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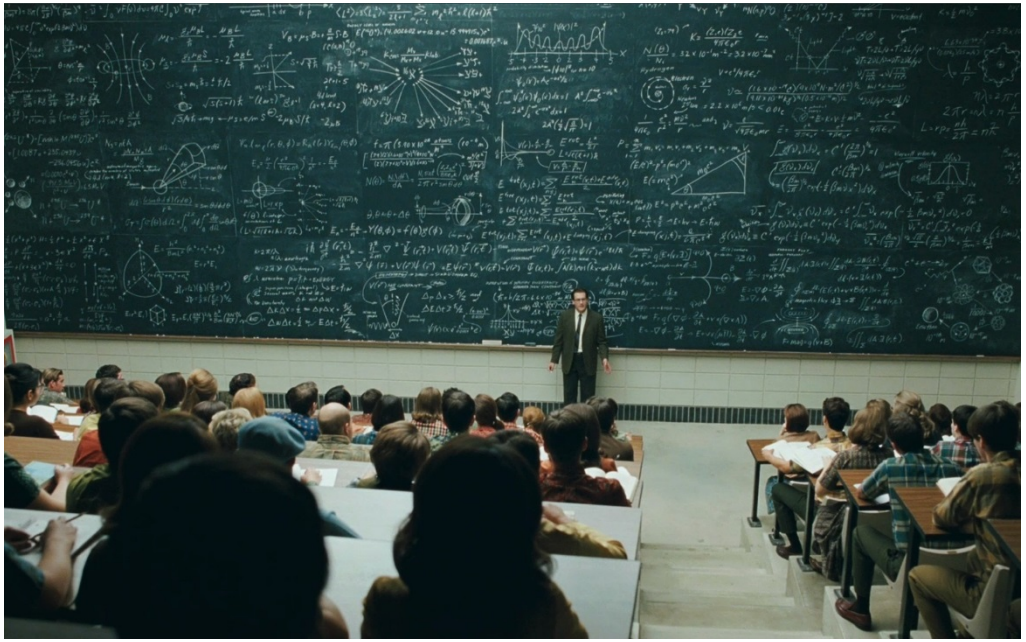
Sussex Drug Discovery Centre

Starting out in Academia

(and flavours thereof)



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About...

Chairs: VOLKER HESSEL - *Eindhoven University of Technology, Eindhoven (The Netherlands)*
LIONEL MAGNA - *Institut Français du Pétrole – Lyon, Solaize (France)*

13:30-14:00 WIM VERBOOM - *Twente University, Twente (The Netherlands)*
Microreactors as a Promising Tool for High Pressure Reactions

14:00-14:15 BENJAMIN WAHAB - *University of Hull, Hull (United Kingdom)*
Novel Approaches in Heterocyclic Synthesis: Micro Fluidic Synthesis of Substituted Indoles

14:15-14:30 RICHARD JONES - *Thales Nano Inc., Budapest (Hungary)*
Optimization of Selective Hydrogenation Reactions Using Automated Catalyst and

ocess Design and

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of substituted indoles using continuous flow micro reactors

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ABSTRACT

Continuous flow micro fluidic devices for organic synthesis ("micro reactors") are becoming established in a number of facets of modern applied chemistry. As part of a concurrent research project with a pharmaceutical company for generation of materials of pharmaceutical interest within continuous flow environments, we present here, for the first time a series of indoles that have been produced within micro reactor systems. We have developed three different approaches to the synthesis, which are compared with traditional batch synthesis as well as each other in terms of ease of optimization, chemical suitability and versatility, and implications as to throughput. Typical throughputs of approach 1 (simulated classical synthesis) were in the region of 2 mgh^{-1} of indoles such as tetrahydrocarbazole and cyclopentaindole. The second approach (based on Eik's modification of Fischer indole synthesis) gave throughputs of 5.7–8.9 mgh^{-1} and the final approach (using heterocatalytic flow reactors) gave the highest throughputs of 12.7–20.1 mgh^{-1}. All throughputs are per single channel reactor system (i.e., one single reactor set up), and the latter two approaches produce viable output quantities for the syntheses of radiolabelled materials (where typically minute amounts of high purity materials are required from a rapid and safe production environment).
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2nd EuCheMS Chemistry Congress

THE UNIVERSITY OF HULL

B. WAHAB, G. ELLAMES, S. PASSEY, P. WATTS* (UNIVERSITY OF HULL AND SANOFI-AVENTIS, ALNWICK, UK)
Synthesis of Substituted Indoles Using Continuous Flow Micro Reactors
Tetrahedron **2010**, *66*, 3861-3865.

Synthesis of Substituted Indoles Using Flow Microreactors

Category: Synthesis of Heterocycles

Key words: microreactors, indoles, flow micro fluidic

Significance: The synthesis of various indoles with throughputs of up to 20.1 mgh^{-1} per single channel reactor has been developed. When ketones **1** reacted with phenylhydrazine (Fischer synthesis) via [3,3]-sigmatropic rearrangement, substituted indoles **2** were obtained in moderate to excellent yields. The substrate scope was moderately studied. Three different conditions were investigated; homogenous catalysis (method 1); neat acid catalysis (method 2), and heterogeneous catalysis (method 3). The heterogeneous approach was shown to be the most efficient.

Comment: The indole unit is a well-established pharmacophore due to the fact that many biological species include this moiety (M. Fredrich, M. Tits, L. Angenot *Trans. R. Soc. Trop. Med. Hyg.* **2008**, *2*62, 153). Substituted indoles have been a topic of interest for over a century since Fischer's first report some 120 years ago (E. Fischer, F. Jourdan *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241). A number of routes to indoles are known, but the most commercially used is still the Fischer method. The heterogeneous approach using Amberlite IR-120 was deemed the most useful of the three conditions as minimal workup of the product and higher throughputs were possible.

Advances in Organic Synth
Substituted Indoles for Pharn
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Being a Thesis submitted for
The Ur

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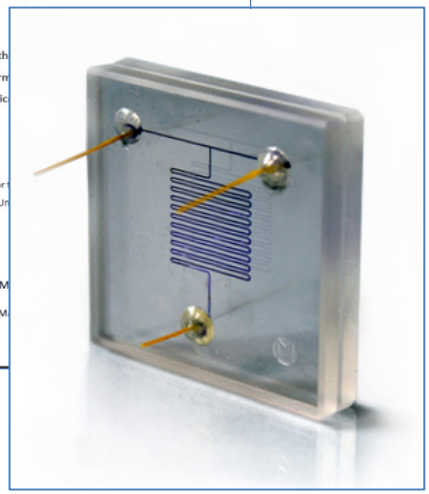

Classical Academia...

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Two classical routes:

Research: The Post Doc -> Fellowship -> ??? Lectureship?!

Teaching: The Lecturer -> Reader -> Professor

Classical Postdoc...

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"Postdoctoral scholars are the lifeblood of any research institution"
Lawrence Berkeley National Laboratory

"As a postdoc, you'll contribute vitally to the progress of science, simultaneously filling the roles of scientist, scholar, and sucker"
Adam Ruben, *The Postdoc: A special Kind of Hell*
DOI: 10.1126/science.caredit.a1300256

There are roughly **7 postdocs per tenured lecturer** in the US, and slightly less in the UK, though this is likely to change.

Postdocs offer a real chance to **explore your research capability** in a competitive academic environment, and allow a chance to take a look at global science

Classical Postdoc...

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Postdoc experiences tend to vary by supervisor, and nation of work –
– it is KEY that you are a good fit for the group / supervisor
– make sure you ask about work/life balance of the group.
Futons in the write up rooms are not a good sign.

Typically, in the UK:

- Usually ONE project, ONE role, ONE group. *e.g.* " a chemist on Kinase X, in the Jones group
- Fixed term appointments (1-3 years), with single point deliverables

- **Devise, run and deliver their own research deliverables**.
- Write grants or support grant writing (on which they are often named)
- Write papers on original research
- Support / manage the group

Classical Postdoc...

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Why Postdoc?

- Post docs typically start on academic **Grade 7 Salaries** (same as trainee lecturers)
- Notional hours (**37.5 hours a week**, though likely you'll put in more)
- A chance to **take control of your own research** within a proper support network
- Can live in academic lifestyle / community
- Post-docs abroad are a way of seeing the world, and global science

There is a wider **community of support:**

- Grant writing advisors / workshops / clinics
- Post-doc forum, post-doc coffee meets
- Skills Support & Development

- There are specialist **"early career" grants** for those just starting out
- There are specialist grants to help you undertake research abroad (*e.g.* within EU)

The Lecturer...

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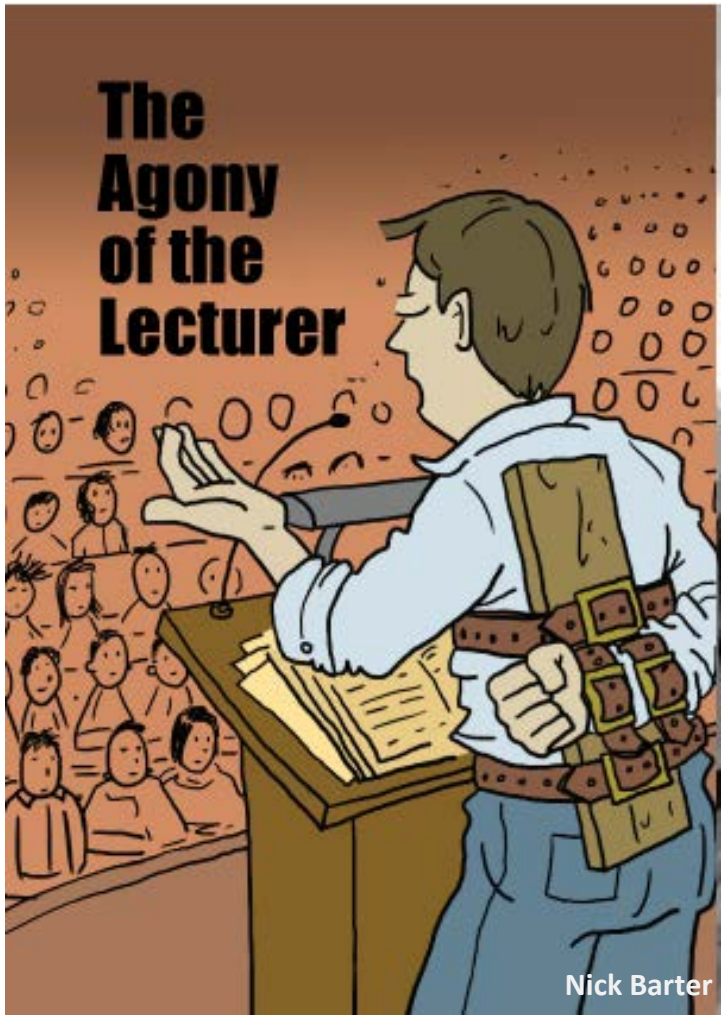
- Usually permanent position
- Role split three ways, typically:

  Lecturing (33%)
  Research (33%)
  Admin (33%)

Commonly it is **research time** that gets squeezed.

Modern lecturers require a PGCHE to lecture – trainee (fast track) positions often run this as part of the probation period.



The Lecturer

Start on grade 7 as probationers (2-3 years, whilst they get their PGCHE) – their teaching load is reduced during this additional workload.

When probation is complete, they scale to grade 8.

Most **Senior Lecturer** positions start at grade 9 (can get there within 3 years from probation).

Student experience is now playing as much a role as actual quality of education in course rankings, and thusly changes the way departments and lecturers operate

Change is coming in the way lectures are delivered in UK intuitions, and as a result, the current notion of "Lecturers" and "Post-Doc" may be a disappearing.

Modern Academia for STEM Subjects: The non-classical research paths

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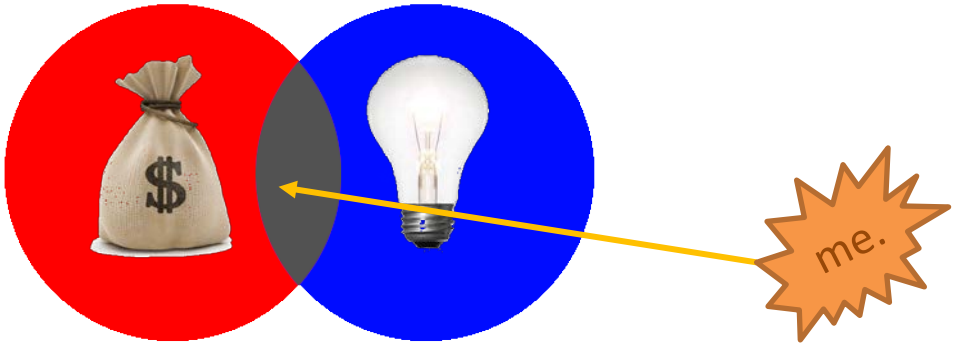

Nano-Factories, KTPs, DDUs, Industrial Interface / Engagement Units, KT/TT Offices, Academic Incubators)

The Knowledge Transfer Partnership

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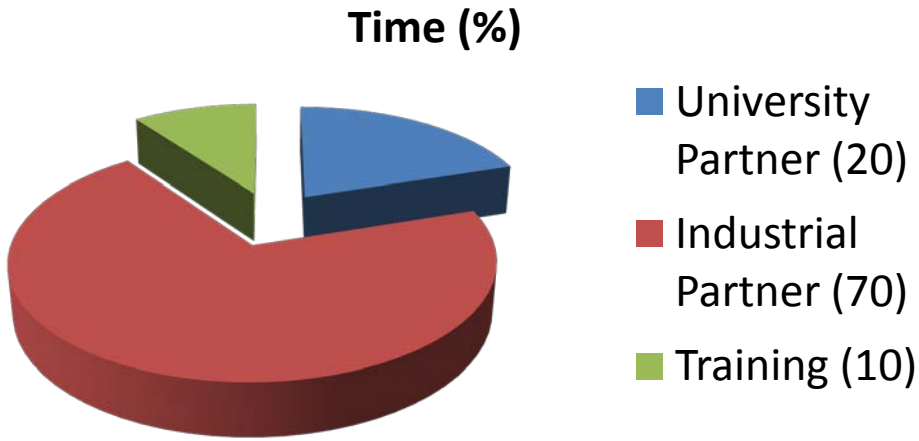
Changing Ideas into Products

Project is run between a university and an SME (often local, but not essential). You work in both environments. Can do as a postdoc or after your first degree (salaries vary)

In the University:
Post Doc role
Developing new technology

In the company:
Deploy technology
Train staff



All academic support systems are there for you (same as if you were a student), but with additional funding for industry relevant professional training.

The Knowledge Transfer Partnership

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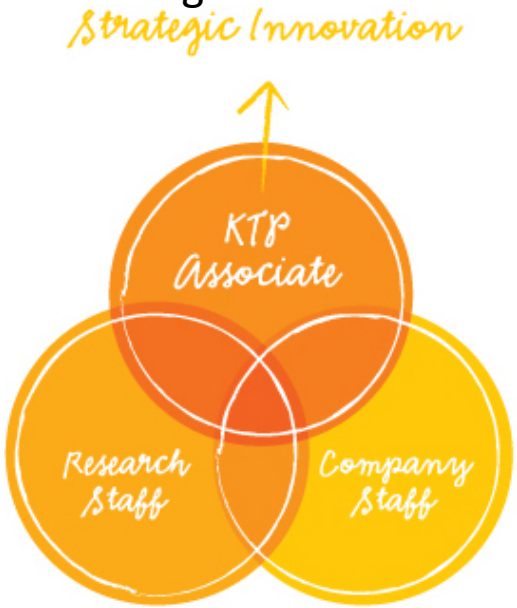
- Government sponsored, **project managed** programs
- **Industry**: new technology or knowledge, academic links, trained staff
- **Academia**: funding, collaborative publications, business relevant teaching



- **Associate (you):**
- **Healthy training and travel budgets**,
  (as well as 10 % time allocated to training)
- **Management** and Leadership **training**

info.ktponline.org.uk/action/search/current.aspx

- Currently: **700 KTPs advertised (April 2016)**, covering revenue management systems to scaling up F1 engines
- Examples of 7,000 completed KTPs on the site

The Knowledge Transfer Partnership

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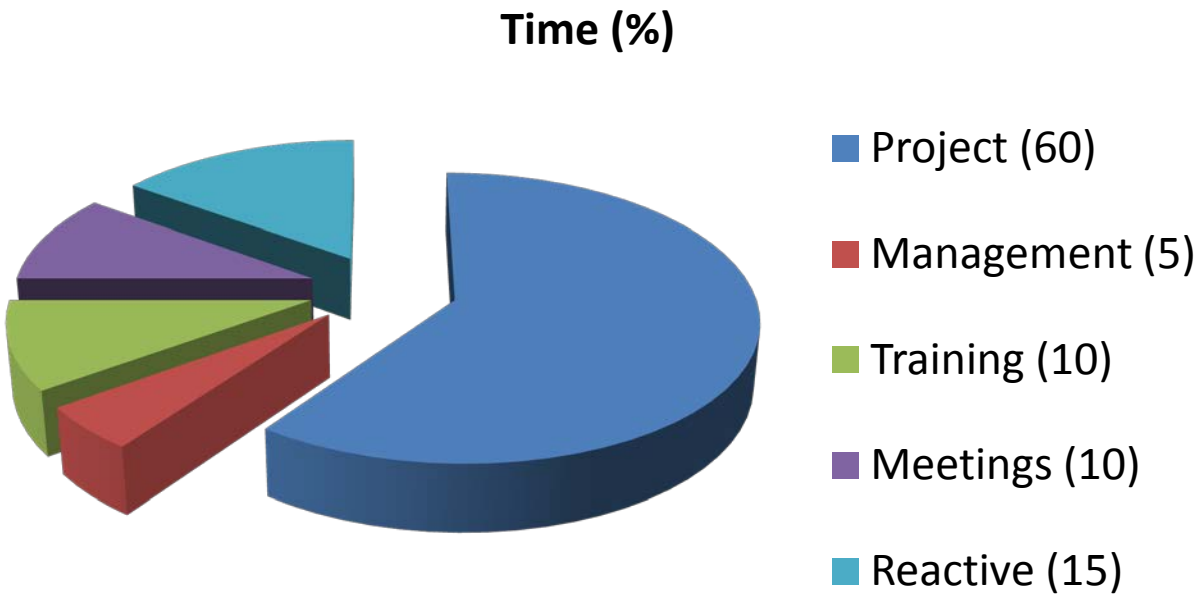
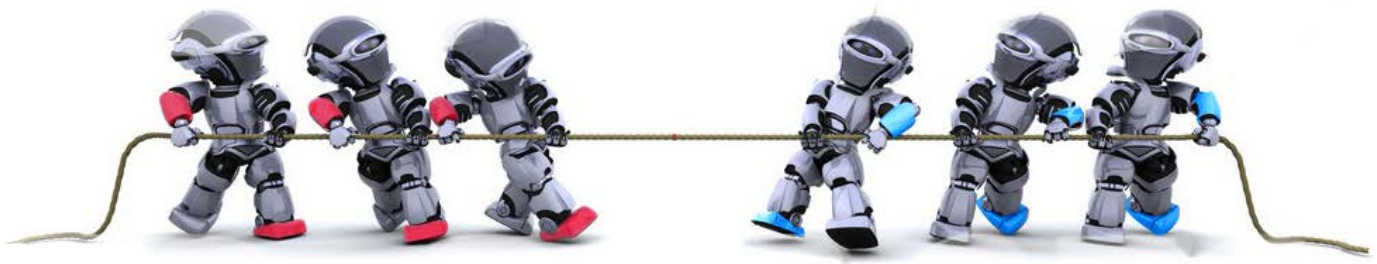


Differences in priority (**publish**, patent, profit, post-doc, **property**, **politics**)
NO teaching, NO grant writing, mild PhD student support



Drug Discovery Units, and Bio-Techs in Academia

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Since the Big Pharma "*reshuffle*", small biotech and biotech-like innovation units emerged…including *academic* drug discovery units…

- Work in academic environments but have mostly industrially trained staff
- **Product oriented** not paper-driven
- Quasi-autonomous
- **Disease area**, not science area
- Properly **project lead** and resourced

SDDC: A group like no other…

(except there are others in London, Cambridge, Leeds, Dundee…)

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100+ years combined industrial experience

7 PhD students (more on the way),
15 research fellows & senior research fellows (more on the way)

Truly multi-disciplinary, from chemists to crystallographers…

SDDC: A group like no other…

(…and Sutton, Manchester and Newcastle and ALL over the US… and Europe…)

University of Sussex
Sussex Drug Discovery Centre

175+ years combined industrial experience

12 PhD students
30 research fellows & senior research fellows (more on the way)
(group size expected to be ~65 by Q4 2016)

We gather “shedded talent”
Very few members have come from non-pharma industry (but there are some)

Working in the SDDC

its like *acadustria*, but more *industremia*…

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Non-Classical Postdoc:

Single role, but **many projects** (project specific chemists, but CADD, biology, crystallography and protein production work across projects)

Multi-faceted teams

Fixed term, but likelihood to roll over to other projects on close.

Less paper and grant writing, but some support to other grant and patent writers.

Some supervision responsibilities, as well as training of staff

Multi-point milestones - projects can fail early, and people may lose their roles

Interactions with many **external organisations**

Priority on **Delivery** and **Quality / Credibility**

Working in the SDDC

its like *acadustria*, but more *industremia*…

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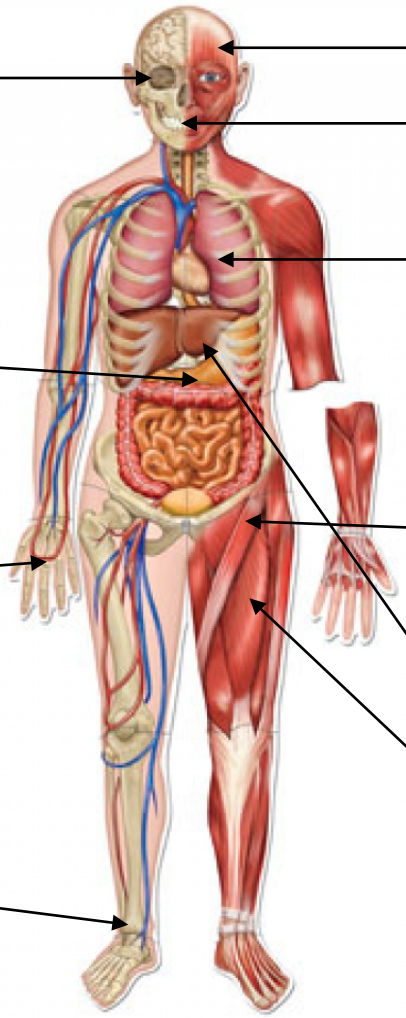
Reading (lots)
academic papers, patents
general competitor awareness

Campus food
cakes at meetings,
someone ALWAYS brings in something

Smart Phone
email is *the* comms method, even if they're next door. Audited record.

Audio..
music is always on somewhere,
headphones in office areas, radio in labs



Meetings & more meetings
(cross-project, cross discipline)
can shell shock

"Big Pharma" safety
stricter, safer policies

Office
air con, comfy office chairs,
correct lighting,
correct computing
wet space / dry space

On campus gym…
On campus bars.

Conclusions

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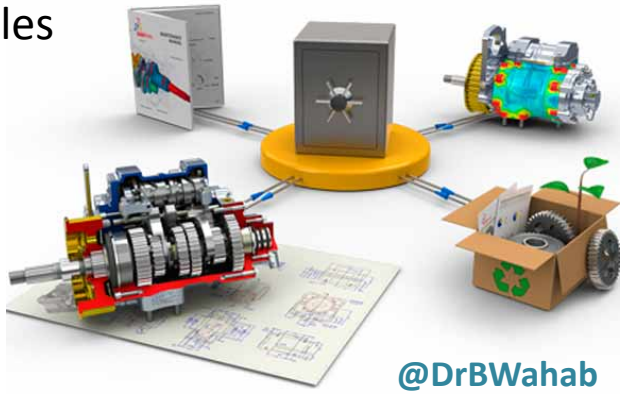
There is **more to Academia** than a classical postdoc or a lectureship role, and its going to get more diverse in the face of changing roles of what a University is and does.

Don't be a postdoc because you want a lectureship **– if you want to lecture, lecture**.

PDRA/F's are fixed term. You will likely have to move a bit if you want to do more than one

Salaries match SME's / CRO's but not classical pharma models (but do they still exist?)
Postdoc salaries don't progress as fast or as high as lecturers (in general)

If you want **application focussed research**, look towards KT roles DDU's, Industrial Engagement roles.



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Acknowledgements

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Dedicated to ending debilitating pain
Sophion
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MARIE CURIE ACTIONS
University of Sussex
wellcome trust
MRC Medical Research Council

Fin.

http://www.sussex.ac.uk/**sddc**