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Materials: the more the merrier!

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gsk
Malvern
PPG
syngenta
Unilever


“you can print anything”


WHAT'S THE PROBLEM?

Phill, we asked a 100 companies what was holding AM back …

Tim, are materials on there?

The UK National Strategy for Additive Manufacturing revealed that lack of materials was the #1 concern for adoption of AM/3DP

http://www.amnationalstrategy.uk/

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So let’s find some materials …

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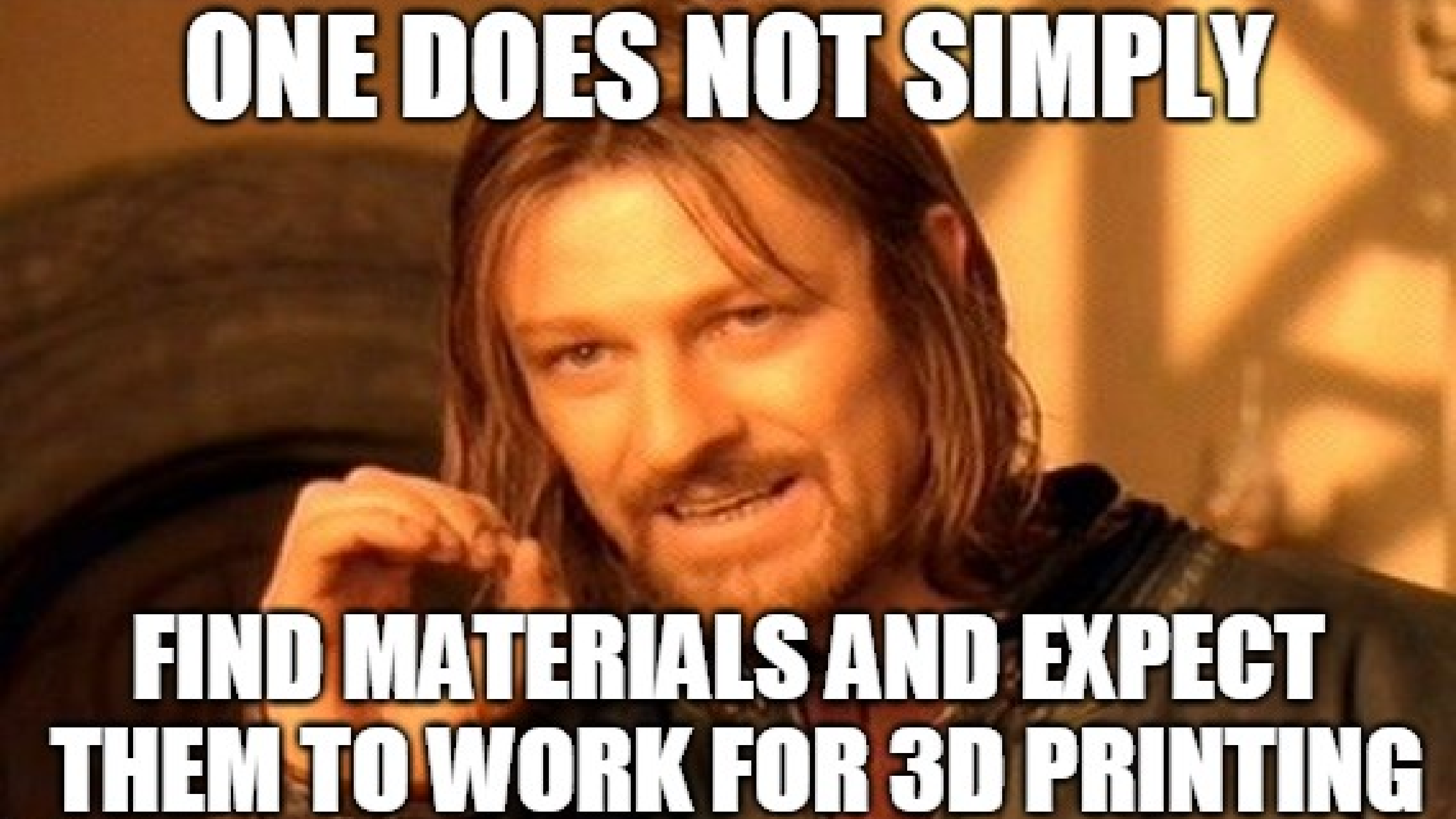
ONE DOES NOT SIMPLY
FIND MATERIALS AND EXPECT
THEM TO WORK FOR 3D PRINTING

An example formulation problem

- Find materials that enable ink jet printing of a highly soluble drug compound
- Demonstrate that drug can elute
- Demonstrate that elution can be undertaken in GI transit times

Ropinirole HCl (Requip™)

For treatment of Parkinson's

Highly soluble in water

Clark et al. '3D Printing of Tablets using Inkjet with UV photoinitiation'
International Journal of Pharmaceutics, 529 2017 523-530

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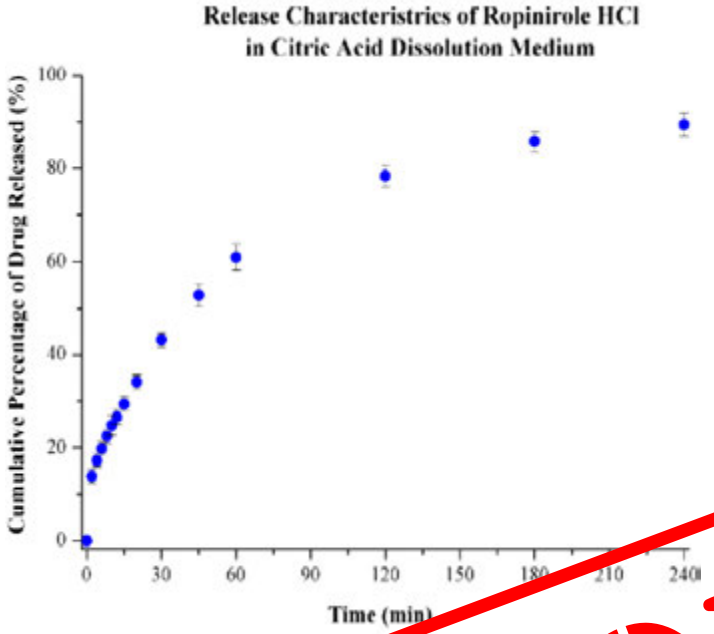
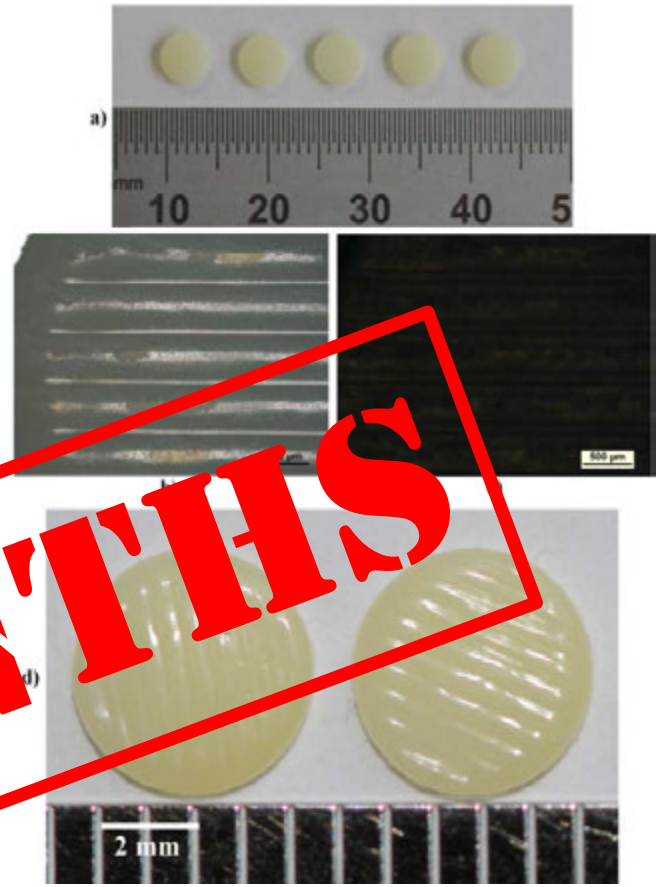
UV curable materials for solid dosage forms

Material	wt %
PEGDA	30
Irgacure 2959	0.5
ropinirole	2
Water	67.5

Formulation:

- Printable
- API stable
- API elutes within prescribed limits





12 MONTHS

but it took a long time to produce a single formulation that may not work for other APIs

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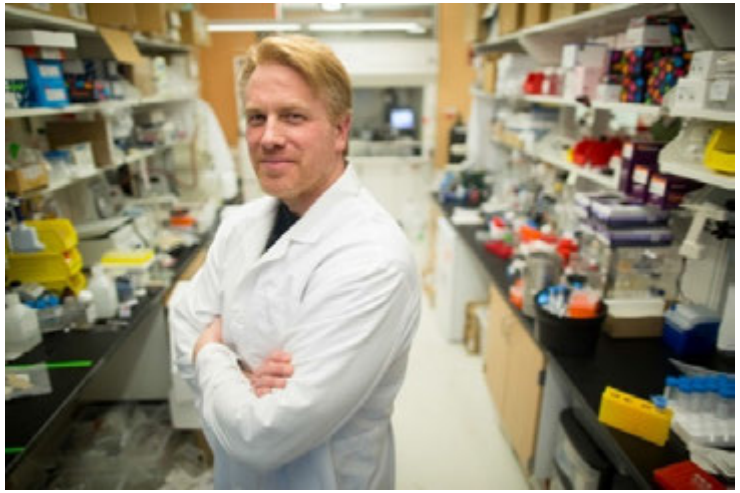
Serendipity

who was inspired by this chap …



Introduced to this guy …

to work with Paul Williams
to fight microbial resistance

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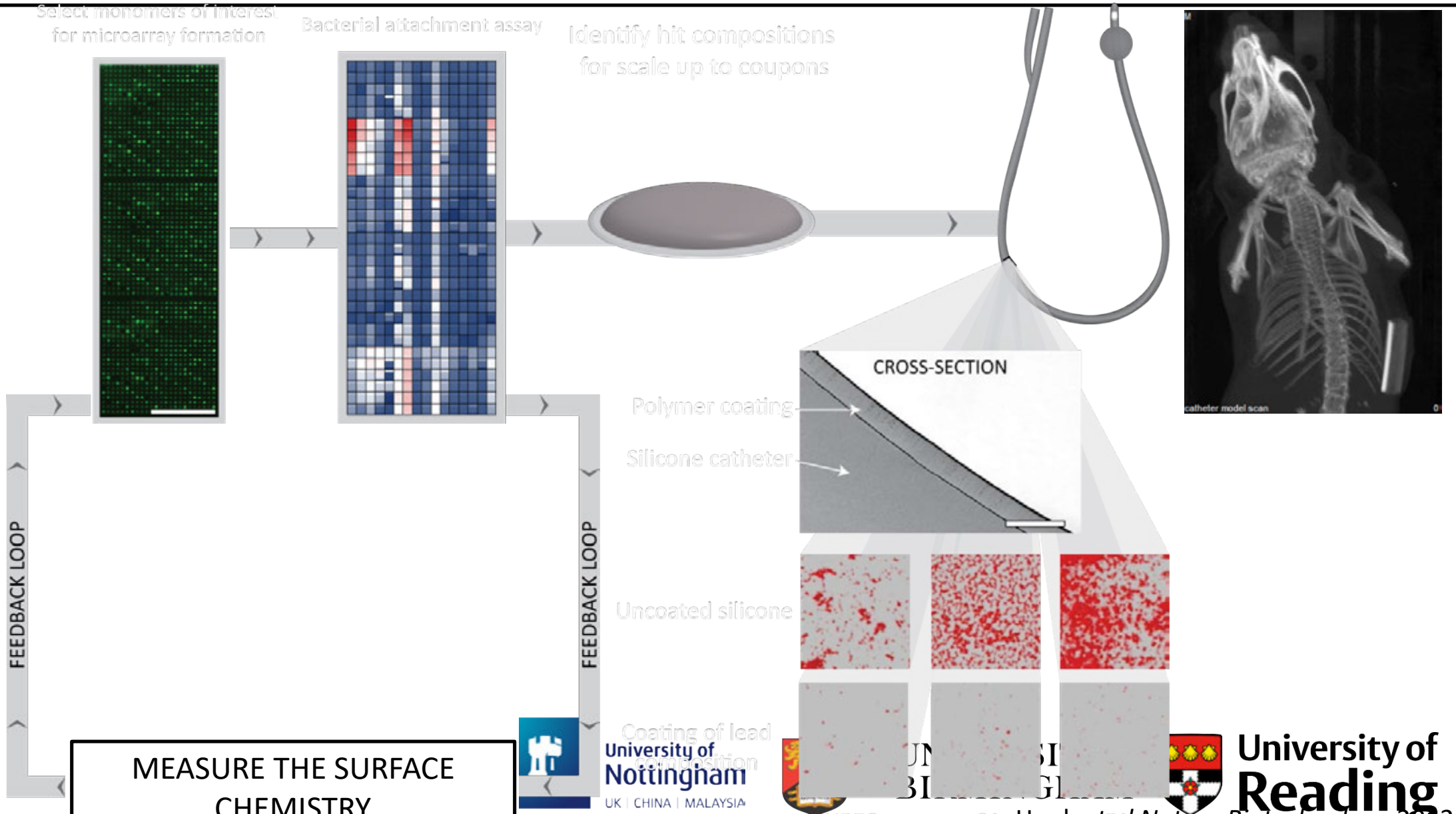
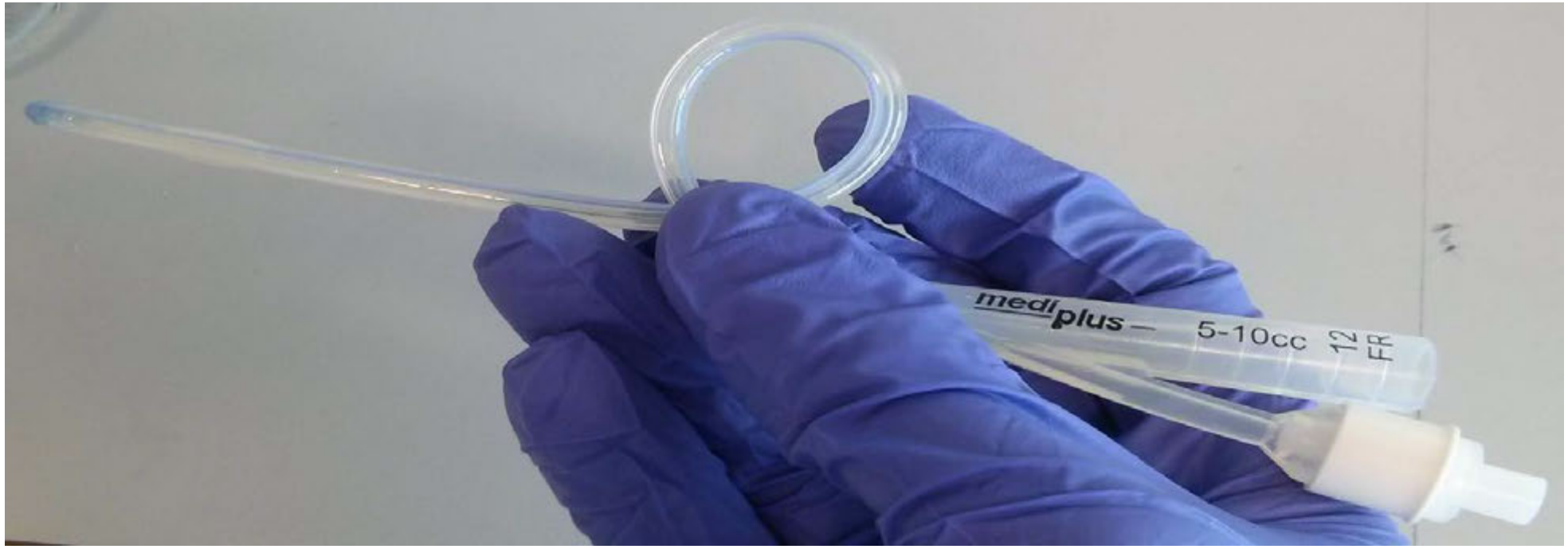
BACKGROUND: High Throughput Materials Discovery of weakly amphiphilic acrylate polymers



Hook *et al Nature Biotechnology* 2012

Product Development to CE mark achieved Q4 2017

In collaboration with UK SME Camstent, CEO Dave Hampton



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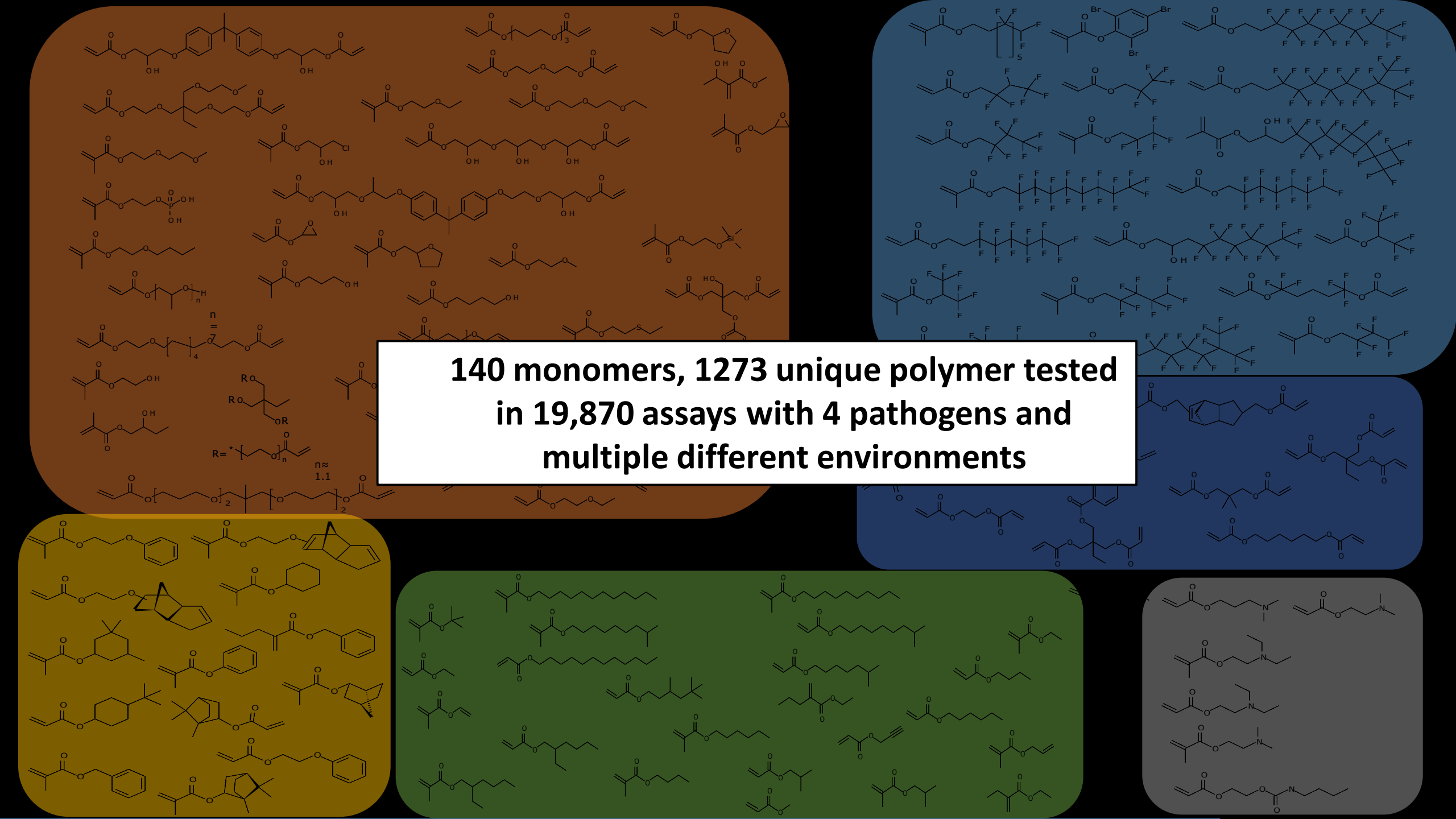
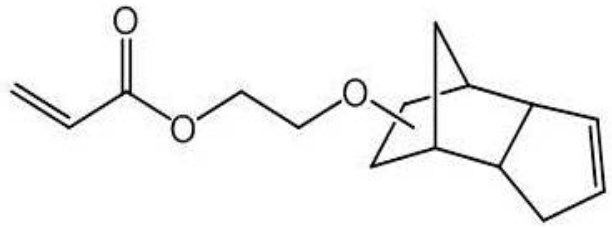
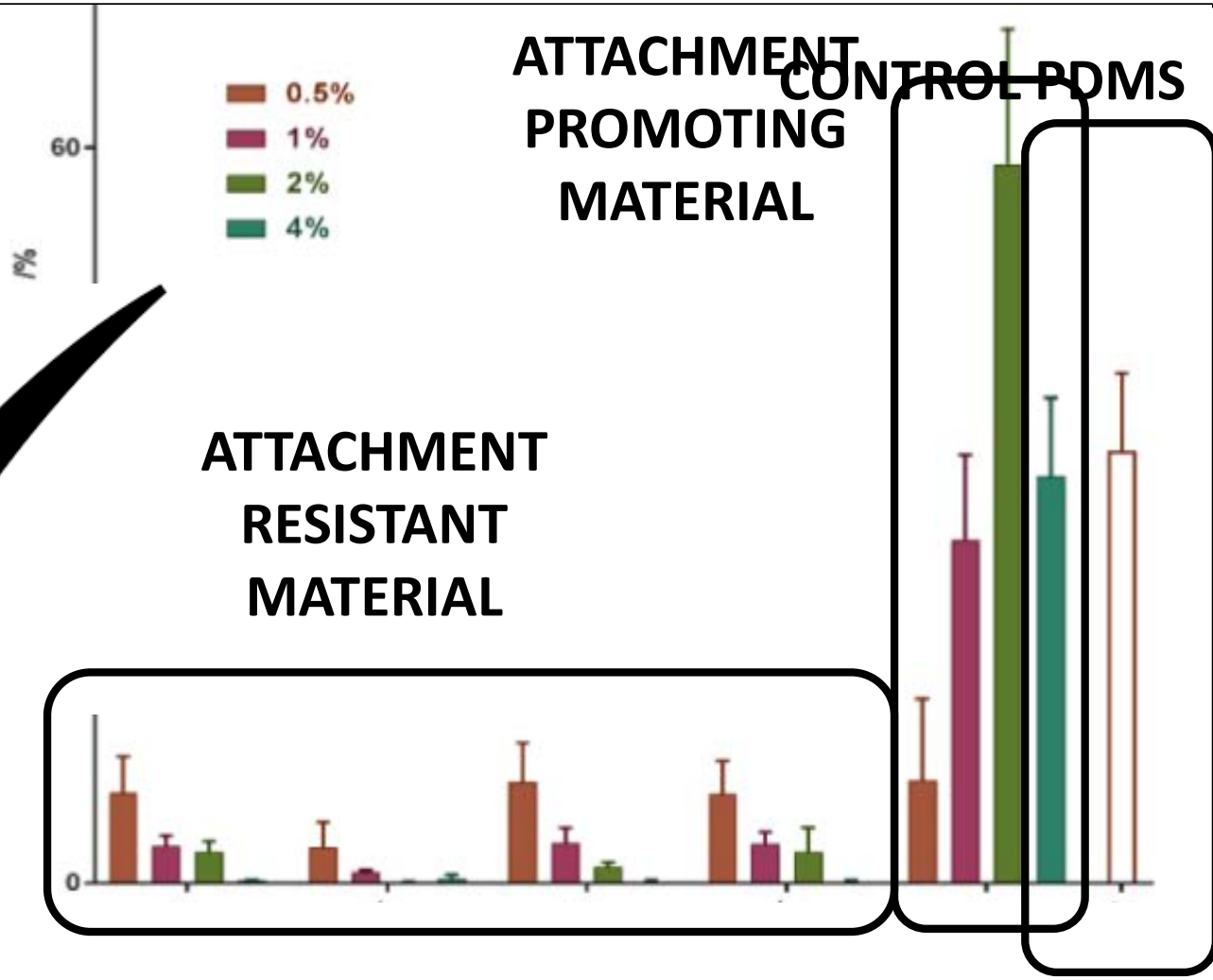

140 monomers, 1273 unique polymer tested
in 19,870 assays with 4 pathogens and
multiple different environments

Borrowing materials shown to have microbial resistance



Tricyclo[5.2.1.0.2,6]
decanedimethanol diacrylate

Scaled up material
RETAIN
functionality



Begines et al 'Development, printability and post-curing studies of formulations of materials resistant to microbial attachment for use in inkjet based 3D printing', Rapid Prototyping Journal, 22, 2016 835-841

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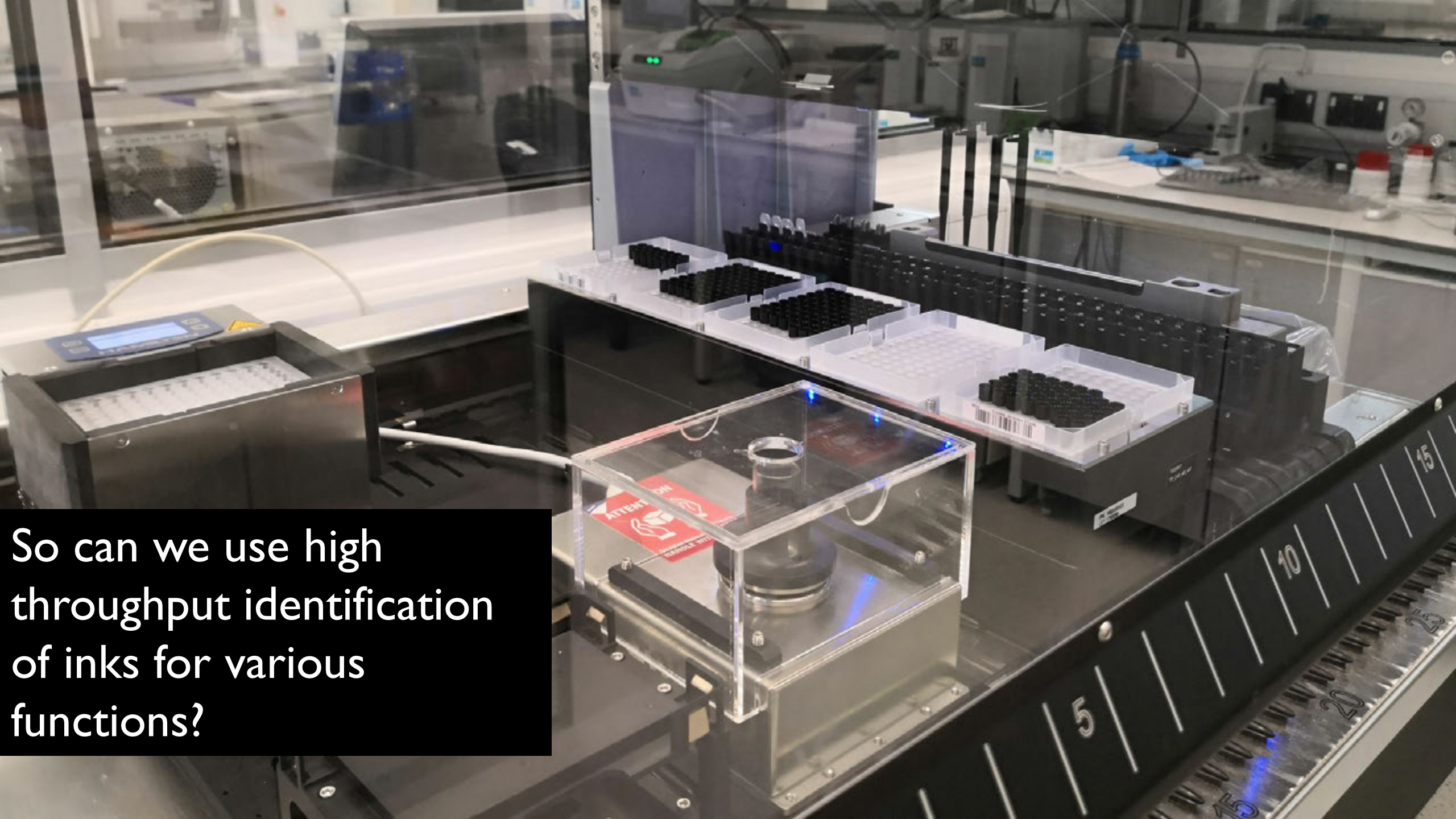

So can we use high throughput identification of inks for various functions?

Formulation for 3D printing:
Creating a plug and play platform for a disruptive UK industry

- EPSRC – £3.53M grant, 4 Years, started 1 Oct 2016
- Project partners:

- Academic partners

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- Industrial partners

gsk

Malvern

PPG

Unilever

syngenta

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The vision

Vision: We will remove the barriers to the uptake of 3D printing through the adoption of high throughput formulation, establishing sector specific material libraries and creating a “plug and play” approach to materials selection, thereby securing the UK at the forefront of the 3D printing revolution

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The solution

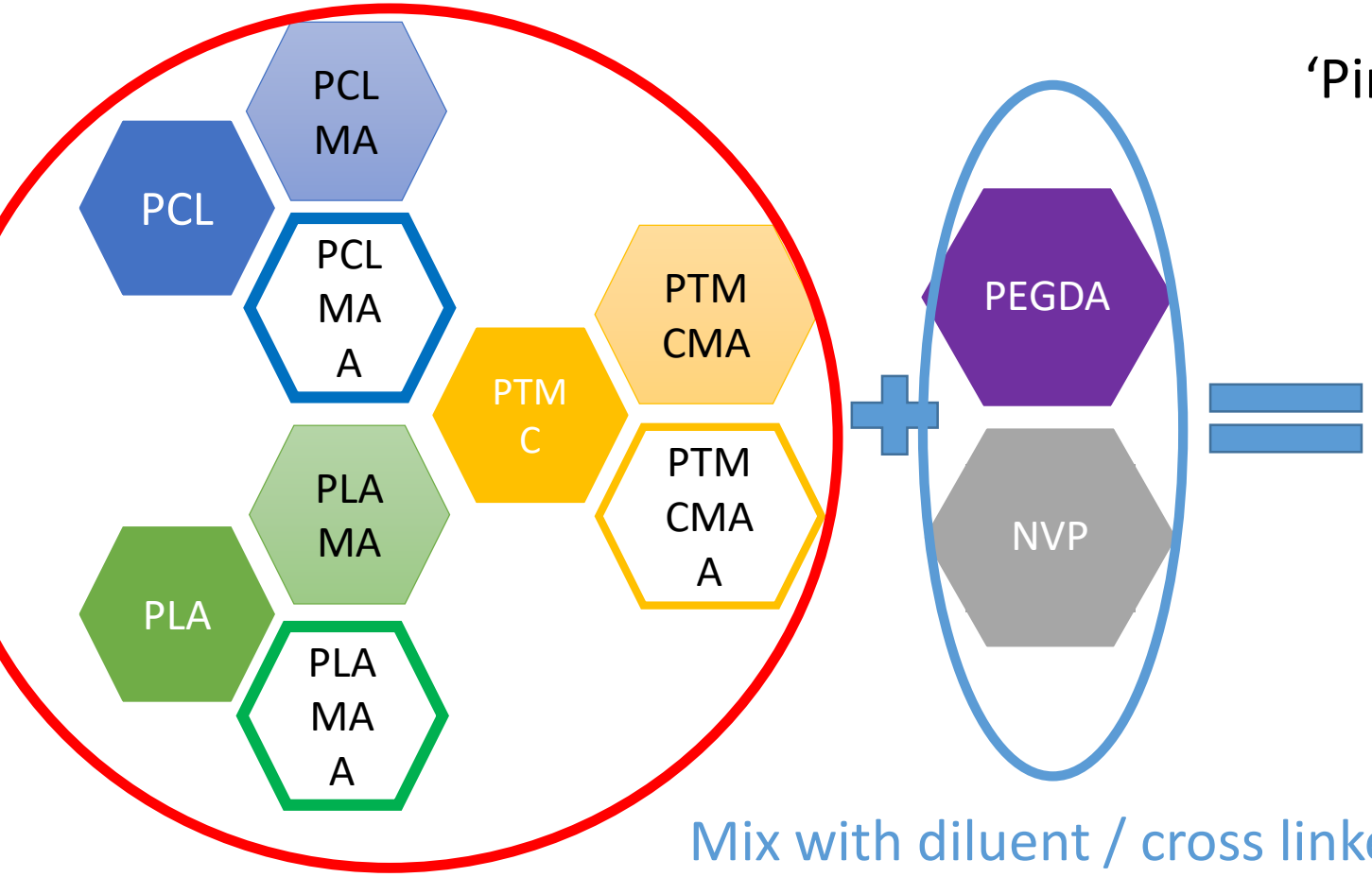
Our experience shows it can take up to 6 months to identify a single formulation for a given function – very intensive

- We can synthesis new materials that are amenable for 3D Printing and retain desired functionality
- We can use high throughput methods can help us narrow down the possible options – allow us to rapidly identify candidate materials
- Demonstrate how these materials can be use to create structure and texture via 3D printing
- Can obtain a library of available formulations and their properties can be shared for all

Materials permutations

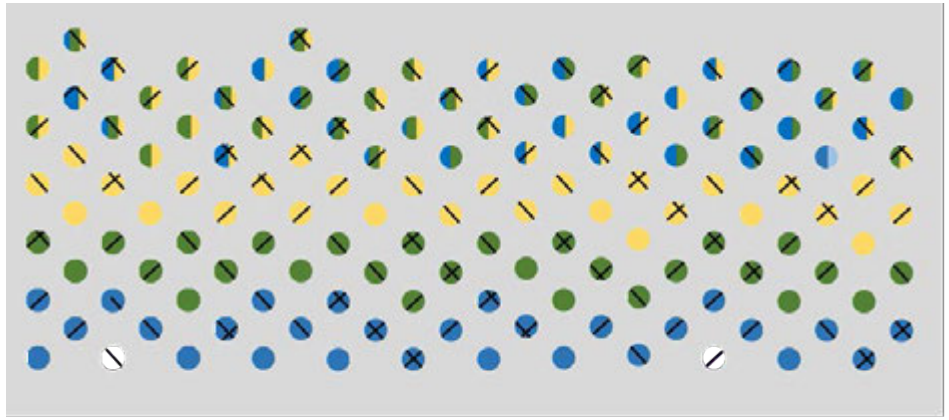
Finding new, printable resins and blends

Synthesize base, resorbable, UV curable material



Mix with diluent / cross linker

‘Pin Print’ array of combinations of materials



PCL PLA PTMC PEGDA NVP

Synthesis of Methacrylate-Terminated Block Copolymers with Reduced Transesterification by Controlled Ring-Opening Polymerization

Laura A. Ruiz-Cantu et al. Macromol. Chem. Phys. 2019, 220, 1800459

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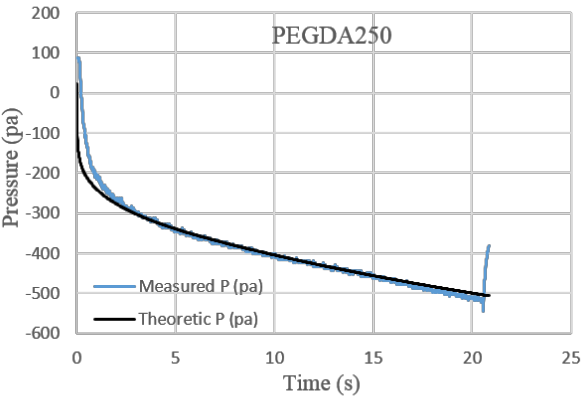
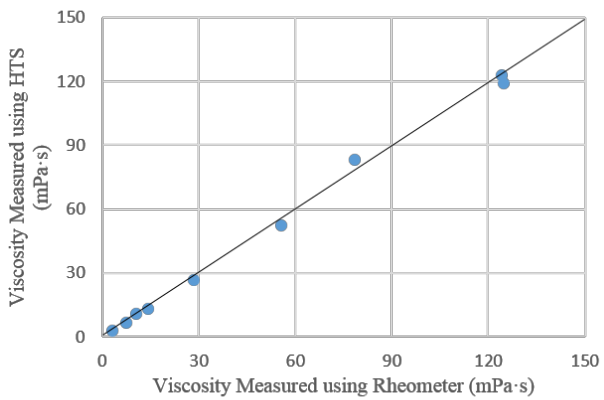
So, how to find out if any of these are printable?

High-throughput Inkjet Printability Determination

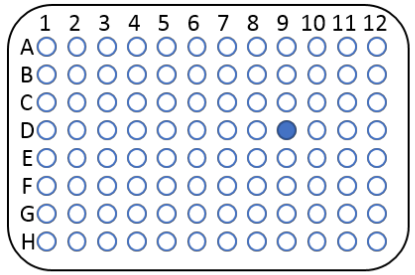


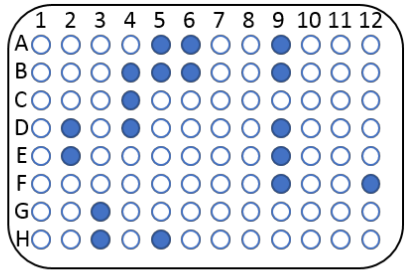


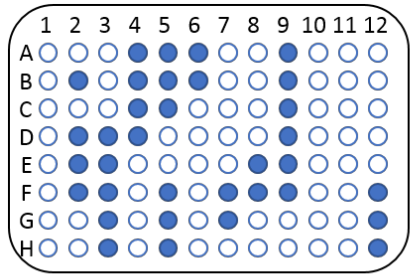
	Viscosity (mPa·s) @ 25°C		
	Measured using Rheometer	Measured using HTS	Difference
PEGDA250	10.52	10.87	3.33%
TCDDDA	124.08	122.82	1.02%
S3	3.26	2.85	12.58%
S6	7.37	6.76	8.28%
N10	14.26	13.24	7.15%
S20	28.39	26.59	6.34%
N35	55.70	52.21	6.27%
N75	124.80	119.13	4.54%

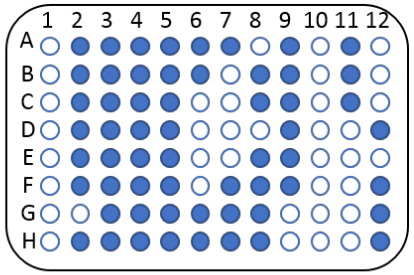
$$P_{gas} = \int_0^H \frac{8\mu Q}{\pi\left(\frac{R_t + R_{(t-0.01)}}{2}\right)^4} dH - \rho g(0.02 - H_t) - \frac{2\gamma\cos\theta}{R_t}$$

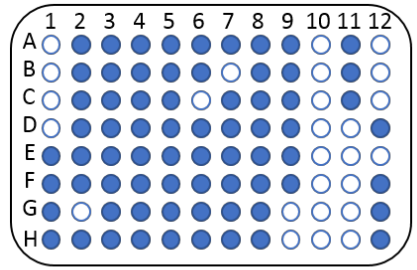
$$\gamma_{sample} = m_{sample}\frac{\gamma_{water}}{m_{water}}$$



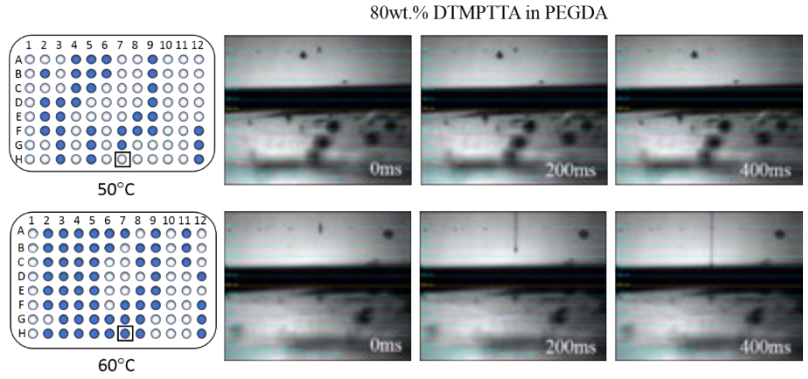








Variation in printability with temperature



Validation of results: demonstration of printability

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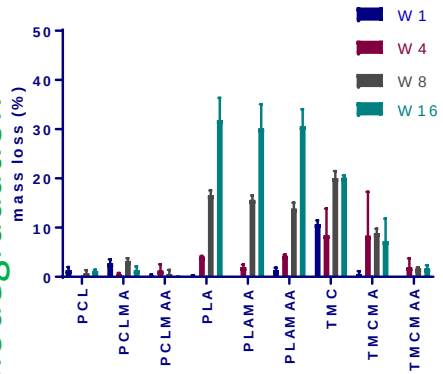
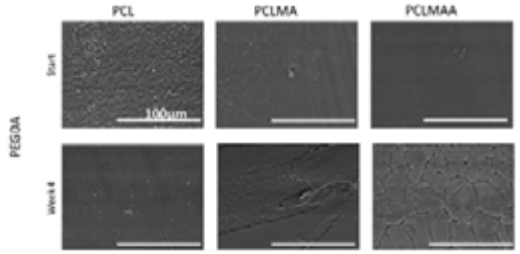
Many materials = many characterisation!

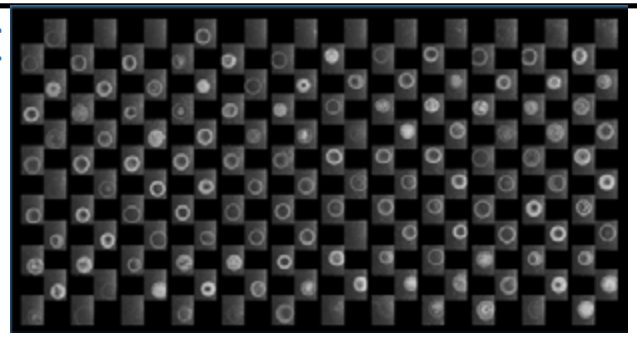
In vitro biodegradation



SEM

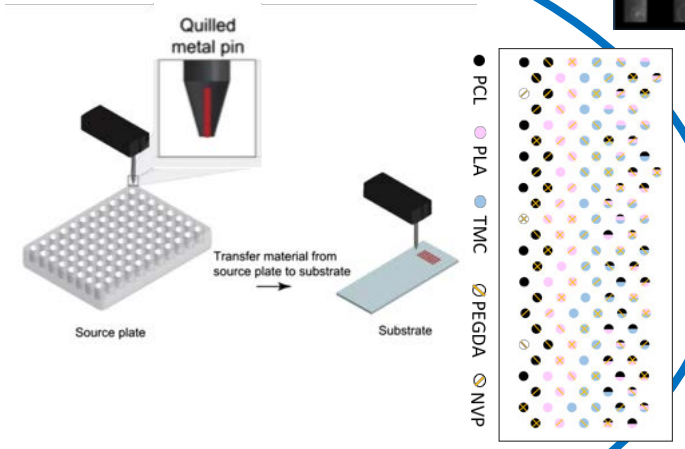


Microscopy

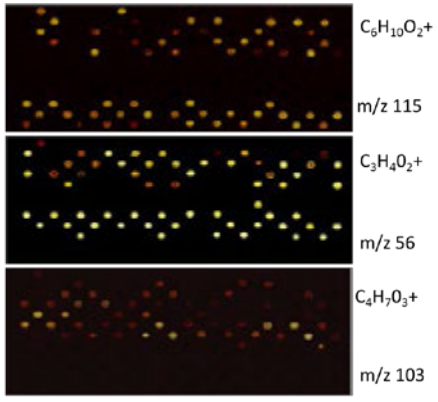


96 well plate format

Micro array format



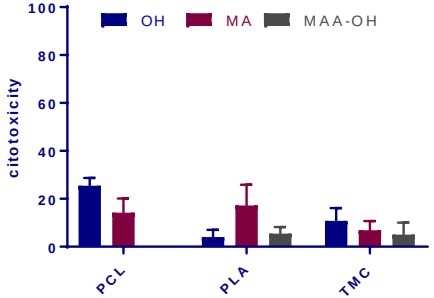
ToF SIMS



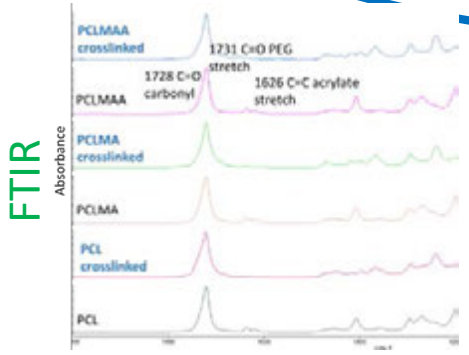
Printability

Drug release

Cytotoxicity

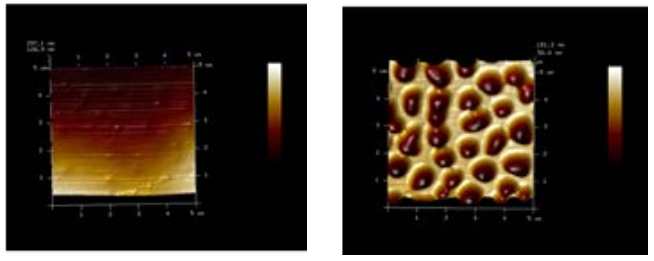


FTIR



Surface topography

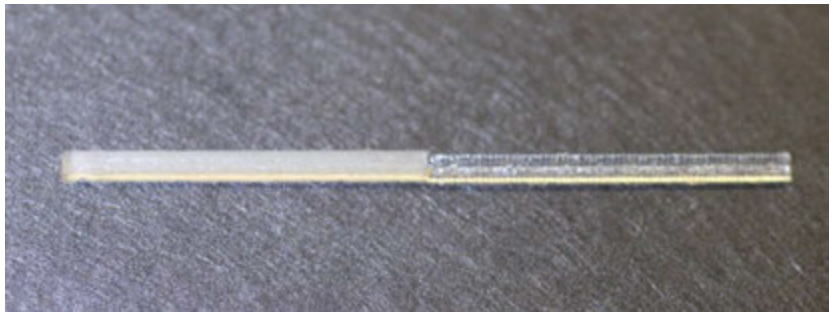
AFM



Printable materials

Material	Solvent	40 °C	50 °C	60 °C	70 °C
PCL	PEGDA	X	X	X	✓
PCL	NVP	✓	✓	✓	✓
PCLMA	PEGDA	X	✓	✓	✓
PCLMA	NVP	✓	✓	✓	✓
PCLMAA	PEGDA	X	X	X	X
PCLMAA	NVP	✓	✓	✓	✓
PLA	PEGDA	X	✓	✓	✓
PLA	NVP	✓	✓	✓	✓
PLAMA	PEGDA	X	✓	✓	✓
PLAMA	NVP	✓	✓	✓	✓
PLAMAA	PEGDA	X	X	X	X
PLAMAA	NVP	✓	✓	✓	✓
PTMC	PEGDA	X	✓	✓	✓
PTMC	NVP	✓	✓	✓	✓
PTMCMA	PEGDA	X	✓	✓	✓
PTMCMA	NVP	✓	X	X	X
PTMCMAA	PEGDA	X	✓	✓	✓
PTMCMAA	NVP	✓	✓	✓	✓

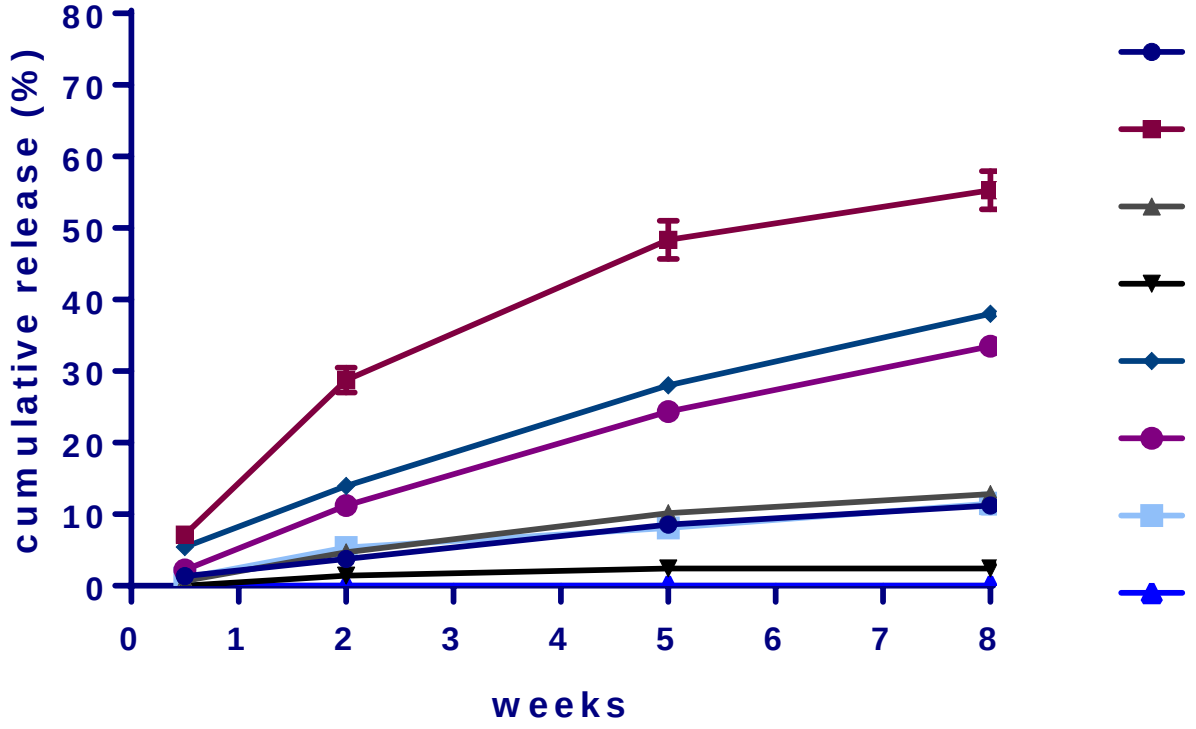
Poly - drug implants



Hypertension Diabetes

Drug release of API

Different combinations lead to different release!



Varying combinations of printed materials

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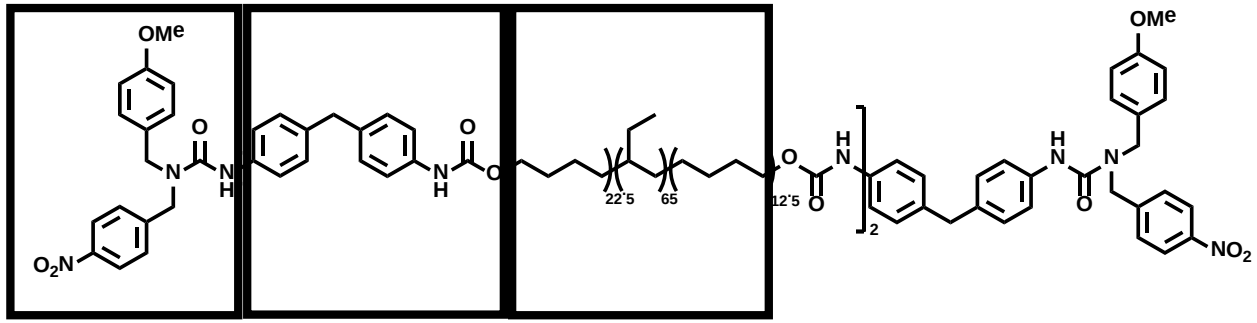
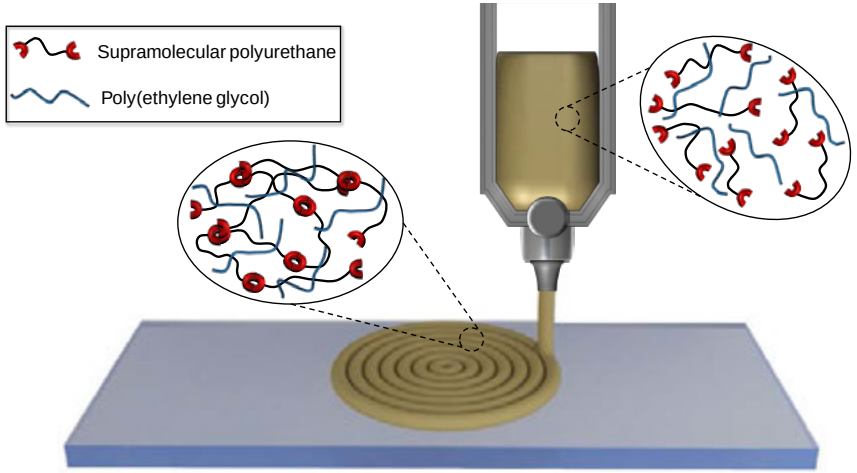
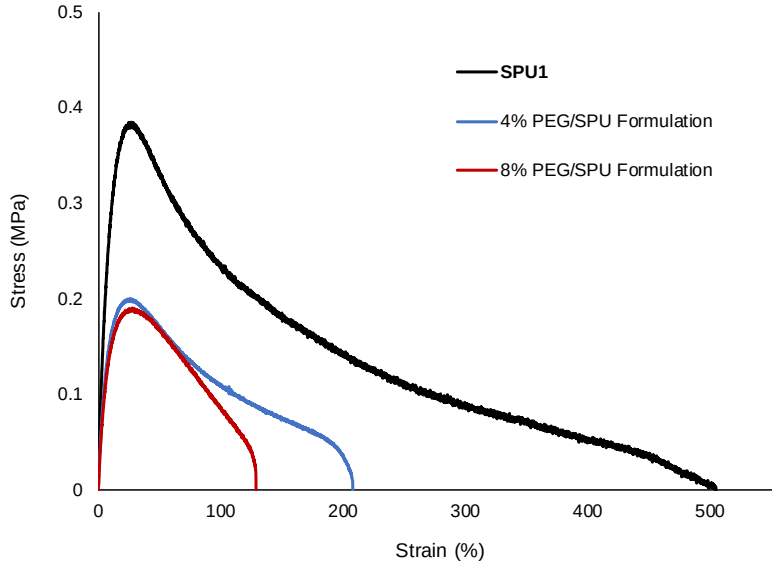
Molecular permutations

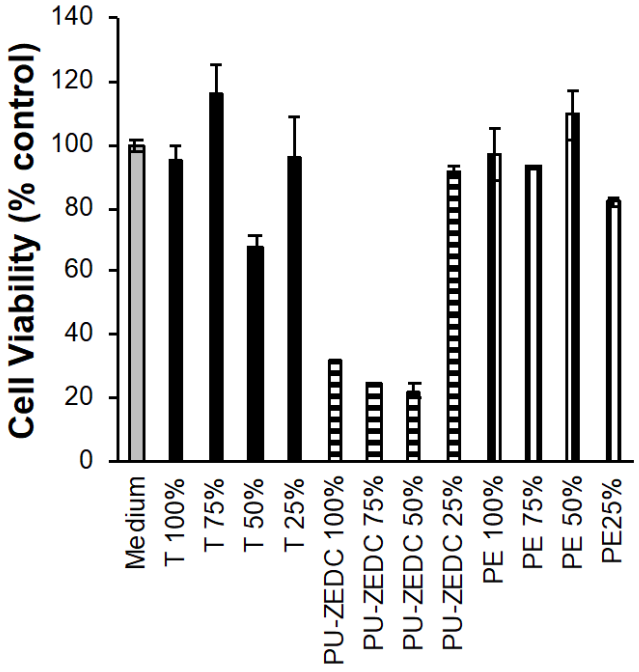
Finding new materials via molecular combinations



We can combine moieties to create supramolecular materials







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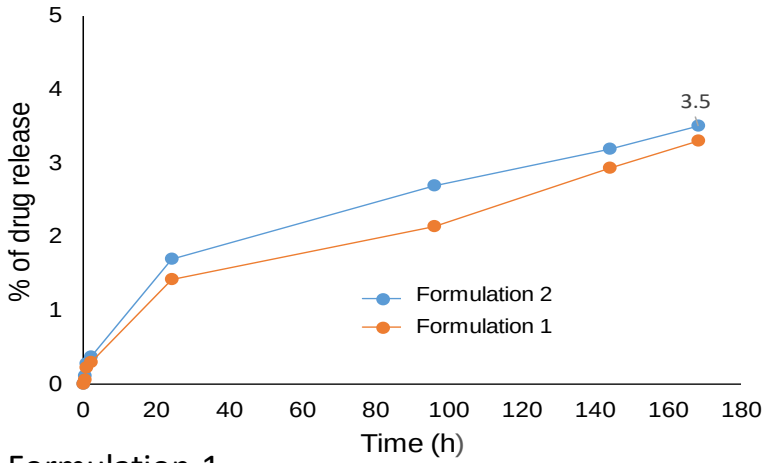
Drug release – from immediate to sustained release

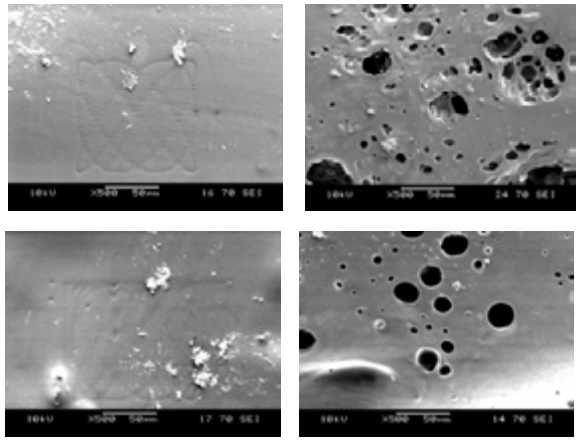
IMPLANT



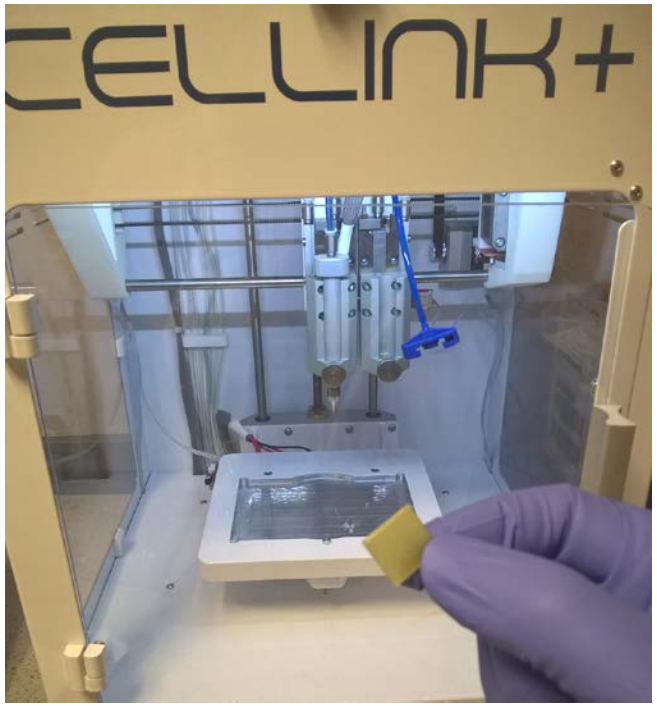
Formulation 1

Before diss.

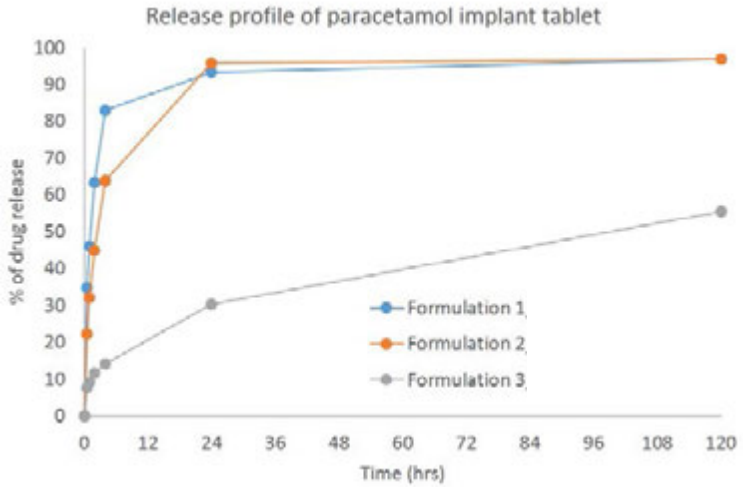
After diss. 7days



Formulation 2



TABLET

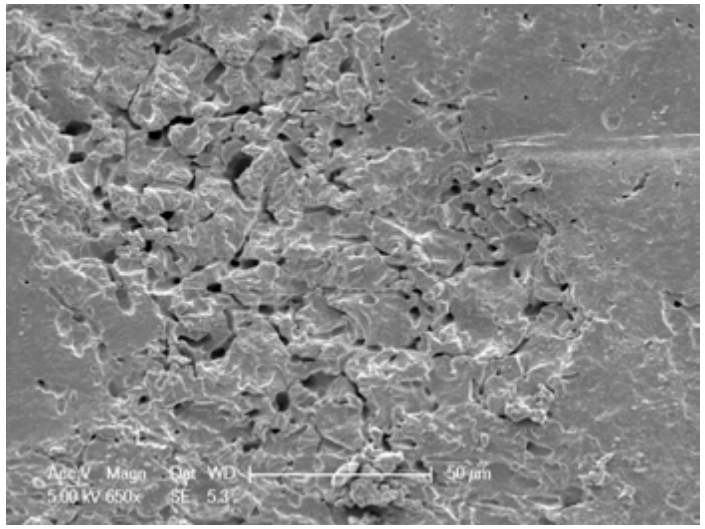


Microstructure permutations

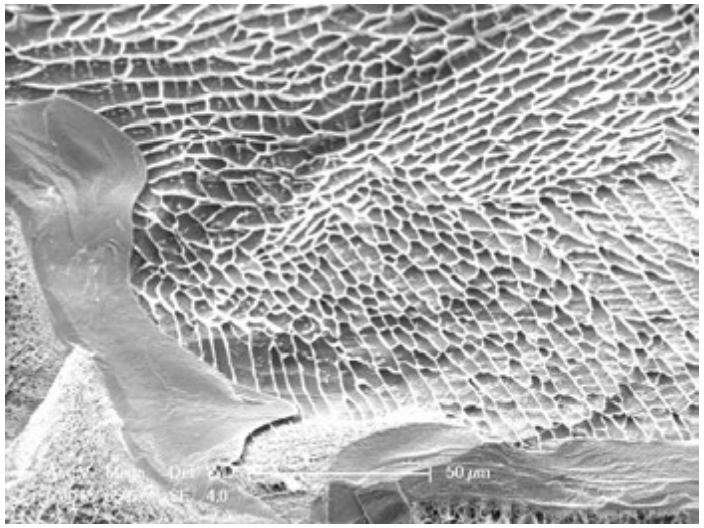
Screening for complex microscructures

The act of printing can create complex structures

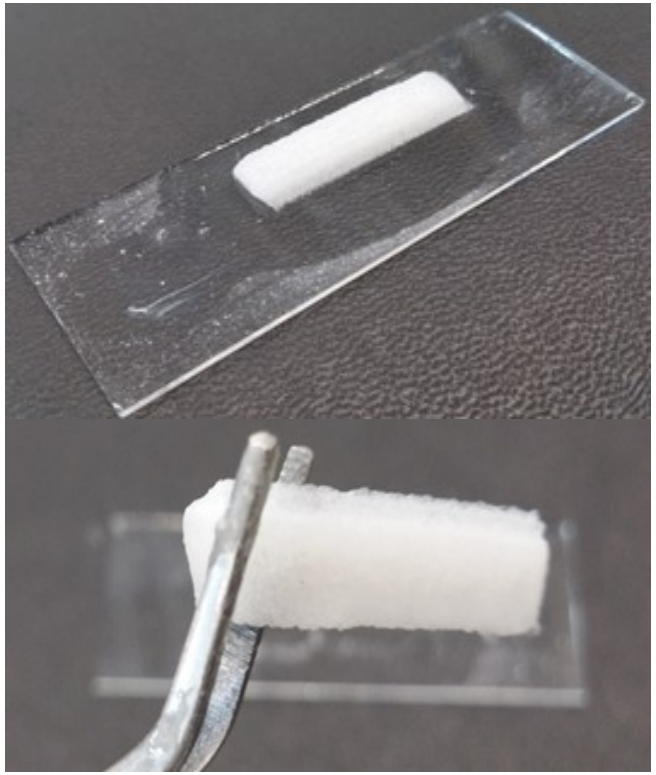
Cast



Printed



Chitosan in 1% acetic acid and sodium dodecyl sulphate in 0.1% xanthan in water.



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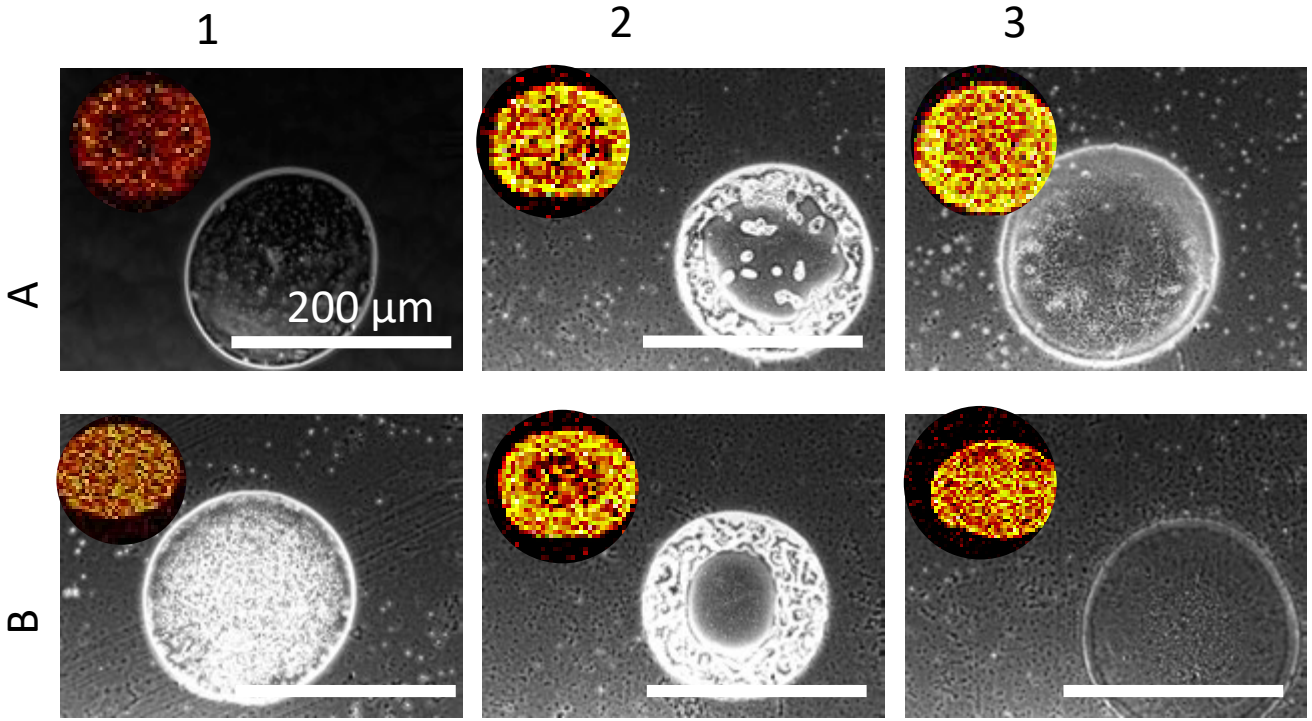
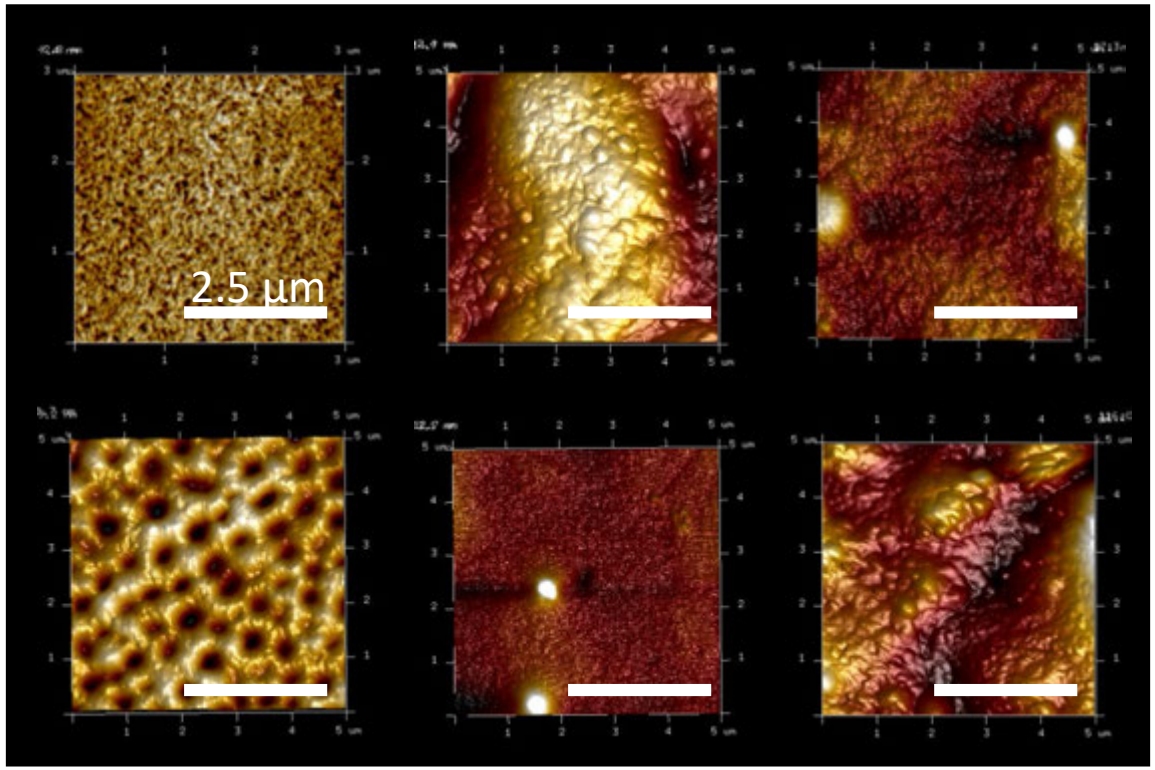
And even in single drops!

Can observe multifaceted phase separation to create complex tomo- and topographies





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Conclusions

- Creation of new materials by combining monomers, oligomers and moieties to has lead to a new suite of 3D printable materials
- High throughput / automated methods can enable rapid identification of materials
- The act of 3D printing can lead to new and complex multiphase structures

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