



Research Infrastructures for the
Life Sciences in Europe
Vienna, June 5-6, 2006

Research Strategies & Needs of the Bio-Industries

Adriano Henney

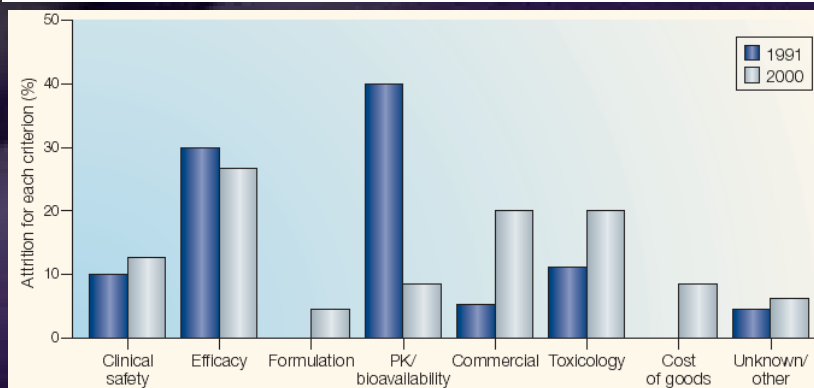
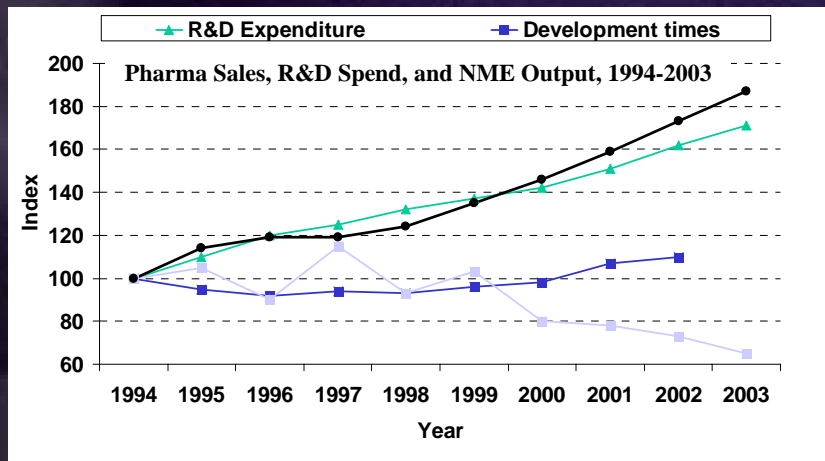
Director

Global Discovery Enabling Capabilities & Sciences

Outline

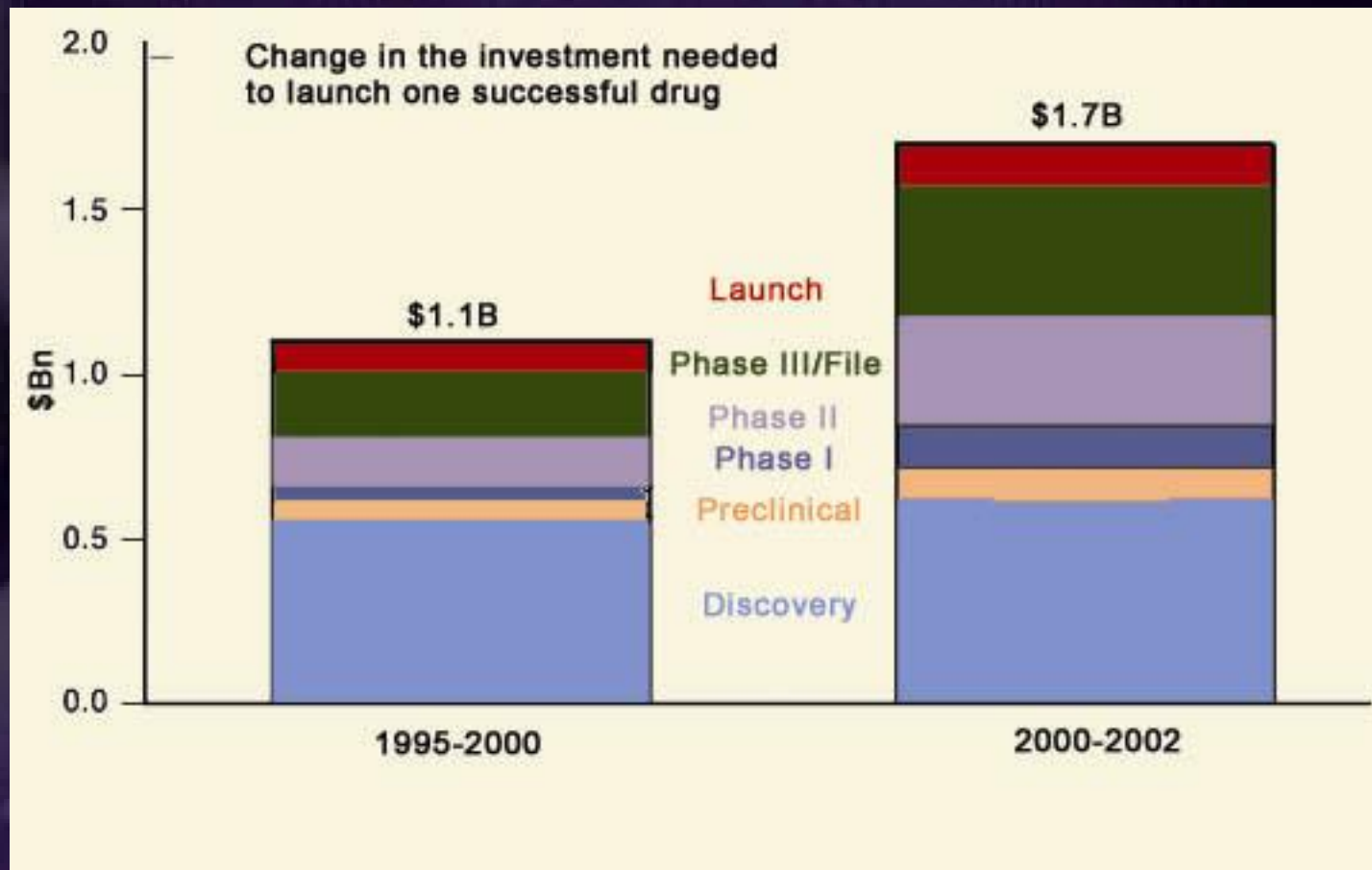
- General points on challenges of pharmaceutical R&D, the demands these impose and potential solutions
 - Information from Corporate & Scientific Affairs
- More specific focus on Systems Biology as a research theme seen to have the potential to impact the development of innovative medicines

Pharma Challenges



- Rising cost of R&D but not paralleled by increased number of NME approvals
- Increased risk due to increased difficulty of developing innovative molecular targets
- Continued attrition due to tox and lack of efficacy
- Regulatory environment more challenging: risk/benefit ratio increasingly difficult to achieve

Pharmaceutical R&D Costs



Windhover's In Vivo: The Business & Medicine Report, Bain drug economics model, 2003

The Genome Revolution: Hope & Expectation

- Huge advances in genetics, molecular & cellular biology and supporting technologies
- Acquisition of highly detailed molecular information in high quantity and quickly
 - Ability to define disease at the molecular level, with expectation that this would increase understanding
 - Hope that this would deliver novel therapies quickly

The Consequences

- Fiercely competitive market
- Technologies -> high throughput screening strategies using 100,000's of compounds and biological assays relevant to disease mechanism
- Refinement of compound structure & activity to enhance benefit and reduce potential for side effects
- Increasing speed and volume through pipeline
- BUT: Significantly increased output from Discovery into Development not mirrored by increased success in development

Pharmaceutical R&D: Facing Major Challenges

Challenges

- More difficult diseases, targets & mechanisms
- Decreasing productivity & increasing costs
- Shifting expectations of efficacy/safety balance
- Patient expectations ever increasing, fuelling demand but squeezing budgets
- Industry reputation weaker; essential animal studies threatened

Adriano M Henney PhD

AZ R&D Priorities

- Access the best science and scientists globally
- Major improvement in productivity
- Create a more balanced pipeline sourced from both internal & external innovations
- Optimise our global organisation to drive projects faster
- Ensure optimal governance and risk management



Need Investment in the Development of Innovative Therapies

Current Picture

Innovation in Europe: the picture today (2004)

- ↑ US spend on research as % of GDP
(2.4% risen to 2.8% in 20 years)
- ↓ EU spend on research as % of GDP
(fallen to 1.9% from 2.4% in 20 years)
- The Lisbon target for Europe
GDP spent on research by 2010
– ⇒ 3% GDP spent on research by 2010

Investment

- US NIH Alone \$27,000 million p.a.
- EU Framework VI €4,5000 million over 5 years
- MRC £394 million p.a.
- BBSRC £249 million p.a
- Wellcome Trust £432 million p.a.

Constraints to Biomedical Research Success

- No integrated European strategy and no clear priorities
- Poor investment in education and training including clinical research
- Market constraints to reward innovation
- Attitudes to entrepreneurship in academia
- Relationships between industry and academia need to strengthen
- Fragmentation of research
- Regulations and Laws

Solutions

- Develop integrated biomedical research strategy and prioritisation
- Funding increased and aligned with the strategy and priorities
- Greater investment in science education – primary, secondary and higher
- Closer collaboration between academia and industry built on mutual respect
- Protection from animal rights terrorists

Opportunities in Europe

- EU Research Area
- Framework Programme 7
- EU Technology Platforms
- EU STEM education and skills base

Innovative Medicines Initiative

- EU needs a strategy for enhancing & accelerating research into the development of innovative medicines
- Requires involvement of all stakeholders academia, industry, regulators, patient organisations, healthcare representatives

Innovative Medicines for Europe:

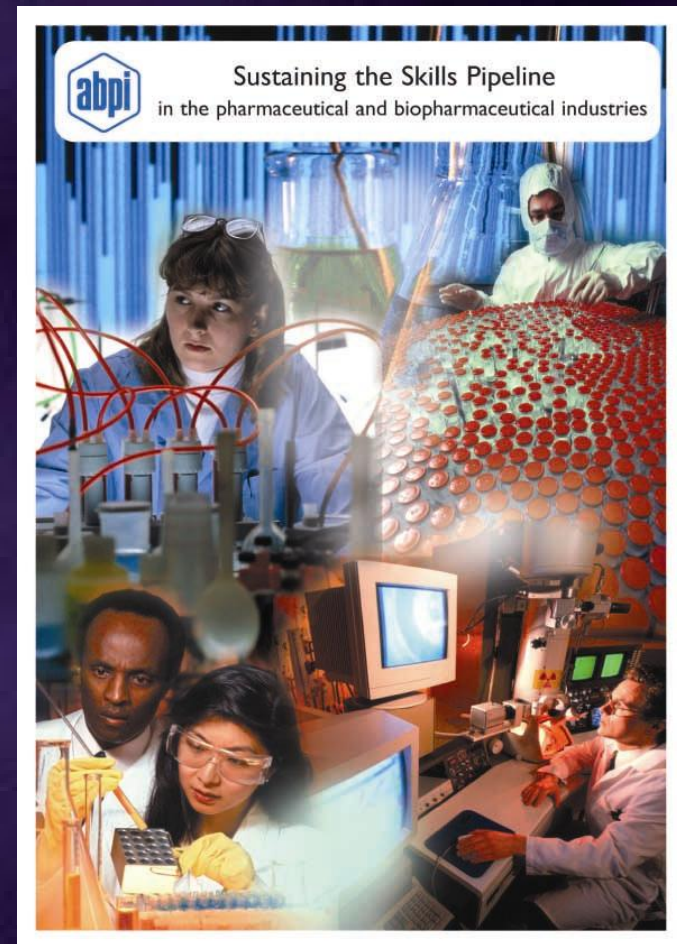
Specific deliverables

- Strategic research agenda – define & set priorities for research activities
- Financial plan – leverage private & public funds
- Public-private partnerships – creation of virtual institutes connecting competence centres
- Patients involvement – information systems linking patients associations with researchers & policy makers
- Innovation – creation of tech transfer offices to exploit results
- Involvement of regulators – establish a structure to enable early involvement of regulatory authorities
- Policy – establish framework for providing input to healthcare policies
- Education – development of STEM skills
- Public information campaign – improve public understanding and perception of pharma

ABPI Science, Technology, Engineering & Manufacturing (STEM) Skills Task Force

Aim:

To review the provision of skilled scientists, engineers and technologists to support pharmaceutical R&D and manufacturing in the UK and highlight issues for the future



STEM Skills: Terms of Reference

- Objectives:
 - Review current and future skills needs for the pharmaceutical industry
 - Assess the effectiveness of the UK education system in meeting these needs, from primary through to postgraduate
 - Identify challenges and targets for Government, the education sector, industry and other stakeholders
 - Leverage support from key organisations
 - Develop a framework for ABPI policy on education including specific initiatives for industry

Weaknesses were identified in core science graduate training

- Issues across a variety of degree courses:
 - Mathematics
 - Practical Experience
 - Exposure to *in vivo* work
 - Chemistry
 - Communication
 - Modular Degrees
 - Computational Analysis



The most significant skills shortages were identified in :

- *In vivo* sciences
- Clinical research and experimental medicine
- Chemical sciences
- Engineering
- Maths & statistics



Clinical Research

- Europe needs to be strong in clinical science to translate scientific advances into patient benefit
- Europe lacks activity and capacity for experimental medicine and large scale clinical trials
 - Bell Report, Academy of Medical Sciences

Clinical Research: Impediments

- Shortage of facilities
- Lack of infrastructure
- Inadequate funding
- Failure to utilize infrastructure that does exist (e.g.NHS)
- Increasingly complex and bureaucratic legal and ethical framework

Clinical Research: Solutions

- Create trans-national networks for clinical research excellence
- Additional funding for clinical research programmes, e.g. original NHS aim to commit 1.5% of turnover to research
- Improved career structures and incentives for clinical scientists
- Improved regulatory environment



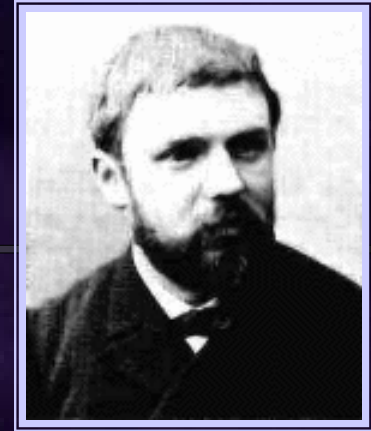
Systems Biology

Post-Genome Issues

- Genetics & Molecular Biology have provided very detailed information on single entities associated with or linked to complex diseases
- Reductionist approach identifies single components and, possibly, their function, but
 - Only parts of a complex system
 - No information on cellular/ system interactions

Henri Poincaré

(1854- 1912)



“Science is built up of facts, as a house is with stones. But a collection of facts is no more a science than a heap of stones is a house.”

Systems Biology

- Need to put targets into context: a biological equivalent of electronics' "wiring diagram" to understand target response within physiological networks, not in isolation
- Systems Biology may offer a solution to this "context" problem

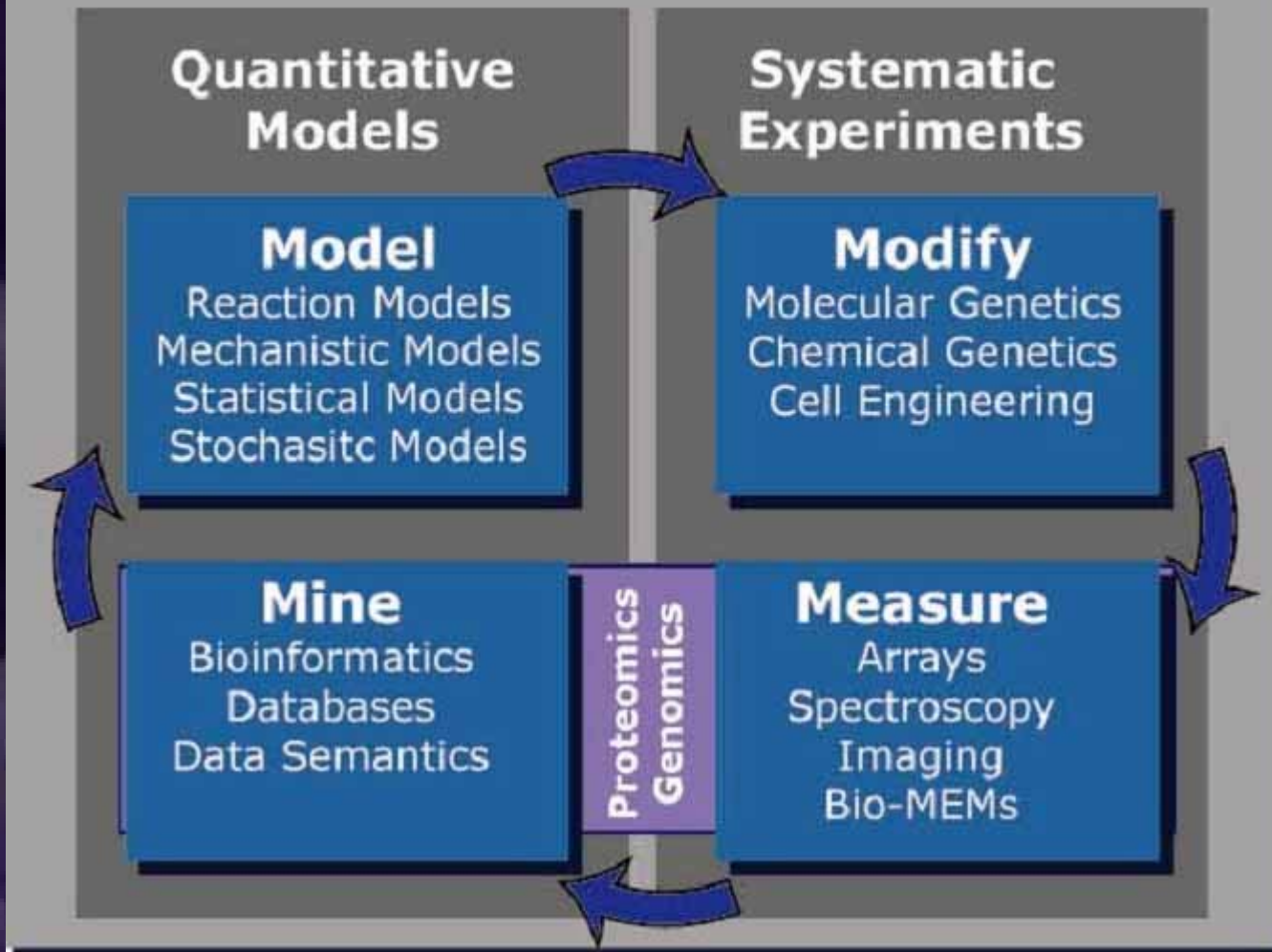
What is Systems Biology?

- The quantitative analysis of how the components of complex biological systems interact dynamically to translate a stimulus into a response.
- Uses a combination of experimentally derived data (parameters), and computational models of a system's behaviour
- Tackles the complexity of multi-parameter interactions that underpin the biological function being studied.
- Contrasts with reductionist methods, focusing in detailed study of parts of a complex system in isolation

Misconceptions

- What it's not:
 - a technology like proteomics or genomics
 - replacing empirical methods and experiments with *in silico* approaches
- What it is:
 - It requires input from *-omics* technologies, but is offers a physiological and mechanistic perspective.
 - It requires computation and experimentation to work together.
 - It organises and connects data taken from a variety of sources & technologies

Computational and systems biology paradigm

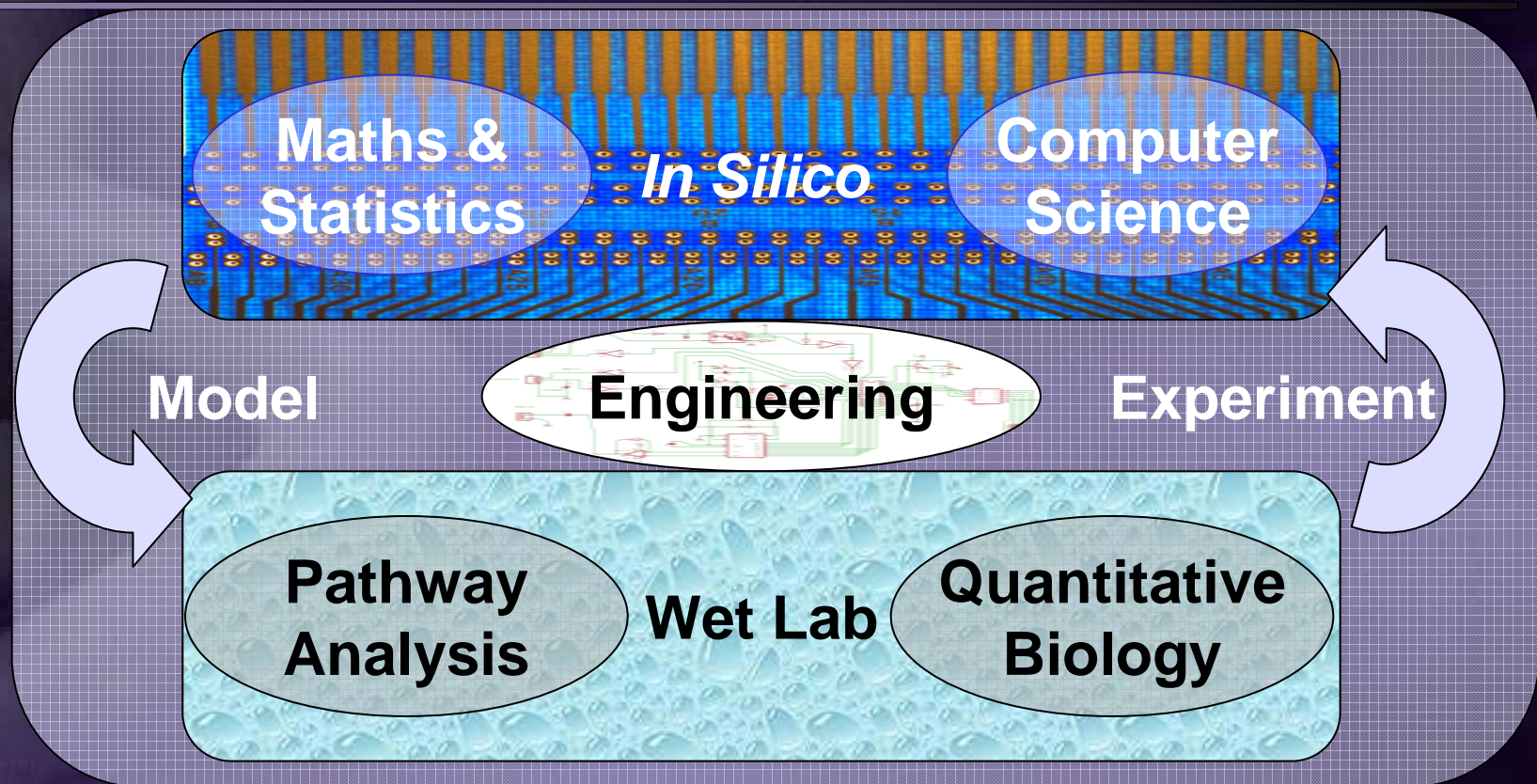


Courtesy of Prof Peter Sorger, MIT

What is needed

- Generation of high quality quantitative data rapidly and in quantity
- Ability to mine existing data rapidly:
 - Text/ literature mining
 - Access to clinical level information
- Skills:
 - Maths for biology & *vice versa*
 - Biology with an engineering perspective
 - Multidisciplinary thinking

Our activities: Internal



Multidisciplinary, cross-functional project teams

Integrated computational biology & pathway analytical components

Our activities: External

- Recognise that key developments in Systems Biology discipline is in academia
 - MIT; Manchester; Cambridge
- Application to health & disease by pharma & biotechs
- Work as a cross-functional project team
- Active involvement of drug discovery and development teams
 - Relevance & impact
 - Access to small molecule “tools” & disease knowledge
- Objectives include both academic (public) & proprietary elements

Where next?

- Continue to develop & build the internal platform
- Further develop Systems Biology within AZ using targeted external partnerships
- Continue to apply approaches to real drug discovery/development problems to offer solutions/options & demonstrate impact
- Build confidence

Some thoughts on Infrastructures

- Promotion & coordination of multidisciplinary SysBio Initiatives
- Consider establishing limited number of major centres for Systems Biology
 - Critical mass in physical, engineering & biological sciences
 - Specific areas of focus but effective networking -> best practice
 - Development of core essential skills & culture
- Promote SysBio benefit to EU health
- Promote benefits to engineering
 - Novel devices & manufacturing



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Summary Points

Industry & Academia

- Academics are more frequently entrepreneurs in the USA as evidenced by the numbers of companies created.
- Some European academics seem to believe that fundamental research untainted by industrial utility is the only worthwhile pursuit
- Many academics think industry gets their valuable ideas cheaply
- Some academics see industrial scientists as second or third rate
- Some industrial scientists see academics as self-indulgent, arrogant and unworldly
- Industry believes most academics overvalue their ideas which require real work to translate into practice

What are we doing about this?

- Industry wide push to promote the Lisbon agenda and competitiveness
- Action plan with clear recommendations for the pharmaceutical sector (G10)
- A stronger EU industry will bring benefits to the biomedical research base
- The biomedical research base underpins future drug discovery and development
- Dialogue with key stakeholders is required to develop and deliver a world-class science education system

Conclusions (both parts)

- Europe is losing competitiveness in biomedical research
- Biomedical research is critical for European pharmaceutical success
- There are no simple solutions

But

- An integrated, prioritised strategy is needed
- Greater investment in education & research must be made
- We must use all of our scientific talent
- Bureaucracy must be eliminated
- Close, true collaboration must be fostered between academia and industry
- **Only concerted effort from academia, industry, government and other funders can reverse the decline.**