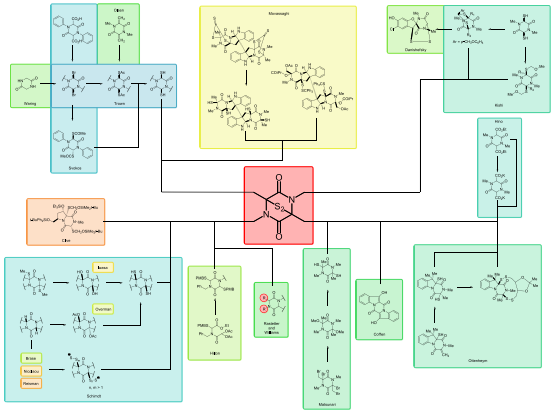
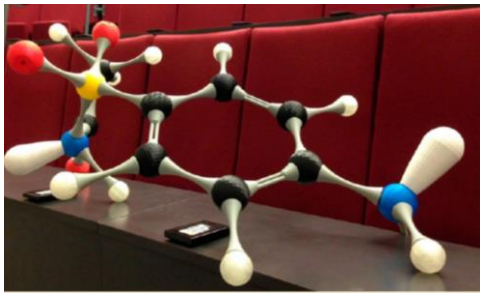
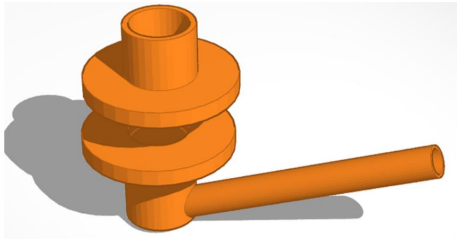
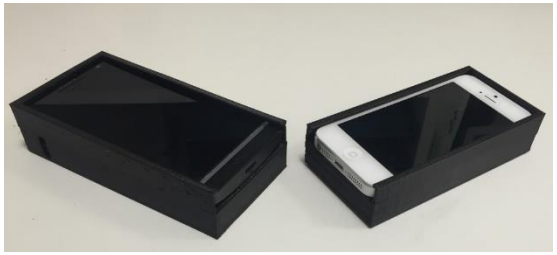
Crossing old barriers and printing new ones

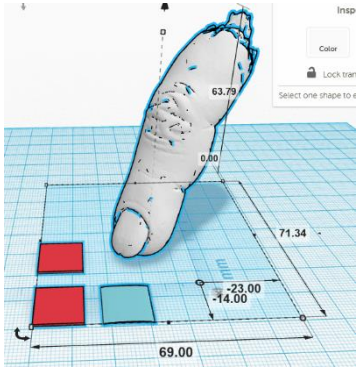
Skin, nails and additive manufacturing





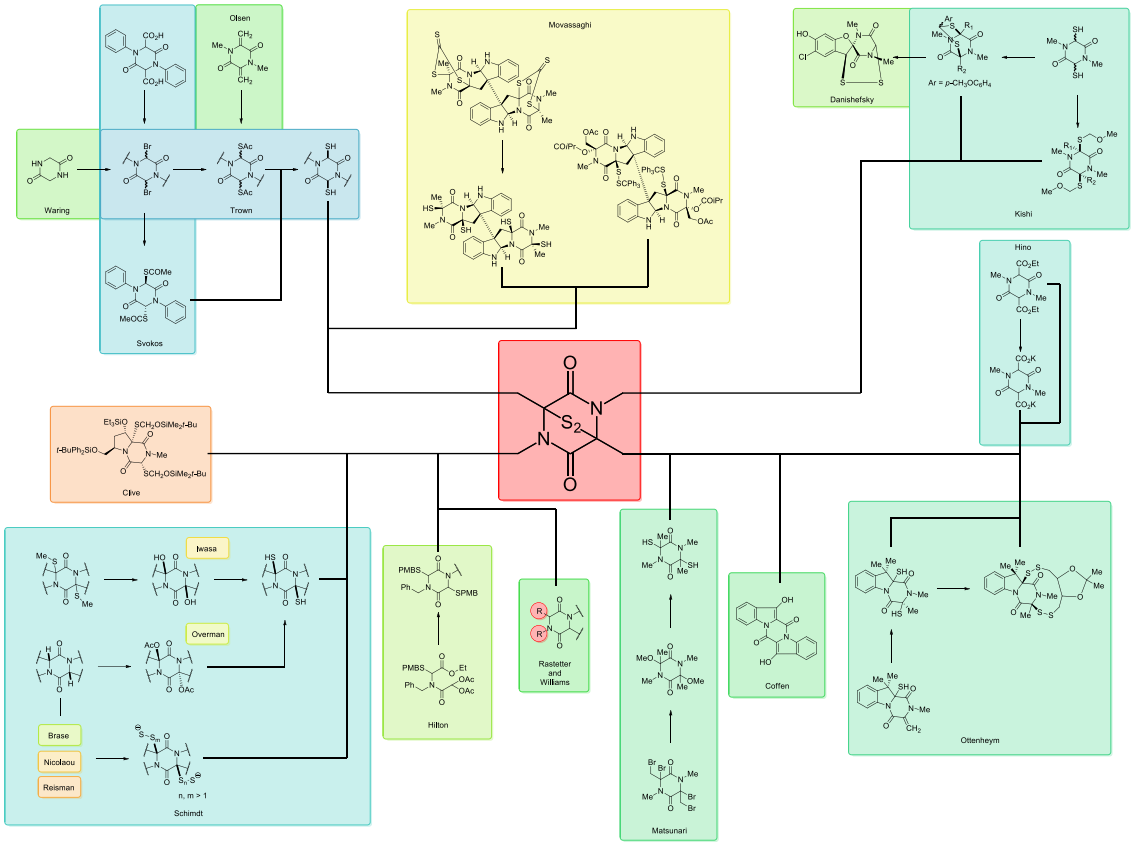






11.09.2019

Medicinal chemistry



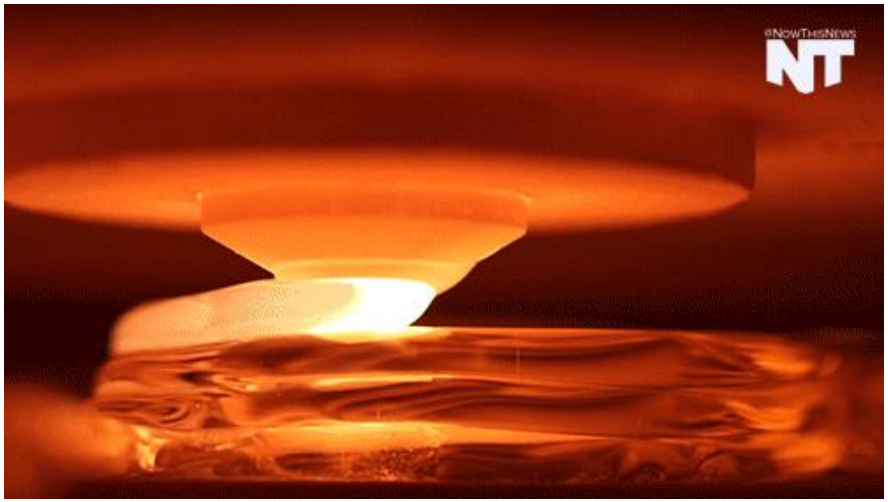
Publications

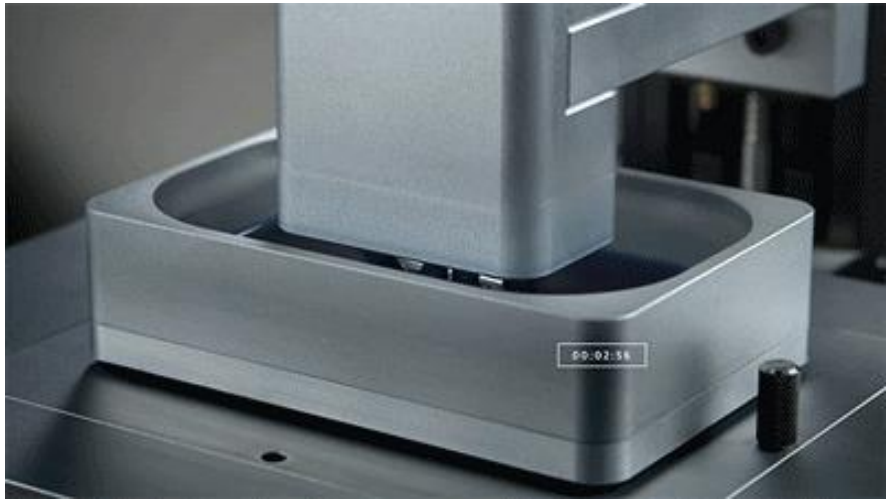
1. B. Sil, S.T. Hilton, A Mild and Convenient Base Catalysed Approach to Disubstituted Epidithiodiketopiperazines, Synlett, 24 (19) 2563 – 2566, DOI: 10.1055/s-0033-1340161. September 2013.
2. Blanka R. Szulc, Bruno C. Sil, A. Ruiz and Stephen T. Hilton, A Common Precursor Approach to Structurally Diverse Natural Products: The Synthesis of the Core Structure of (±)-Clausenamide and the Total Synthesis of (±)-Hyalodendrin, European Journal of Organic Chemistry, DOI: 10.1002/ejoc.201501256. September 2015.
3. Jing Li, Yaru Zhang, Bruno Da Silva Sil Dos Santos, Feng Wang, Yuyong Ma, Christian Perez, Yanling Yang, Junmin Peng, Seth M. Cohen, Tsui-Fen Chou, Stephen T. Hilton, Raymond J. Deshaies; Epidithiodiketopiperazines Inhibit Protein Degradation by Targeting Proteasome Deubiquitinase Rpn11, Cell Chemical Biology, 25, 1–9, DOI: https://doi.org/10.1016/j.chembiol.2018.07.012. August 2018.
4. Christopher Asquith, Bruno Sil dos Santos, Tuomo Laitinen, Graham Tizzard, Simon Coles, Antti Poso, Regina Hofmann-Lehmann, Stephen Hilton; Novel Epidithiodiketopiperazines as anti-viral zinc ejectors of the Feline Immunodeficiency Virus (FIV) nucleocapsid protein as a model for HIV infection, Bioorganic & Medicinal Chemistry, DOI: https://doi.org/10.1016/j.bmc.2019.07.047. July 2019.

3D Printing

3D printing, also known as additive manufacturing (AM), refers to processes used to synthesize a three-dimensional object in which successive layers of material are formed under computer control to create an object.

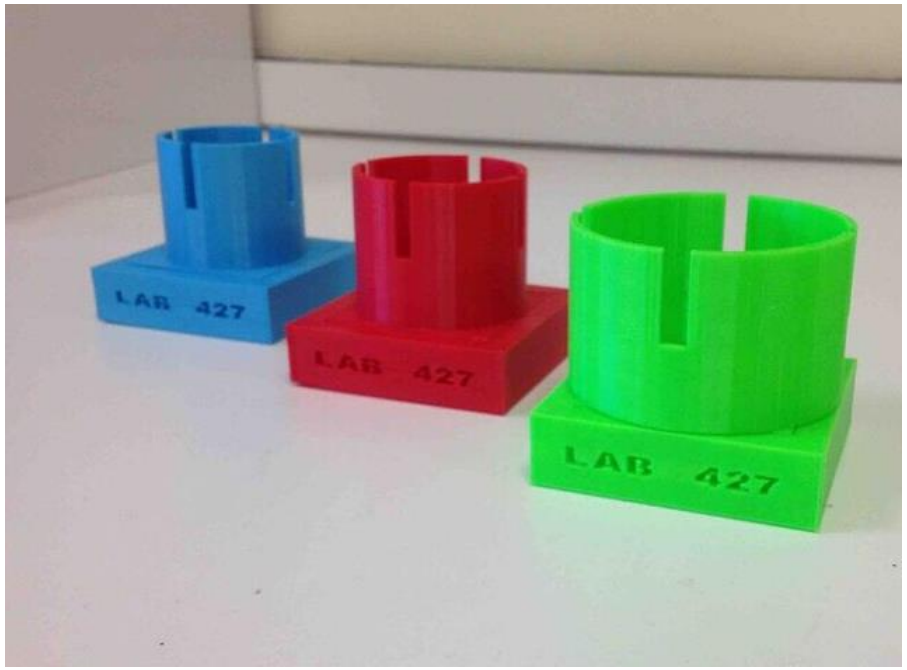
Source: Wikipedia



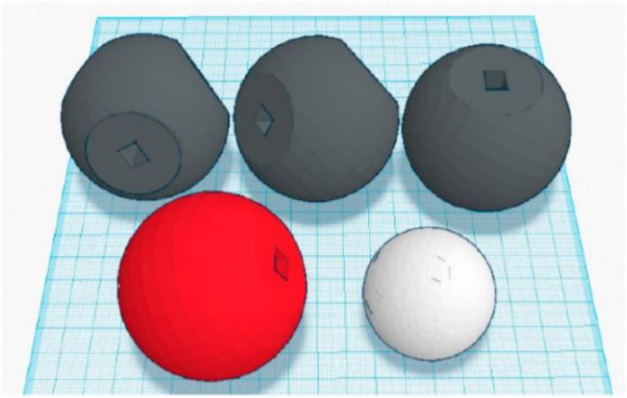


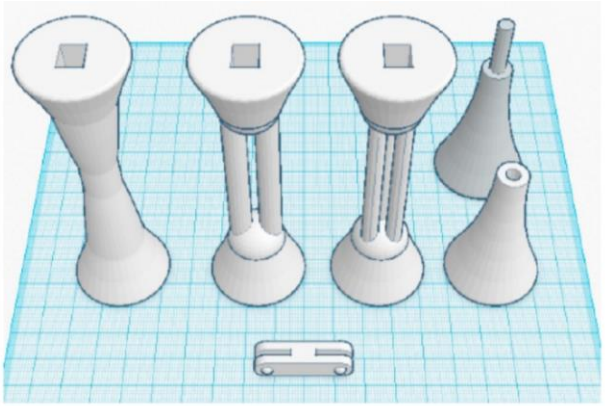
Laboratory equipment

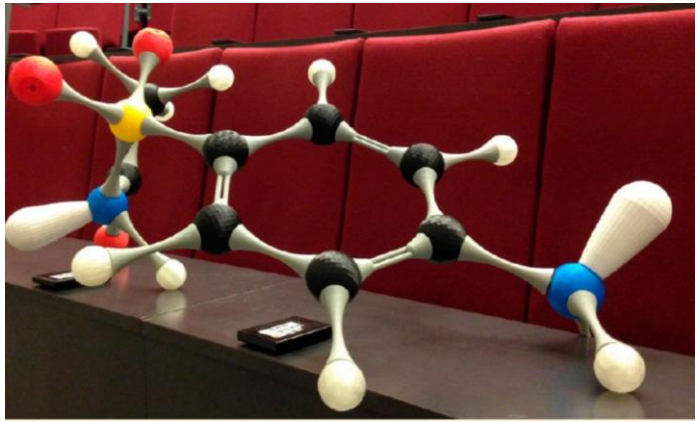
"Lets go around the lab and see what's needed"
"Can we print something that's expensive?"
"Can we customise?"
"Research? Teaching?"



Educational tool





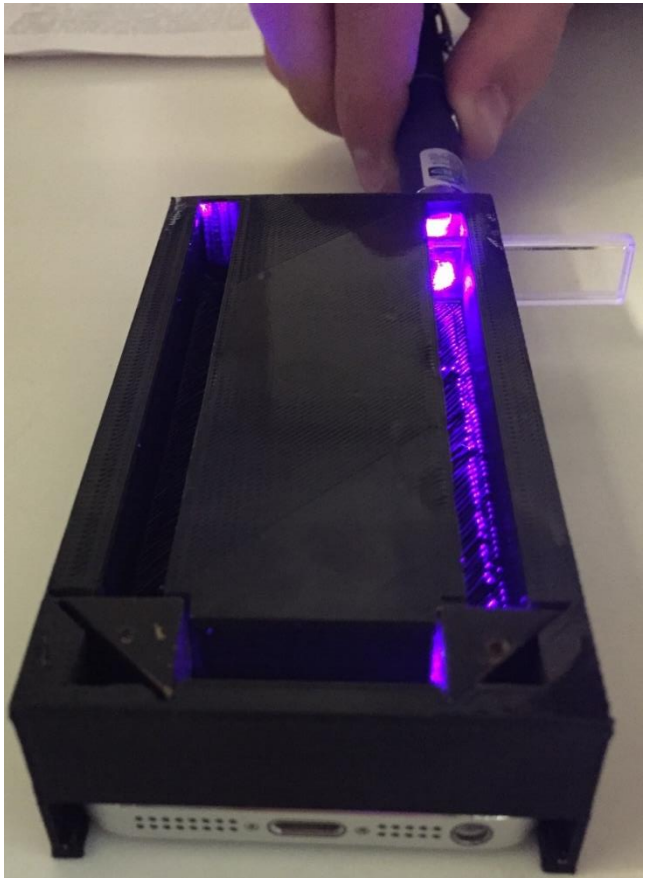


Matthew R. Penny, Zi Jing Cao, Bhaven Patel, Bruno Sil dos Santos, Christopher R. M. Asquith, Blanka R. Szulc, Zenobia X. Rao, Zaid Muwaffak, John P. Malkinson, and Stephen T. Hilton; Three-Dimensional Printing of a Scalable Molecular Model and Orbital Kit for Organic Chemistry Teaching and Learning, Journal of Chemical Education, 94, 9, 1265-1271, DOI: 10.1021/acs.jchemed.6b00953. August 2017.

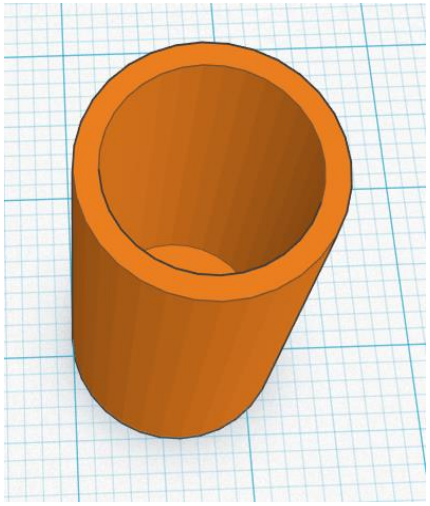
UCL iSense Group

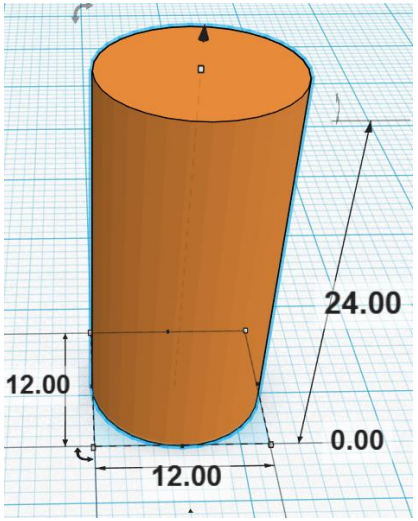
Early-Warning Sensing Systems for Infectious Disease

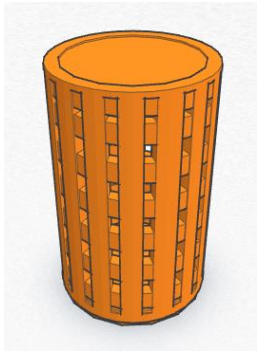
A Novel Sensor System for Influenza (mobile spectrometer)

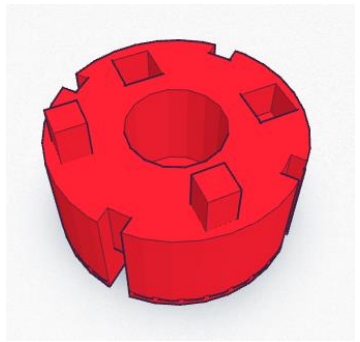


Impregnated plastics for chemical reactions





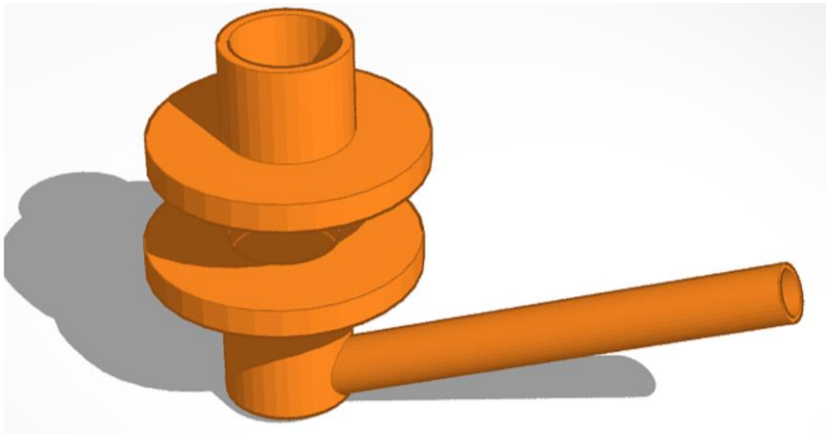


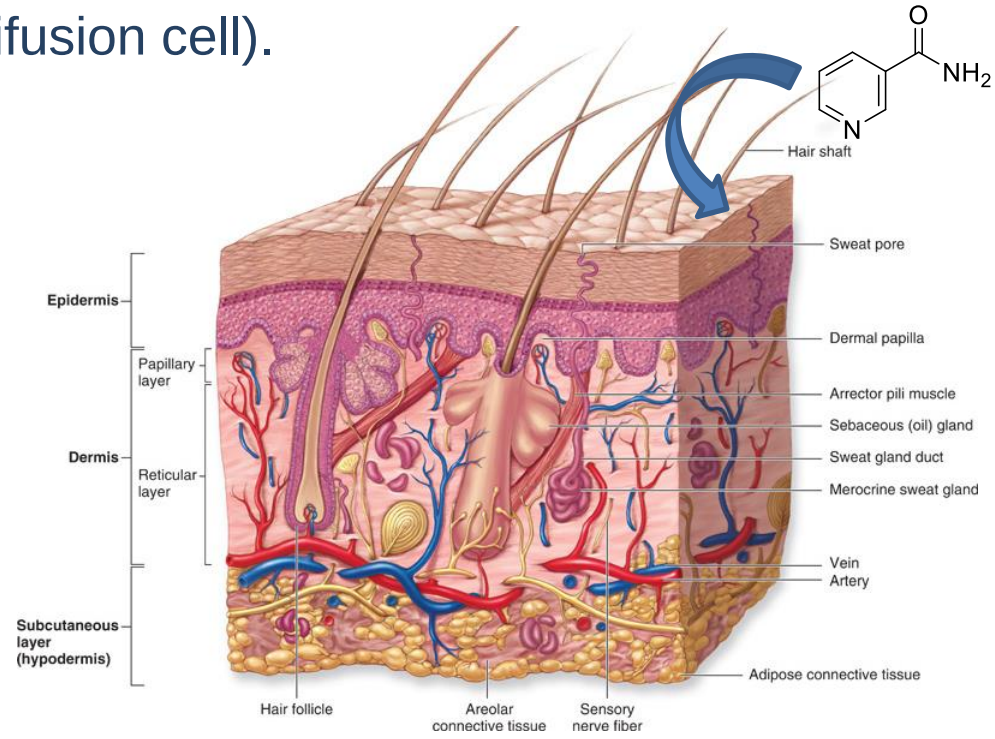


Patent PCT/GB2017/050685, Three-dimensional printing of impregnated plastics for chemical reactions. December 2017.

UCL Skin Research Group

- Niacinamide permeation studies in novel biomimetics.
- Drug delivery systems (Franz difusion cell).

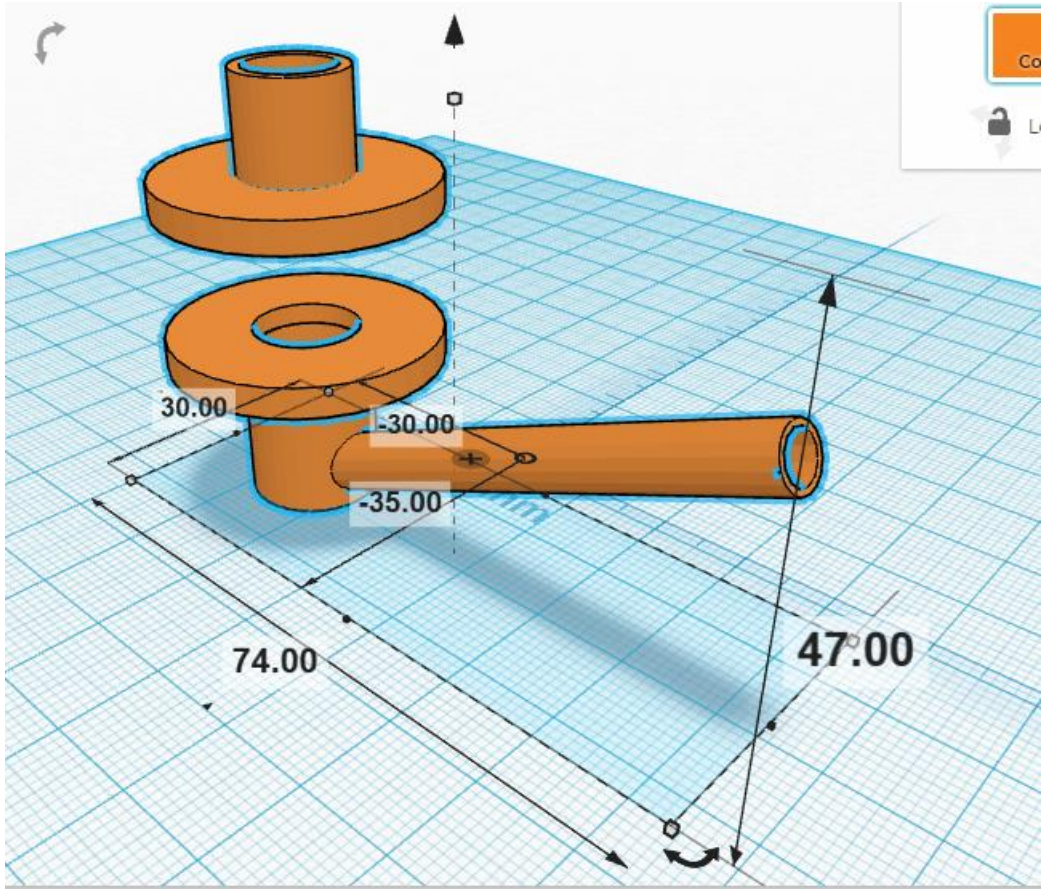




Publications

1. Tasnuva Haque, Bruno C. Sil, Majella E. Lane, Jonathan M. Crowther, David J. Moore; In vitro permeation and disposition of niacinamide in silicone and porcine skin of skin barrier-mimetic formulations, International Journal of Pharmaceutics, Volume 520, Issues 1–2, Pages 158-162, ISSN 0378-5173, https://doi.org/10.1016/j.ijpharm.2017.01.054. March 2017.
2. B. C. Sil, D. J. Moore, M. E. Lane; Use of LC-MS analysis to elucidate by-products of niacinamide transformation following in vitro skin permeation studies, International Journal of Cosmetic Science, 1–5, DOI: 10.1111/ics.12486. September 2018.
3. Fotis Iliopoulos, Bruno C. Sil, David J. Moore, Robert A. Lucas, Majella E. Lane; 3-O-ethyl-l-ascorbic acid: Characterisation and investigation of single solvent systems for delivery to the skin, International Journal of Pharmaceutics, DOI: https://doi.org/10.1016/j.ijpx.2019.100025. July 2019.
4. Yanling Zhang, Bruno C. Sil, Chin-Ping Kung, Jonathan Hadgraft, Michael Heinrich, Balint Sinko, Majella E. Lane; Characterization and topical delivery of phenylethyl resorcinol, International Journal of Cosmetic Science, DOI:. August 2019.
5. Chin-Ping Kung, Bruno C Sil, Jonathan Hadgraft, Majella E. Lane, Bhumik Patel, Renée McCulloch; Preparation, Characterization and Dermal Delivery of Methadone, Pharmaceutics, DOI. August 2019.

UCL Skin Research Group



Glass

3D

<1 £

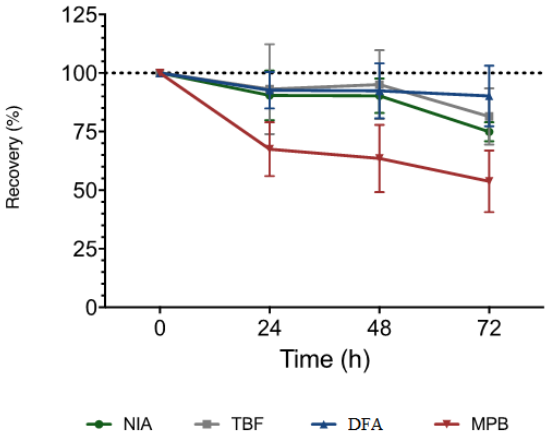
Expensive

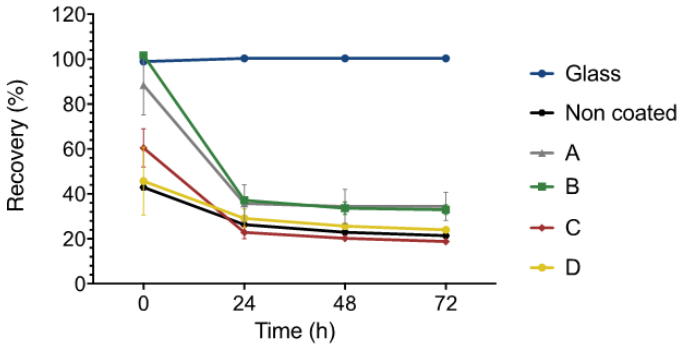
Quick

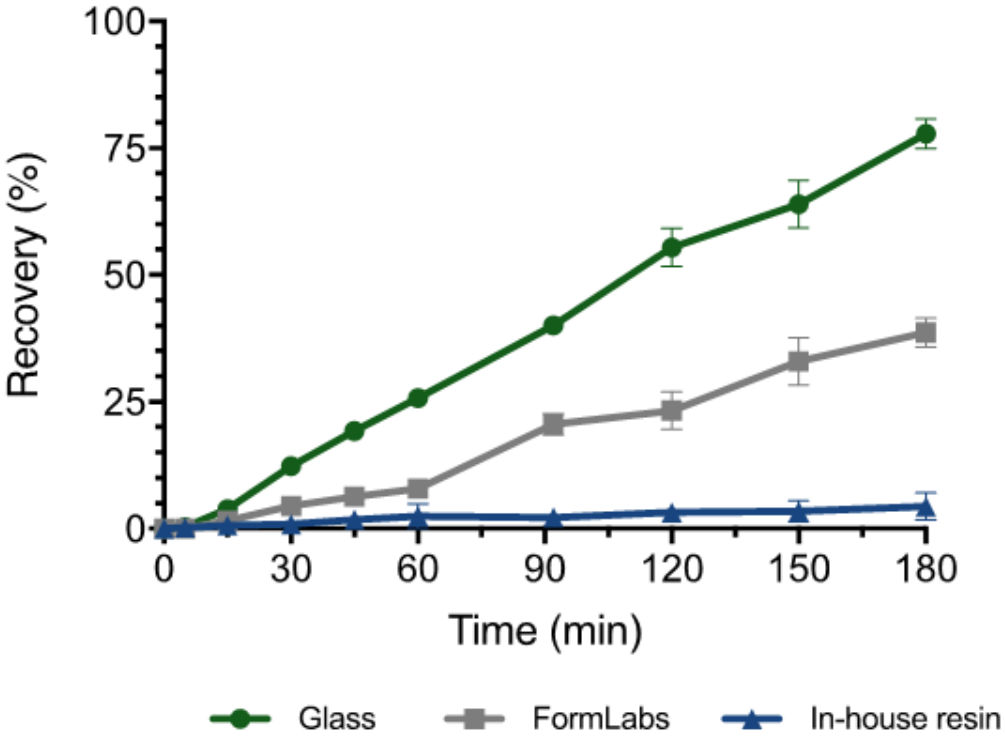
Outsource

Do it yourself

UCL Skin Research Group (3D FC)







- Permeation of methylparaben (1.5 mg/mL) evident, but not at the same rate for conventional glass cells and 3D printed Franz cells .

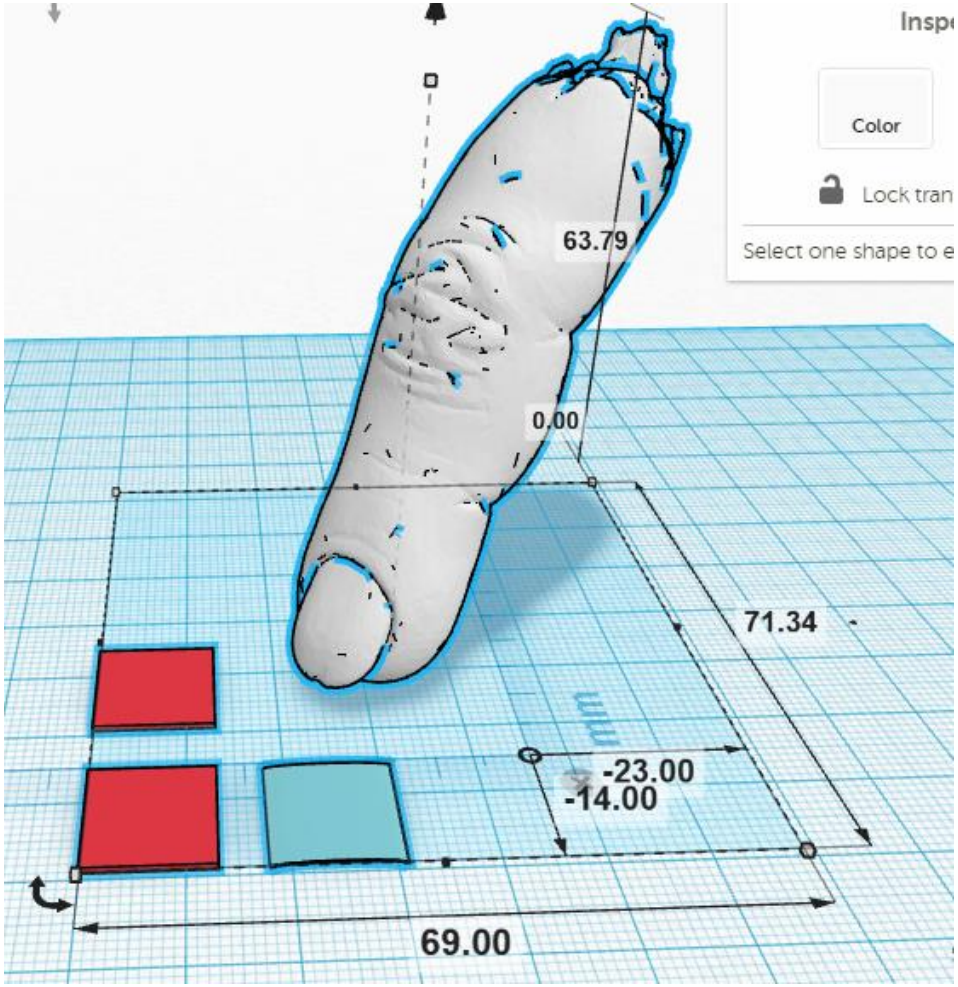
Bruno C. Sil, Miguel P. Alvarez, Yanling Zhang, Chin-Ping Kung, Monjur Hossain, Fotis Iliopoulos, Lin Luo, Jonathan M. Crowther, David J. Moore, Jonathan Hadgraft, M. E. Lane, Stephen T. Hilton; 3D-printed Franz type diffusion cells, International Journal of Cosmetic Science, DOI: 10.1111/ics.12504. December 2018.

UCL Skin Research Group (3D Nail)

Rationale of the project

- Assessment of the efficacy of new formulations for treatment of nail diseases requires the provision of human nails or an appropriate surrogate tissue.
- Human nails are difficult to source, variable in quality and their use is associated with ethical and safety issues.
- Diseased nail models not available.
- In recent years, 3D printing has evolved to develop bioprinting of tissues including skin, bone, cartilage and skeletal muscle.
- Costs of biocompatible resins allied with the complexities of biological tissues have limited the widespread use of the technology.

UCL Skin Research Group (3D Nail)



Nails

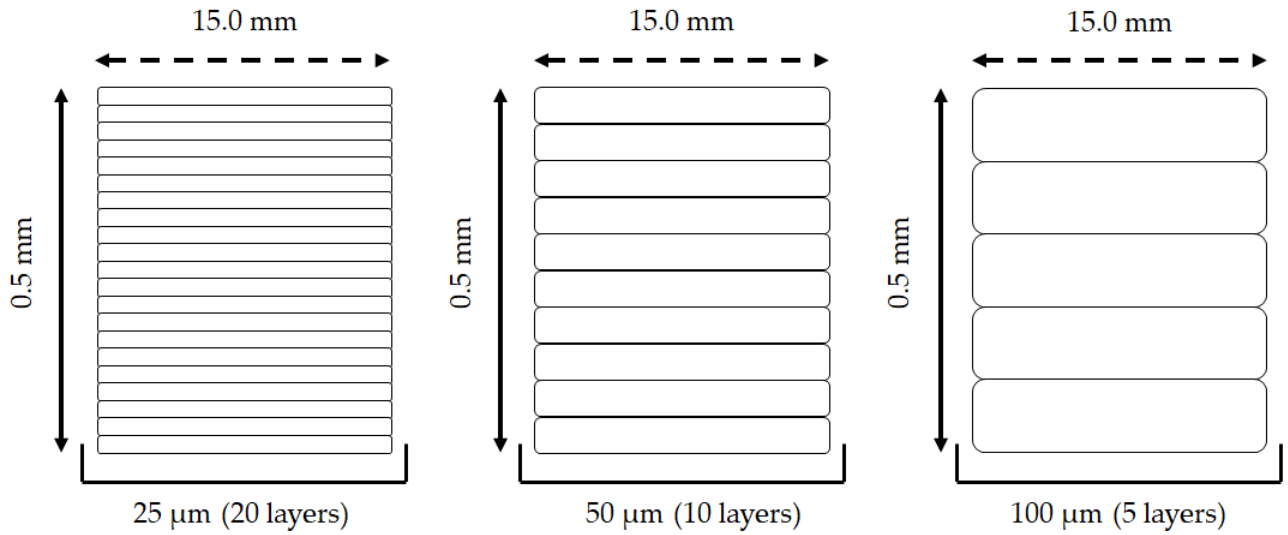
≈ 0.5 mm

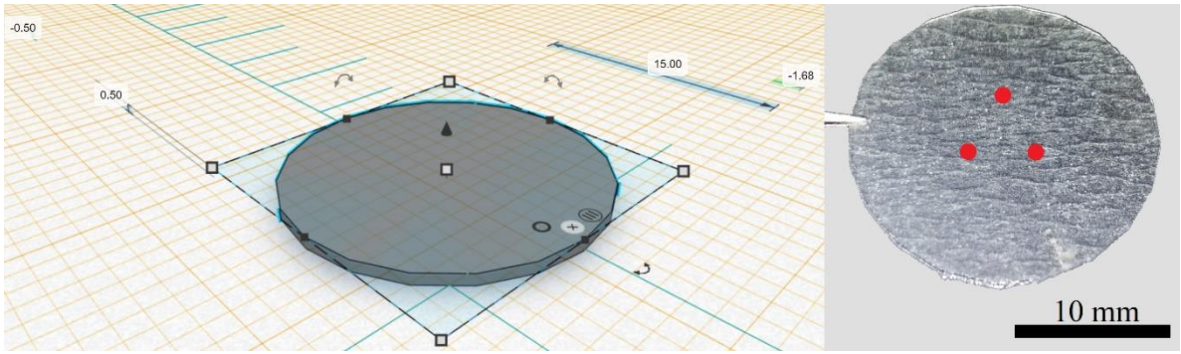
25 layers

Resolution of Form 1+ is 25 µm

Allows usage of custom resins

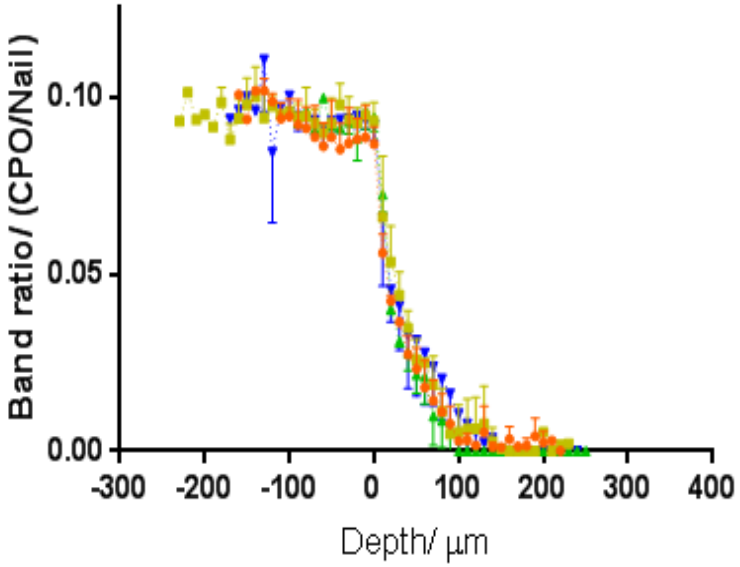
UCL Skin Research Group (3D Nail)



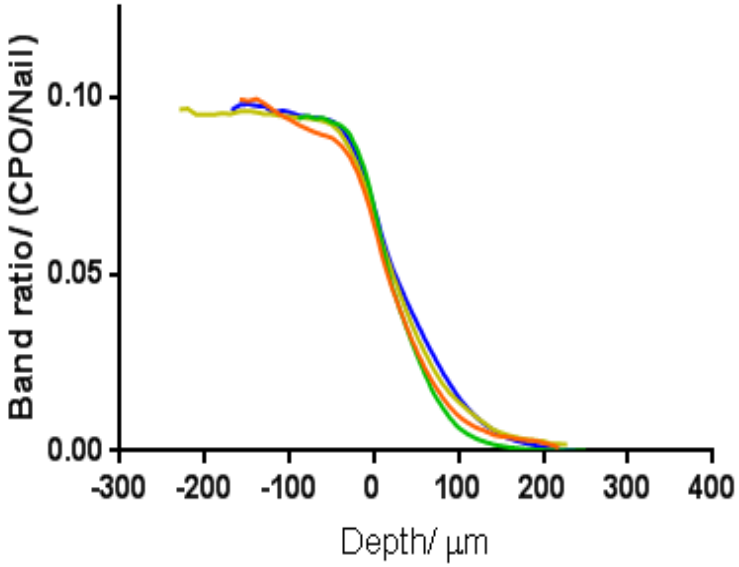


UCL Skin Research Group (3D Nail)

MYCOSTER with film



Curve: LOWESS of MYCOSTER with film

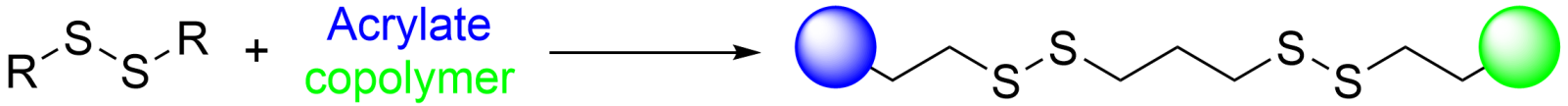


Bruno C. Sil, Avnish Patel, Jonathan M. Crowther, David J. Moore, Jonathan Hadgraft, Stephen T. Hilton, Majella E. Lane; A Preliminary Investigation of Additive Manufacture to Fabricate Human Nail Plate Surrogates for Pharmaceutical Testing, Pharmaceutics, DOI:10.3390/pharmaceutics11060250. May 2019.

UCL / LMU (3D Nail)

Rationale of the project

- Make nails more “human-like”: introduction of **disulfide bonds** and **increase hydrophilicity**.
- Chemistry:



- Nails to test: **Commercial resin**, **commercial resin S-S** and **“hydrophilic polymer”**.
- Literature review for actives with well studied permeations profiles: **methylparaben** and **caffeine**.

UCL / LMU (3D Nail)

Permeation studies

- Application of **different amounts** of the chosen compounds: saturated solutions, 1.5 mg/mL, 500 µg/mL, 200 µg/mL and 100 µg/mL.
- **Permeation study:** 3 prep days + 21 permeation days (last day includes mass balance).
- So far: commercial resin and “hydrophilic resin” nails (**some permeation**).
- Currently running: “hydrophilic resin” and commercial resin S-S nails.
- Future work: different “hydrophilic resins” and the real stuff!

Terbinafine
Amorolfine
Tioconazole
Ciclopirox

UCL / LMU (3D Nail)

Permeation studies (MPB and CAF solutions)

Resin type	Nail resolution (µm)	Tested compound (n=3)	Applied solution (top of nail)	Nail extraction (inside the nail)	Permeation (pass the nail)
Commercial	25	Saturated MPB	56.13%	34.26%	-
	50		54.57%	37.63%	-
	100		60.58%	34.82%	-
Commercial	25	1.5 mg/mL MPB	33.07%	55.44%	-
	50		27.98%	63.34%	-
	100		41.41%	53.08%	-
Commercial	100	200 µg/mL CAF	91.01%	1.10%	-
Hydrophilic nail	100	200 µg/mL MPB	42.88%	23.34%	16.76%
Hydrophilic nail	100	200 µg/mL CAF	89.76%	1.14%	-