Both sides now: An intimate perspective on research collaborations

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Outline

• Background
• Some Recent History
• Pros & Cons on Both Sides
• Lessons Learned

• There are only 22 slides
Cheminformatics Implications of Collaborations between Academia and Industry

Why should we care?

Because it is where the most critical innovations come from.
Who am I to Talk About It?

• 8.5 years in academia
• 10 years at Monsanto
  – biochemistry, synthesis & screening
• 13+ years at Tripos (International)
  – QSAR & combi-chem software development
  – applications research (Discovery Research)
  – algorithm & new methods development (IRC)
• Projects I have been intimately involved with
  – Advanced CoMFA® Consortium
  – OptiSim, OptiDock & OptDesign®
  – CScore™ for consensus scoring
  – Pharmacophore Tuplets™
  – GALAHAD®
  …
Types of Collaboration at Tripos

- **Software development**
  - typically enterprise-scale projects
  - science is already known
  - application-specific
  - written to spec
  - “software consulting”: Schering, BMS, Wyeth…

- **Applications research**
  - science is already known
  - project-specific
  - Tripos Discovery Research, field scientists …

- **Basic applied research**
  - the problem is known but the solution isn’t
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What is Research?

• It means many things to many people
  – Google yields 771,000,000 hits (“about”)

• It is not:
  – (very) predictable
  – easily budgeted ahead of time
  – carried out in the Boardroom

• But it can be:
  – very useful
  – very productive
  – very rewarding in intangible ways

“If we knew what it was we were doing, it would not be called research, would it?”

- Albert Einstein
Caveat Auditor

• Names have been changed to protect the innocent
  …and the not-so-innocent
• Conclusions are generalized
  …but not overly so (I hope)
• Opinions expressed are solely my own

“The questions have been painstakingly researched,
but the answers have not”
– Michael Feldman, NPR
(Some) Collaborations I Have Known

• Pfizer, Inc.
  – 1998-2001 (Groton & Sandwich sites) → DAP

• Parke-Davis (→ Pfizer, too)
  – 2000-2003 (Ann Arbor) → CScore

• Novo Nordisk A/S
  – 2001-2003 (Copenhagen) → Tuplets

• University of Sheffield
  – 2002-2004 (Peter Willett & Nicola Richmond) → LAMDA

• Biovitrum AB
  – 2003-2004 (Stockholm) → GALAHAD

• Bayer HealthCare AG
  – 2005-2007+ (German & US sites) → PiX System
Types of Academic-Industrial Collaborations

• Good
  – everyone is happy at the end of the day

• Bad
  – good answer to the wrong problem
  – no publications

• Ugly
  – no useful code, nothing presentable

• Really ugly

• Really good
  – more often than not, for us

• “Fair to middling” is (surprisingly?) rare

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A Little History

• **Mantras of the 90s**
  – “New platforms & technologies are going to be the keys to drug discovery & development in the 21st Century.”
  – “If you don’t get there first, you won’t get there at all.”
  – “You can patent anything.”

• **Realities of the 90’s**
  – bigger is not always better
  … and is only rarely *proportionately* better
  – strategic partnership management ⇒ fewer $$$ for collaboration
  – you do not have a patent until you have defended it
  – you can’t patent everything

• **Mantras of the 00’s**
  – “It is all about getting access to data”
  … but try to keep the *informatics* in cheminformatics
  – “Outsource it if you can.”
A Little More History

• New technologies did not deliver
  – HTS & combinatorial chemistry
  – molecular diversity
  – in silico ADME/Tox

• Effects at the industrial bottom lines:
  – too few new drugs are being produced
  – a lot of new tech is (too?) expensive

• Too little attention was paid to (flexible) validation benchmarks along the way
  – should have been built in from day one
  – courses changed without being able to measure how much things improved…if, in fact, they did
  – stakeholders, committees & nice guys took over
Bureaucracy

• **Strategic partnership management**
  – puts you cheek-to-jowl with outsourcing projects
  – accounting pressure to look to the lowest-cost “provider”

• **Getting IT/IS departments involved**
  – essential for enterprise-scale projects
  – performance & cost outrank features as criteria
  – linked to a “revenue sink”
    … chemist support is critical but it’s not sexy

• **Intellectual property problems**
  – University wants downstream commitments
  – invention vs work-for-hire
  – Industry limits on data sharing
  – cross-licensing hassles & open source
Collaboration

• What does industry bring to the table?
  – experience in medicinal chemistry & drug discovery
  – a large quantity of data
  – high quality data
    …but usually not both at the same time

• What do academics bring to the table?
  – naïveté about the problem
  – innocence about what “won’t” work
  – scholarship: “How come you know stuff like that?”
Collaboration

• What *can* industry bring to the table?
  – experience in medicinal chemistry & drug discovery
  – a large quantity of data
  – high quality data
    …but usually not both at the same time

• What *can* academics bring to the table?
  – naiveté about the problem
  – innocence about what “won’t” work
  – scholarship: “How come you *know* stuff like that?”
“What we have here is a failure to collaborate!”*

• What academics should not do
  – expect blue skies & ivory towers to be encouraged
  – broadcast that “We’re here to tell you how to do it right!”
  – be lazy about making sure that programs are robust
  – think that the relationship is exclusive or forever
    • you haven’t gotten married

• What industry should not do
  – plan on having a “product” at the end of the project
  – expect delivery of industrial-strength code
    • be wary of freeware, open source and Matlab
  – be too promiscuous
    • you are committed to living together for a while

*with apologies to the chain gang captain in “Cool Hand Luke”
Some Take-Home Lessons

• Optimize communication
  – that’s what committees are really good for
• The more the merrier…
  …but there is strength in small numbers
• Each project needs a champion…
  …on both sides of the collaboration
  …in it for the long term
• Aim for publishability from the start
  – essential on the academic side
  – (very) valuable on the industrial side
  – a useful reality check in any case
• The “co” in collaboration is critical
  – cultivate a sense of group & individual ownership
• Do not plan on failing, but be prepared to do so
Some More Take-Home Lessons

- Share everything.
- Play fair.
- Don't hit people.
- Put things back where you found them.
- Clean up your own mess.
- Don't take things that aren't yours.
- Say “Sorry!” when you hurt somebody.
- Wash your hands before you eat.
- Flush.
- Warm cookies and cold milk are good for you.
- Live a balanced life.

“All I Ever Really Needed to Know I Learned in Kindergarten”
- Robert Fulgham
A Few of the People Who Have Made Things Work...

- **Tripos**
  - Peter Fox
  - Frank Stahl
  - Lakshmi Akella
  - Charlene Abrams
  - Philippa Wolohan
  - Michael Berthold
  - Dave Patterson
  - Alex Strizhev
  - Andreas Witte
  - Roman Dorfman
  - Fred Soltanshahi
  - Edmond Abrahamian

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  - Jerk Vallgårda
  - Anna-Lena Gustavsson
  - Maria Wirstam
  - Peter Brandt

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  - Peter Willett
  - Nicola Richmond
  - John Holliday
  - Val Gillet

- **UCSF**
  - Ajay Jain

- **Parke-Davis**
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  - George Cowan
  - Dan Ortwine
  - Alain Calvet
  - Jack Bikker
  - Mark Snow
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  - Jim Dunbar

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Conclusion

“I’ve looked at clouds from both sides now,
From up and down and still somehow,
It’s clouds illusions that I recall,
I really don’t know clouds…at all.”

“[V]iew the boundary between the [academic] and [industrial] cultures not as a territorial line but as a broad and mostly unexplored terrain awaiting cooperative entry from both sides.”

- paraphrased from E.O. Wilson
Thank you...

...for your kind attention.