

Building a Business Case for more *in silico* Modelling in the Pharma Industry

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Abstract

How one can use examples from other industries to make a business case for the employment of more *in silico* techniques in drug discovery and development.

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1 Initial Ideas

Ideas generated by group members at the initial meeting:

- What do we mean by *in silico* modelling ?
- → Population/genetic differences ?
- → How different people react to different drugs ?
- → Do we stick just to atomistic and molecular modelling of suitable drug targets that can then be synthesised in the lab ?
- What successes can we see from previous industries ?
- It is *in the interest* of the regulatory bodies to reduce costs.
- Do we want to focus on specific areas whereby attrition rates are already lower than other treatments being developed and which modelling can reduce the attrition rates even further ? But do we then also want to try and convince our audience that the modelling tools can be applied to a very general group of treatments as well ?
- What software exists already (in pharma and other industries) ?
- → What can we have in five years' time ?
- → What are the next steps in the software and the hardware that will be available ?
- Be aware that when developing simulations for nuclear bombs in France, there also needed to be an increase in experiment as well so this did not lead to savings. Try to convince our audience that increased modelling will reduce the need for so much experiment (reducing time and costs) due to the strength of the science involved in the methods.
- Think about the communication between the FDA, pharma firms and scientists.
- What simulations *can not be done yet* ? How can overall improvement happen ?
- What are the timescales involved and the potential benefits ?
- How can you harness distributed computing ideas such as FoldIt or Folding@home ?
- In the nano-technology industry, huge investments were needed to be made in training people to learn new skills and money was needed for new manufacturing and fabrication facilities. We need to convince our audience that *in silico* modelling will aid existing facilities in the lab to synthesize new drugs and other targets and that an investment in software and hardware will pay back this initial investment within at least 15 to 20 years.
- Examples of Pfizer sponsoring PhD students, having industrial supervisors linked to the company and potentially employing them after they have submitted their thesis.
- Highlight Pfizer plans to slash its research and development spending by billions and cut thousands of jobs

- Would we be killing innovation by taking people out of the labs and getting them to work in industry on pharmaceutical simulations ?
- Operationalising the *in silico* modelling: What are the dangers ? Is it feasible ? What would it cost to move in that direction ?
- Equipment issues, company issues, increasing collaborations with universities
- Can we find stable software already in existence that can meet the pharma industry's needs, like ABACUS in engineering or CASTEP in materials science. Could ONETEP be the future for atomistic quantum mechanics simulations of biological systems ?
- Empirical Approach to testing
 - → Need yield from your investment
 - → What is it investigating ? Pathways ? Reactions ?
- On the timescales being considered, will the software options being considered still be a viable solution ?
- Application, application, APPLICATION
 - → We need to generate the interest of investors.
 - → Who is interested in this (apart from MedImmune) ? Where can profit be made ?
 - → Are there less attrition rates in certain treatments ? What rates can be *most* reduced, thereby giving greater revenue ?
 - → Will competitors be a use or a hassle ?
 - → What are the timescales of the company benefiting from an initial investment ?
- Must consider **Opportunity Cost**
 - → If - for example, one would need to eliminate 100 R&D areas to put money into *in silico* modelling, how much would be gained from focussing on this area ?
 - If this were approved, how would this give an individual company (i.e. MedImmune) a competitive advantage ?

The four main areas we thought would be useful to focus on:

1. What is the state of the art ? What is the scientific and commercial feasibility of existing *in silico* modelling techniques from academia or industry ? We need to be sure to cover both optimistic and pessimistic areas, in order to present a balanced argument but also highlight the strengths of going in favour of more modelling.
2. CASE STUDIES: Examples from the Pharama industry of existing emphin silico modelling techniques and examples from other industries and illustrations OF NUMBERS highlighting the significant savings that have been made in other industries.

3. What are the future costs of moving in this direction ? What are the benefits that can come from a move in this direction ? What are the timescales involved ? What is the genuine feasibility of *in silico* technologies becoming a reality ? What are the possible pitfalls ?
4. INVESTMENT: Who is interested ? OPERATIONS: How would you organise the required people, skills and equipment ? COLLABORATIONS: How would we harness collaborations between pharma companies and university labs ? What can the pharma industry offer scientists they can not get in academia ? However, we must be sure not to put too much effort into this point as the team addressing *Challenge 1: How to put in place a very broad collaboration between multiple academic groups at Cambridge University and MedImmune Research?* will be working on solutions to this issue.

Additions from Pablo

For the business case I recommend you to:

- Try to be PRECISE, something great does not need to be complicated to understand. The judges want quality of an innovative product, but they will need to fully understand it in just ten minutes.
- Do not forget the Marketable and Profitable characteristics of the product, the judges will act as INVESTORS.
- How Time and Resources will help us to develop the product?

Additions from Saturday 12th March Meeting

- Illustration of hill you would have to climb but with pathways around it
- → illustrating that *in silico* modelling will allow you to get around the tough challenges coming from increasing total R&D spending when approval rates are decreasing.
- Around 30 percent of spending is done before Phase I clinical trials
- QSAR is software implementing neural network techniques looking into similarity of different drugs, effectively the homology approach on a large scale as it can be applied to huge databases of existing molecules.
- We need to convince the head of research that we UNDERSTAND the steps involved in the process of initial drug discovery and each phase up to marketing a finished product
- Within pre-clinical development you need to check the stability of your target proteins within different environments such as water, blood and stomach acids. Software can implement a range of implicit solvent models for the same types of molecules you are investigating.
- Changing the processes involved up until pre-clinical development (which could instead benefit from 50/50 modelling-experiment processes) with the use of selective filtering from harnessing the predictive power of *in silico* models

- Otherwise look to presentation slides for further ideas

Our three main ideas that we wish to present as the core of our argument involve:

1. Acquisition of existing R&D sections of companies
2. Harnessing collaboration between industry and academia
3. Starting in-house software teams

2 Presentation

The presentation will need to be TEN MINUTES in length (should we need no more than one slide per minute ?) and well will need to present up to THREE IDEAS. We will be assessed by a panel of three key MedImmune figures, including the Head of research at the Cambridge site, the Head of Operations (Vice President) and the Clinical Project Manager We will be judged on some key areas:

- **Novelty** - they want to hear new ideas they won't have previously thought about
- **Feasibility** - perhaps this won't work, it doesn't need to be a finished product but it needs to be *innovative*.
- **Quality** - they want *quality* ideas and *quality* presentations.
- **Ideas** - they are interested in learning what we can come up with and how we think about creative solutions to tough problems.