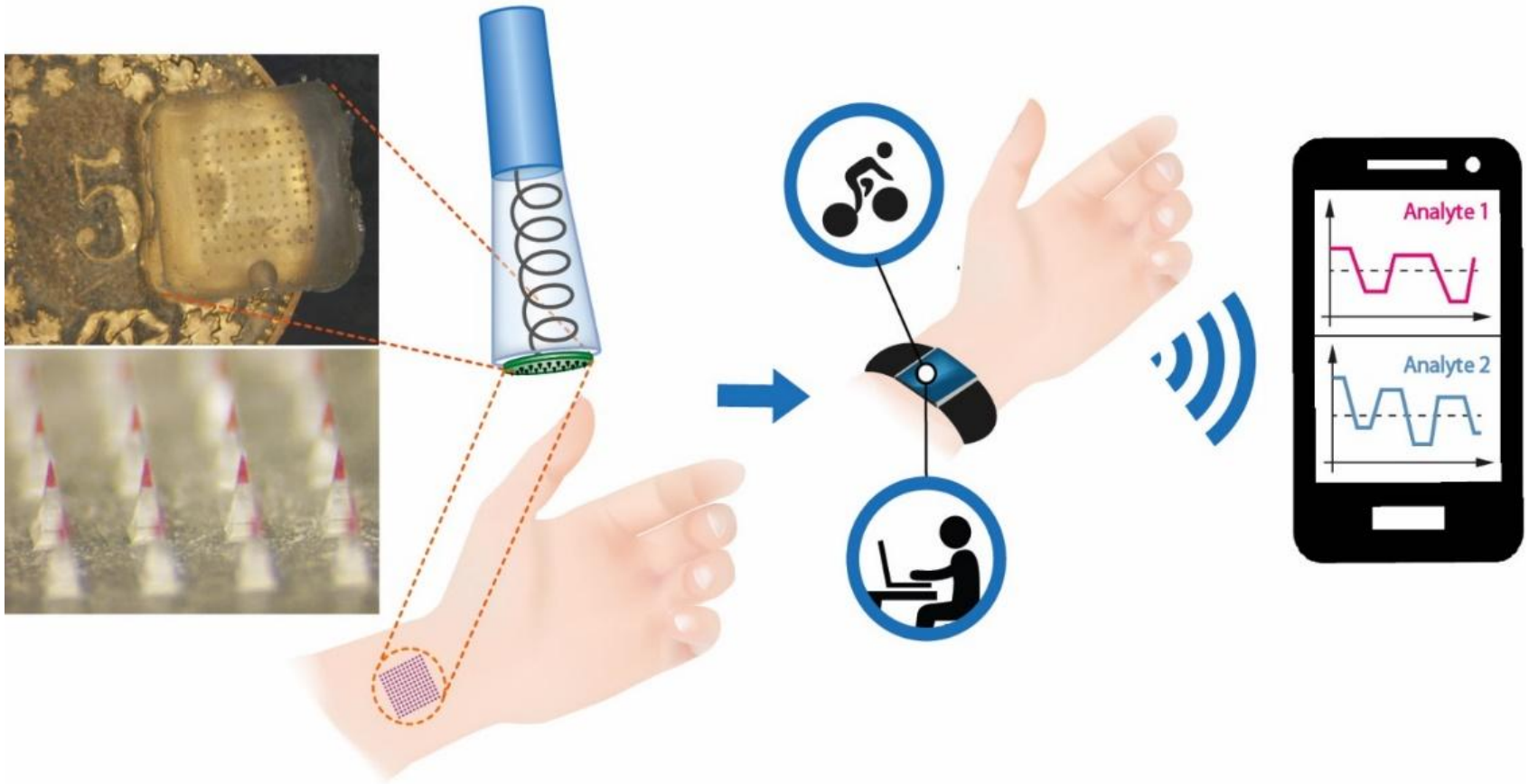
Health monigtorng is a rapid growing field of research and market



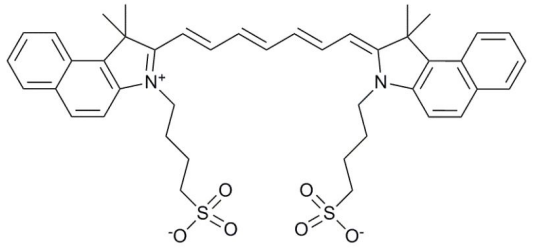
Babity S. *et al*. *Small*, 2018

Medical microTattoo: minimally-invasive monitoring of physiological parameters

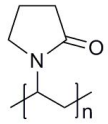
Can we collect informations about health and diseases from the skin non invisively and remotely?
EEG, O_2, HR...



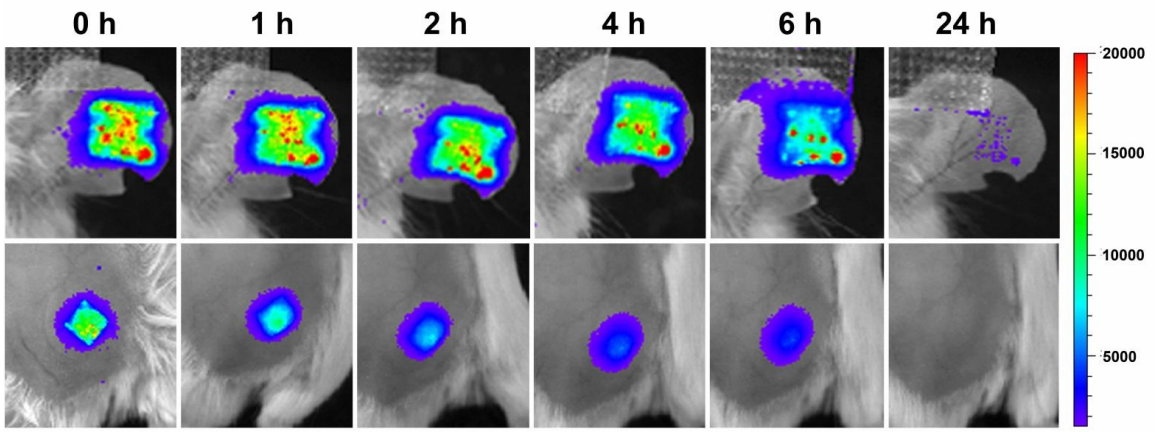
Lymphatic drainage quantification

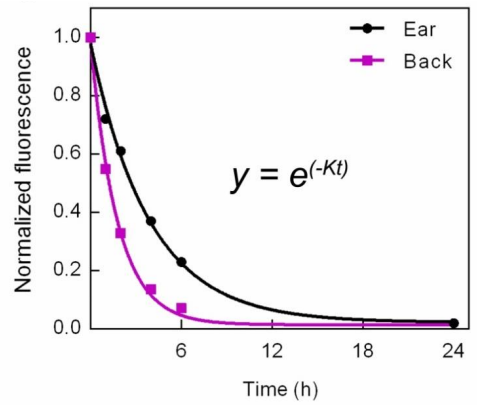


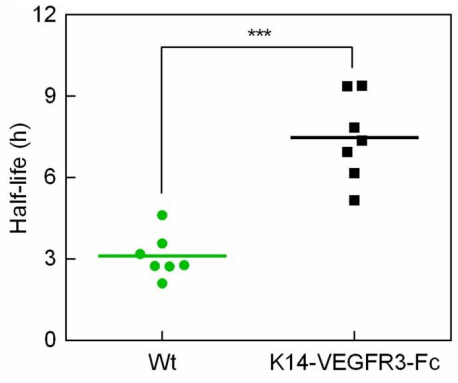
NIR imaging
Injectable



Solubilizer
Described for MNs
Injectable (low MW)





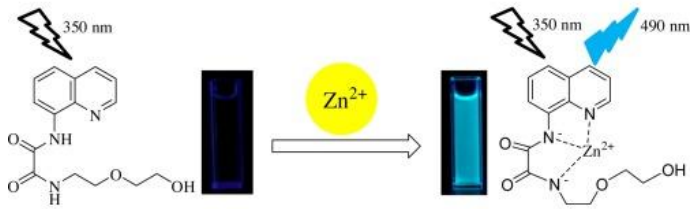


Monitoring of lymphatic drainage
Early stage identification of lymphedema

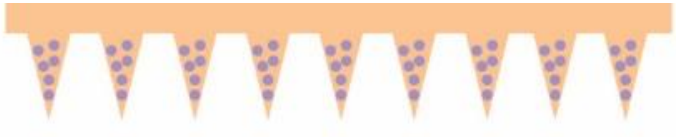
Expand the concept to other parameters?

Brambilla S. *et al*. *Small*, 2016. WO2016180835A1. *Babity et al. J Contr. Release 2020*

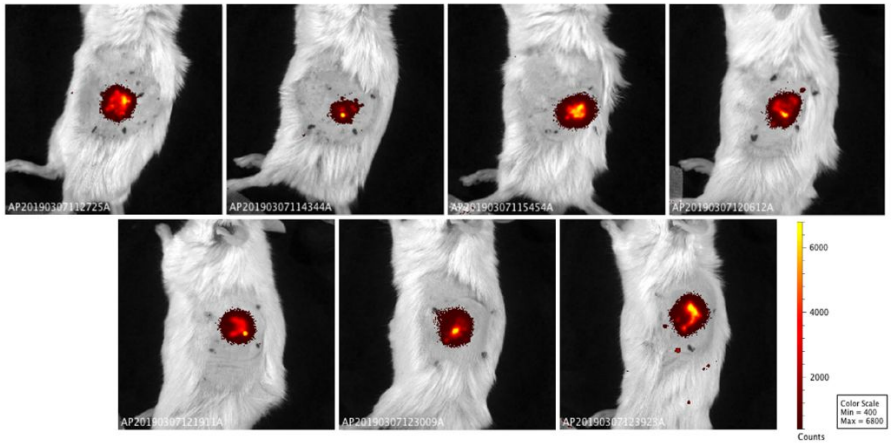
Bioresponsive tattoos

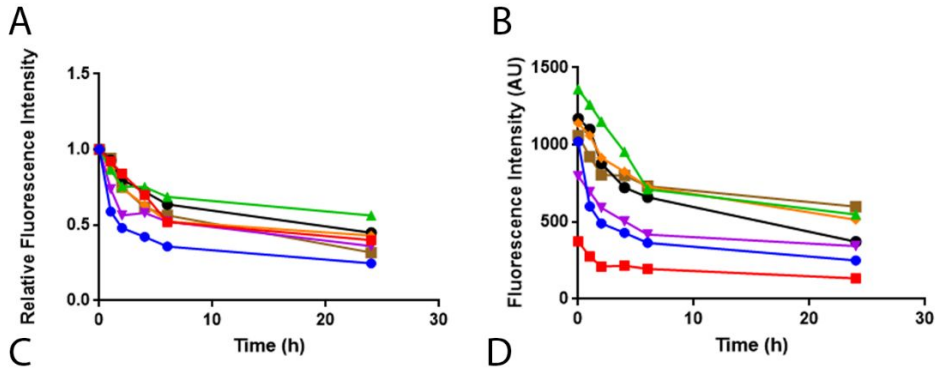


Delivery of switch-on probes to the ISF



Fluorescent intesity-based organic probes: <u>simple and inexpensive detection</u>



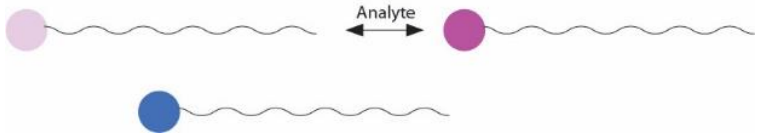


Ratiometric, low skin background (low amount delivered), soluble and stable

Our approach: a ratiometric tattoo

The probe

The stable reference

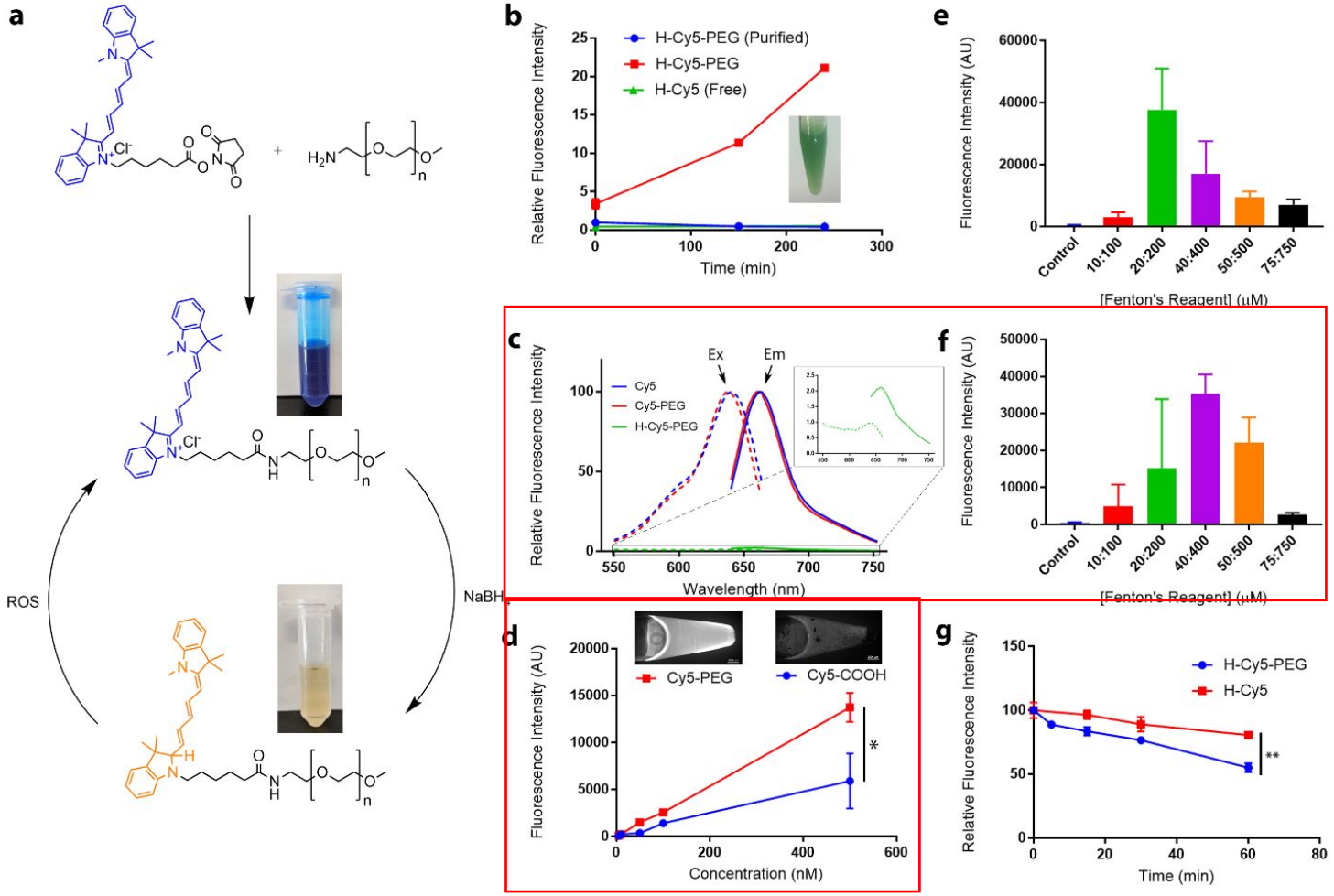


Same physico chemical properties (size, LogP, *etc.*): comparable delivery and diffusion

No fluorescence signal cross-talk

Skin inflammation: *proof of concept*

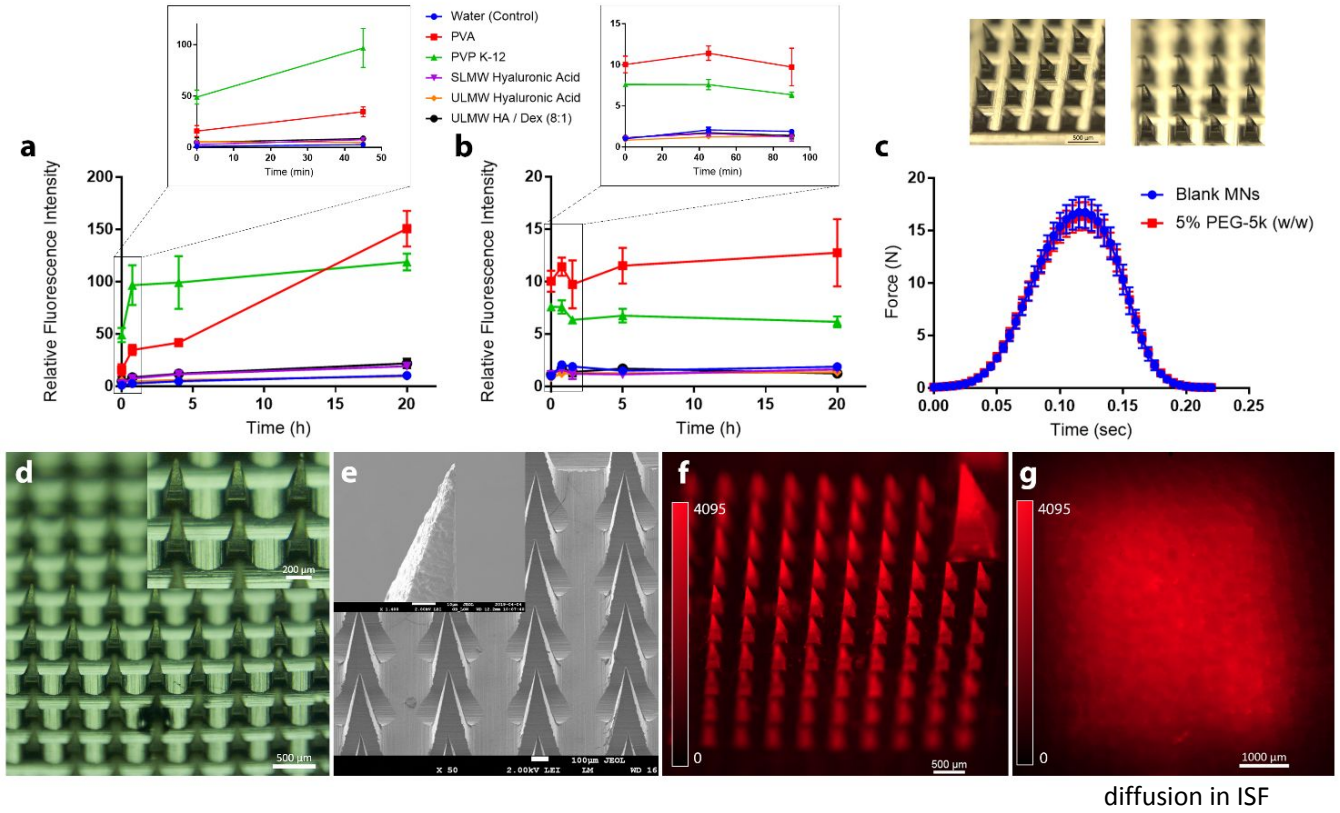
The sensor



Kundu K. *et al. Angewandte*, 2009; Andina D. *et al., Chem: A European Journal*, 2018;
Babity B. *et al. Data Brief*, 2020; Babity S. *et al. Adv. Healthc. Mat*. 2021

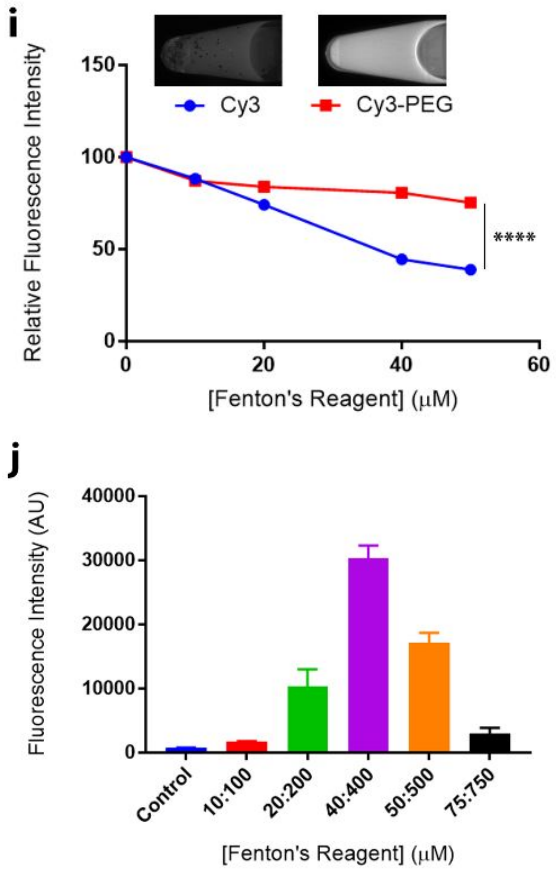
Skin inflammation: *proof of concept*

The microneedles



diffusion in ISF

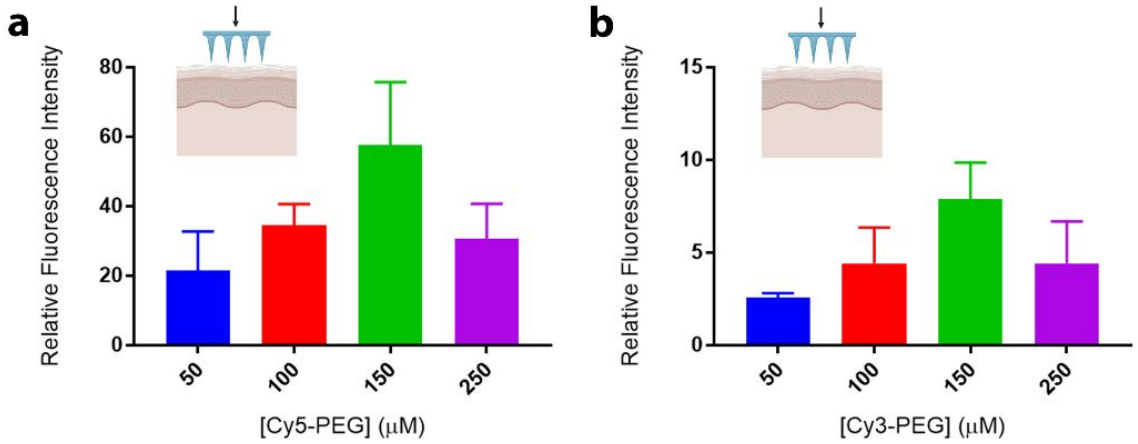
The reference dye

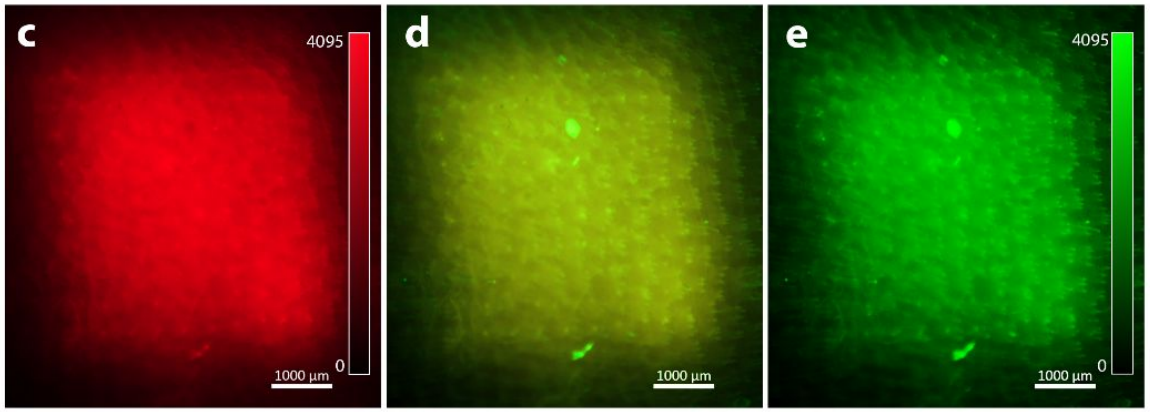


Babity S. *et al. Adv. Healthc. Mat*. 2021

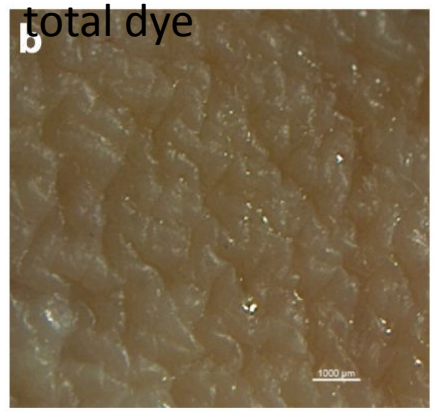
Skin inflammation: *proof of concept*

The tattoo





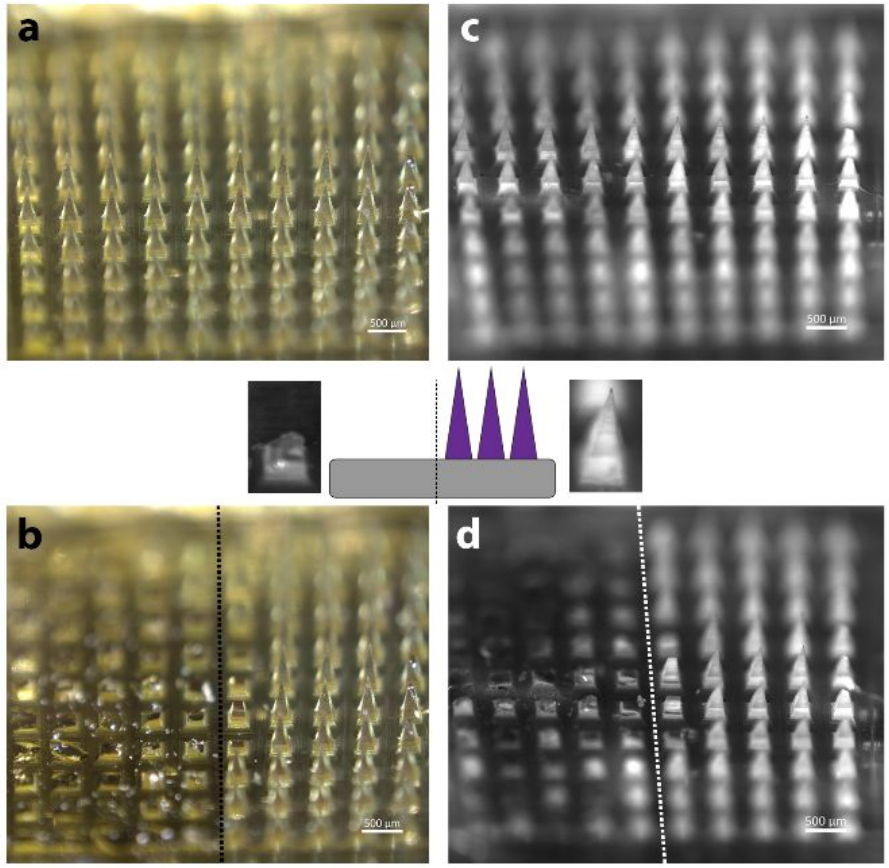
± 1 μg of total dye

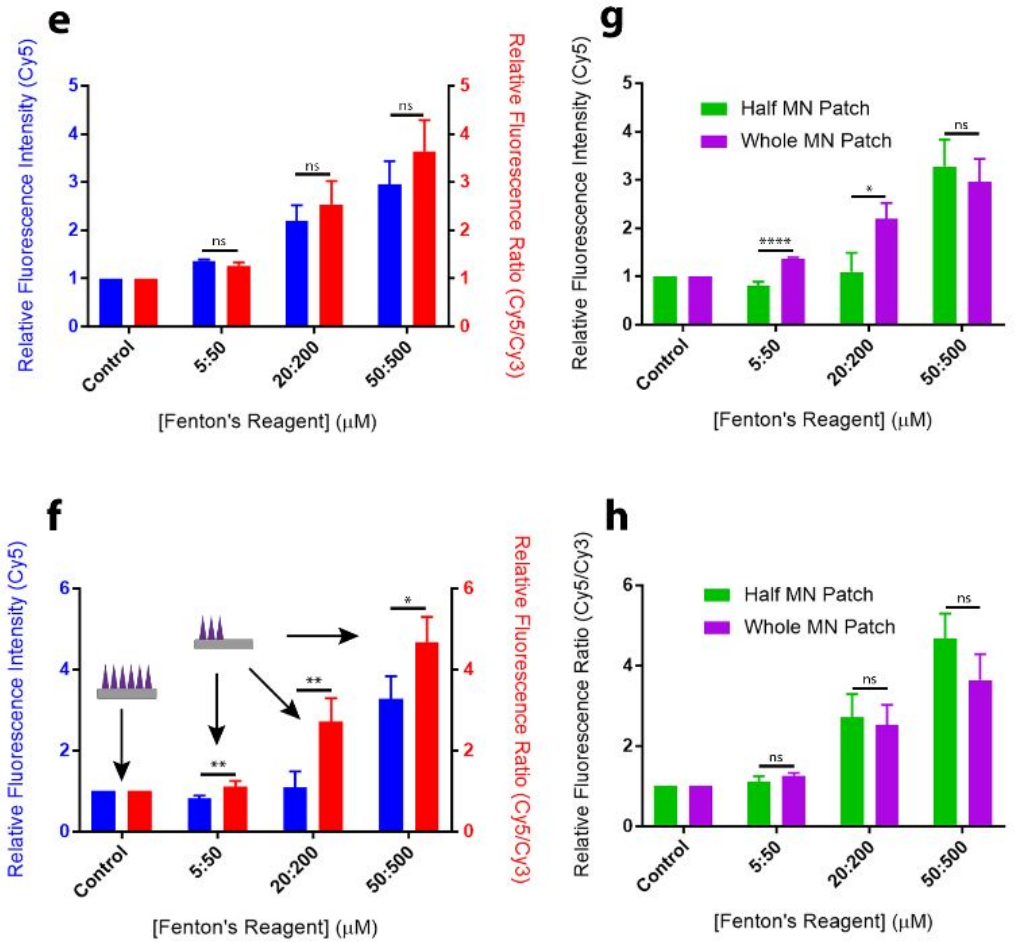


Babity S. *et al. Adv. Healthc. Mat*. 2021

Skin inflammation: *proof of concept*

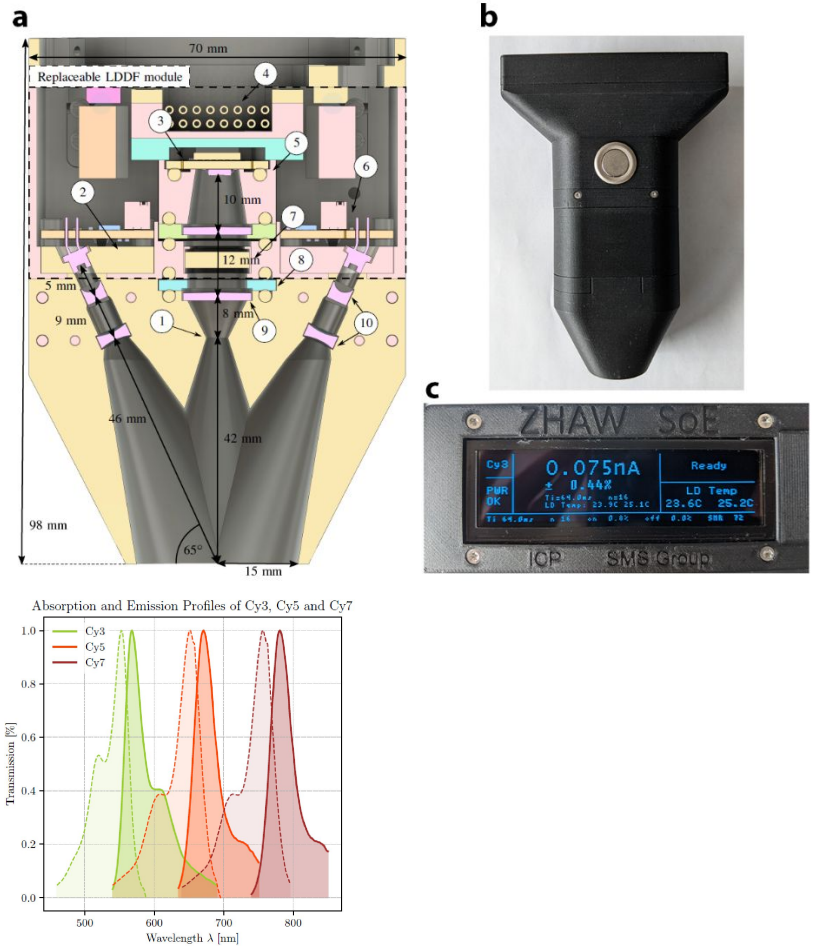
Ratiometric concept

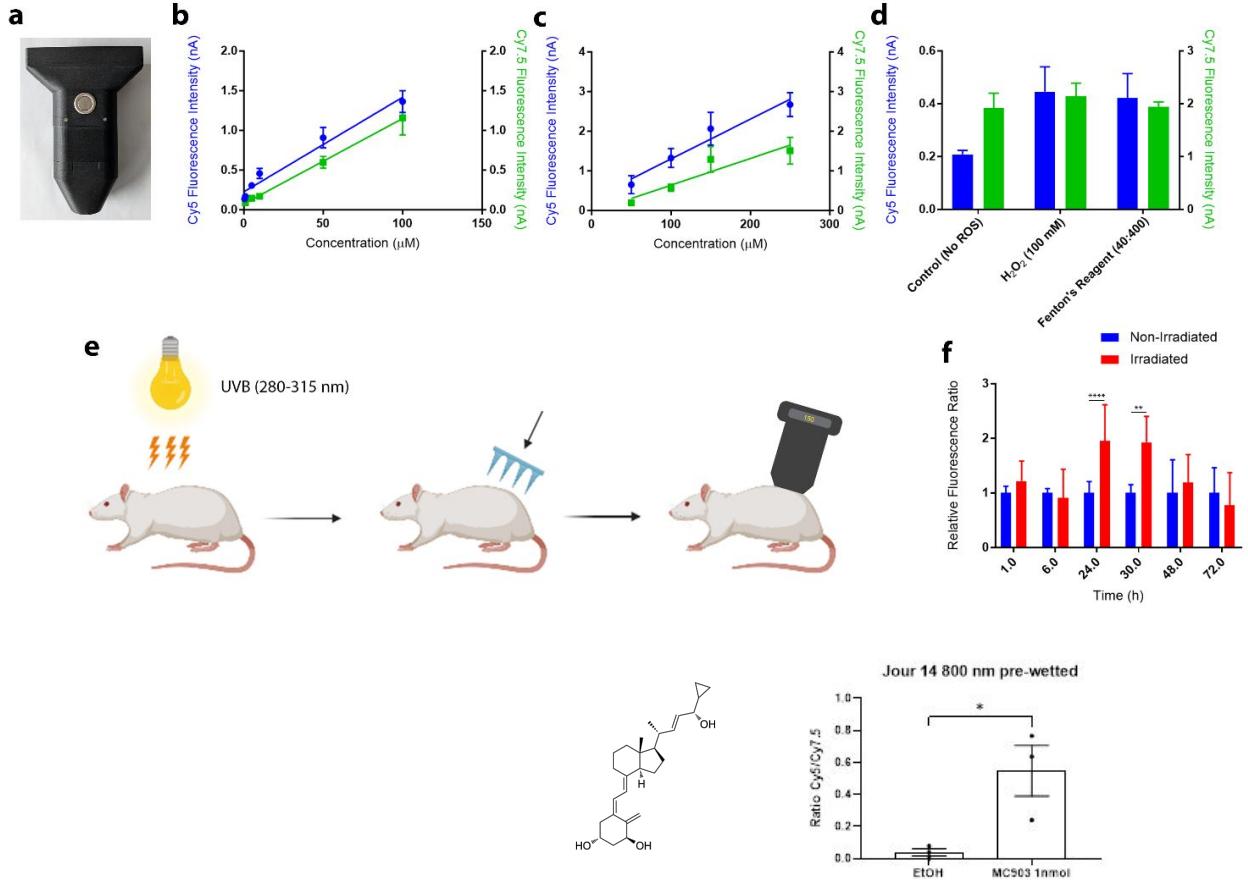




Babity S. *et al. Adv. Healthc. Mat*. 2021

Skin inflammation: *proof of concept, atopic dermatitis model*





Babity S. *et al. Adv. Healthc. Mat*. 2021

Conclusions

- MNs can be used to generate ratiometric micro-tattoo for monitoring physiological parameters non-invasively (potentially home based)
- A simple and versatile method for the fluorescence sensor signal normalization was developed: potentially allows the « quantification » of biological entities withouth the use of complex ratiometric probes

- We followed a linear path: inert dye (drainage), portable (wearable) equipment, implemented a responsive dye (implement normalization)..

Next

- Develop similar concept for biologically relevant molecules: disease biomarkers (more complex biosensors)
- Improve sensitivity
- Add two more aspects: **Quantification** and **Reversibility** (tune dermal residence time)

Acknowledgment

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