Bionanotechnology

Commercialisation of Bionanotechnology

resources

- Bridging the valley of death: improving the commercialisation of research, House of Commons Science and Technology Committee, 2013 [http://www.publications.parliament.uk/pa/cm201213/cmselect/cmsctech/348/348.pdf]

Topic examples

- Artificial blood cells - Red blood cell-mimicking synthetic biomaterial particles Nishit Doshi [http://www.nature.com/articles/ncomms12828]
- Synthetic gecko foot-hairs for future wall-climbing and surgical robots Sitti and Fearing [http://www.tandfonline.com/doi/abs/10.1163/156856103322113788]
- Bio fabrication principles- DNA-Directed Self-Assembly of Graphene Oxide with Applications to Ultrasensitive Oligonucleotide Assay Longhua Tang, Ying Wang, Yang Liu, and Jinghong Li [http://pubs.acads.acs.org/doi/abs/10.1021/nm200147n]

Evaluation criteria

<table>
<thead>
<tr>
<th>Grade Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>20-30%</td>
<td>A very good, clear and concise introduction to the technology. Describes the broad area of the technology and the specific research area. Has a very brief introduction to the technology and the specific research area.</td>
</tr>
<tr>
<td>30-40%</td>
<td>A good introduction to the technology. Describes the broad area of the technology and the specific research area. Describes some advantages of the technology/what problem it solves. Describes the broad area of the technology and the specific research area.</td>
</tr>
<tr>
<td>40-50%</td>
<td>A very good, clear and concise introduction to the technology. Describes the broad area of the technology and the specific research area. Describes some advantages of the technology/what problem it solves. Describes the broad area of the technology and the specific research area.</td>
</tr>
<tr>
<td>50-60%</td>
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</tr>
<tr>
<td>60-70%</td>
<td>A very good introduction to the technology. Describes the broad area of the technology and the specific research area. Describes some advantages of the technology/what problem it solves. Describes the broad area of the technology and the specific research area.</td>
</tr>
<tr>
<td>70-80%</td>
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</tr>
<tr>
<td>80-90%</td>
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Note: The evaluation criteria are based on the quality and clarity of the introduction, the coverage of the technology, and the relevance of the specific research area. The criteria are designed to assess the effectiveness of the introduction and its alignment with the requirements of the technology.
Overview

- What is bionanotechnology?
- Research -> Product
  - Quantification of progress – TRL
  - Valley of death
- Intellectual Property
- Regulation
- Case study – Affymetrix
- Topic examples

What is bionanotechnology?

- A subset of nanotechnology
  - Use biological starting materials, biological design or biological fabrication principles
  - Applied in medicine or biotechnology.

Research -> product

Technology readiness level (TRL)

- An estimate of the maturity of a technology.
- Conceived by a NASA researcher, Stan Sadin in 1977 (7 levels).
- Formalised in 1990s NASA - nine levels widespread acceptance across industry.
- Precise definitions adapted to suit needs.
Valley of death

• “Valley of Death” - the gap between the lab and the marketplace
  Significant roadblocks; funding gaps; long clinical trials; lack of access to
  the right skills, support and infrastructure.

• “Commercialisation is particularly challenging in the life sciences sector,
  due to the long time frames, significant capital requirements, and the
  higher regulatory barriers associated with products intended for use in
  humans.” – House of Commons Science and Technology Committee

Crossing the valley of death

A “three pillar bridge” to address the difficulty in translating ideas to products

1. Technological research
   • Use advantage of European scientific excellence
   • Proofs of concept demonstrations
   • Proprietary – Protect IP

2. Product development and demonstration
   • Exploitation to make innovative product prototypes
   • Need pilot lines (prototyping facilities)
   • Validation - demonstration and deployment operations European sites,
     protecting the technological advance.

3. Advanced manufacturing
   • Competitive production facilities
   • Scale up product prototypes
   • Develop new manufacturing technologies

Focus on Key Enabling Technologies (KETs)

• “Technology bricks”
• Knowledge and capital intensive technologies
• High (R&D) intensity
• Systemic relevance and multidisciplinary

European Commission - High-Level Expert Group on Key Enabling Technologies (2011)
What do investors want to know?

- The technology
  - What does it do?
  - Competitive landscape
  - The USP – Unique Selling Soint

- How can investors make money
  - Target market
  - Market size – how to estimate – research firm. E.g. profit/test * x tests/year * estimated market share
  - Research firm surveys

The business Model Canvas

The business Model Canvas

Intellectual property rights (IPR)

Intellectual property rights include patents, copyright, industrial design rights, trademarks, trade secrets

Patents
- An exchange: given protection, but no longer secret
- Must be Inventive and Non-obvious

• Costs – Attorney + filing
• Sometimes best to keep “know-how” secret
Typical route to protection

- CE marking (Conformité Européene)
  - Meets safety, health or environmental requirements
  - Product can be sold anywhere in Europe
- Electromagnetic Compatibility (2004/108/EC)
- General Product Safety Directive (92/59/EEC)
- Medical Electrical Equipment (BS EN 60601)

Medical directives
- CLIA (US)
- Medical Device Directive MDD (EU)
  - Directive 90/385/EEC regarding active implantable medical devices (AIMD)
  - Directive 93/42/EEC regarding medical devices (MDD)
  - Directive 98/79/EC regarding in vitro diagnostic medical devices (IVDD)

Why medical regulation?
- E.g. *in vitro* diagnostics (detect diseases, conditions, or infections)
- Safety
- What if the test is not accurate, not calibrated, wrongly performed?
  - E.g. cholesterol wrongly reported as low – risk heart attack
  - HIV test
  - Wrong blood grouping? (ABO system)

Case study – Affymetrix GeneChip®
- Invented in the late 1980's by a team of scientists led by Stephen P.A. Fodor, PhD.
- Using semiconductor manufacturing techniques with advances in combinatorial chemistry to build vast amounts of biological data on a small glass chip.
- This technology became the basis of a new company, Affymetrix, formed 1991.
- March 2016 Acquired by Thermo Fisher Scientific (1.3 billions USD)
Multiple funding rounds
• Series A private placement - $21M
• Series B placement - $39M
• 1996- IPO - valuation of $300M


Revenues from payments from collaborative research and development agreements and government research grants ($4.63 million in 1995).

As of March 1996- Sold nine GeneChip systems – all solely for research use
• Year ending 31st Dec 1996 – revenues of $12.0M net loss $12.2 million
By 2000, Affymetrix's R&D expenses were $57.4 million and its product sales for that year were $173 million.

By September 2001, the majority of the top pharmaceutical companies, over a dozen biotech firms, and more than 1000 academic institutions were customers for the firm's GeneChip and other technologies.

Miniature Haematology Analyser

- Automated processing of 30 µl whole blood to produce full blood count (finger-prick)
  - RBC, WBC, PLT, Hb
- Reagents pre-loaded onto disposable cartridge
  - £5-6 per test
- Bench-top portable reader processes sample and analyses data for output
  - (screen, printer, upload to patient record etc.)
- < 5 minutes to result

Competitor Products

<table>
<thead>
<tr>
<th>Measures</th>
<th>Disposable cartridge</th>
<th>Time per test</th>
<th>Cost per test</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Cells</td>
<td></td>
<td>&lt; 5 min</td>
<td>£5-6</td>
</tr>
<tr>
<td>Red Blood Cells</td>
<td></td>
<td>&lt; 5 min</td>
<td>£1.85</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>&gt; 3 min</td>
<td>£4.50 (x 2)</td>
</tr>
<tr>
<td>Haemoglobin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sysmex pachy-100i</td>
<td></td>
<td>~2.5 min</td>
<td>£1</td>
</tr>
</tbody>
</table>

Point-of-care test

Lab test
Market Needs / Proposed Product

**Market Need:**
- Full, or complete, blood counts (FBCs):
  - Counts the numbers of red and white blood cells, platelets and haematocrit level in blood
  - An FBC is the most commonly requested diagnostic test in the developed world
  - FBCs are currently routinely sent to centralised haematology laboratories for analysis on large, automated machines
  - Slow turnaround time
  - Inconvenient for patients

→ Need to provide a point-of-care device so that FBCs can be carried out at the point-of-need with immediate results

**Proposed Product:**
- Disruptive technology to meet identified market needs
- Diagnostic, point-of-care FBC disposable chip and reader
  - Each test self-contained
  - All reagents integrated into disposable chip
  - Simple to use
- Used by:
  - GPs in surgeries
  - Doctors and nurses in hospitals
  - By community care nurses in the community
  - In care homes for the elderly
  - For home self-testing

**Large lab based Haematology Analyser**

**Disposable Haematology Chip**

**Handheld / desktop reader, one per clinician / nurse:**
- Disposable chip
- One per test

**Potential Service Model:**
- Pay-per-test, service contracts

**Proposed Product:**
- Diagnostic, point-of-care FBC disposable chip and reader

**Market Segmentation and Opportunities**

**Market:**
- Global haematology market is expected to grow from $5.7 trillion in 2010 to $8.1 trillion by 2017
- CAGR of 5%
- Development of high sensitivity point-of-care tests is expected to drive the growth of the global haematology market
- USA is largest contributor to the market, contributing over 50% of the global market in 2010
- Market is likely to expand due to:
  - Increasing elderly population
  - Adoption of point-of-care testing equipment
  - Companion diagnostics

**Investment and Opportunities:**
- Requires a ~£4 million investment over 4 years
- Product launch: FY2015
- Profitable / self-sustaining business: FY2017
- Return on investment / breakeven: FY2018
- Revenue at 2022: £20 million (Global)

**Summary:**
- Target market share by 2022
- No of tests / year (million)
- Target revenue (£)

<table>
<thead>
<tr>
<th>Country</th>
<th>% of Share</th>
<th>No of Tests</th>
<th>Target Revenue</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>2%</td>
<td>1</td>
<td>£5million</td>
</tr>
<tr>
<td>USA</td>
<td>2%</td>
<td>10</td>
<td>£10million</td>
</tr>
<tr>
<td>GLOBAL</td>
<td>2%</td>
<td>20</td>
<td>£20million</td>
</tr>
</tbody>
</table>

**Source:** Hematology Reagents and Analyzers – Global Pipeline Analysis, Competitive Landscape and Market Forecasts to 2017, GlobalData, April 2011

**Components demonstrated on whole human blood samples**
- Impedance chip:
  - Proven to reliably count red blood cells, white blood cells, and platelets
  - Concordance data using healthy human blood
- Blood preparation device:
  - Microfluidic blood preparation device designed and tested
  - Proven proof-of-concept using whole human blood
  - WBCs, RBCs, and PLTs
- Integration of impedance chip into blood preparation device was demonstrated in December 2013
- Patents filed

**Technology Status & IP**

**IP Status:**

<table>
<thead>
<tr>
<th>Patent Number</th>
<th>Assignee</th>
<th>Priority Date</th>
<th>Content of 1st Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>GB201306913D0</td>
<td>UoS</td>
<td>16/04/2013</td>
<td>Method of electrically measuring cells flowing in a liquid</td>
</tr>
<tr>
<td>GB201306914D0</td>
<td>UoS</td>
<td>16/04/2013</td>
<td>Apparatus for electrically measuring cells flowing in a liquid</td>
</tr>
<tr>
<td>US 13/865,215 (will be split)</td>
<td>Sharp</td>
<td>09/08/2013</td>
<td>A fluidic device for preparing a blood sample</td>
</tr>
</tbody>
</table>

**Topic examples**

- **Synthetic microswimmers.** Nanolocomotion—Catalytic Nanomotors and Nanorotors Mirkovic et al
  [http://www.nature.com/articles/ncomms12828 -swim towards light (Phototaxis)](http://www.nature.com/articles/ncomms12828)

- **Artificial blood cells** - Red blood cell-mimicking synthetic biomaterial particles
  Nishit Doshi [http://www.pnas.org/content/106/51/21495.short](http://www.pnas.org/content/106/51/21495.short)

- **Synthetic gecko foot-hairs** for future wall-climbing and surgical robots

- **Bioinspired Materials** for Controlling Stem Cell Fate
  Omar Z. Fisher, Ali Khademhosseini, Robert Langer and Nicholas A. Peppas
  [http://pubs.acs.org/doi/abs/10.1021/ar900226q](http://pubs.acs.org/doi/abs/10.1021/ar900226q)

- **Bio fabrication principles**- DNA-Directed Self-Assembly of Graphene Oxide with Applications to Ultrasensitive Oligonucleotide Assay
  Longhua Tang, Ying Wang, Yang Liu, and Jinghong Li
  [http://pubs.acs.org/doi/abs/10.1021/nn200147n](http://pubs.acs.org/doi/abs/10.1021/nn200147n)
# Resources


The following table outlines the grade criteria for the introduction, state of the technology, critical evaluation, and resources sections of the report.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Introduction to the Technology</th>
<th>State of the Technology</th>
<th>Critical Evaluation of the Gap between the Technology and a Product</th>
<th>Writing Style, Balance, Clarity, Referencing</th>
</tr>
</thead>
<tbody>
<tr>
<td>30-39%</td>
<td>A very good, clear and concise introduction to the technology. Describes the broad area of the technology. An adequate discussion on the potential impact of the technology.</td>
<td>A very good and realistic analysis of the technology readiness level of the product. A detailed discussion of the rationale for the decision supported by appropriate references from a range of sources.</td>
<td>A very good discussion on the gap between the research and product. Some critical analysis supported by appropriate references.</td>
<td>Well written. Appropriate language for the lay audience in the vast majority of the introduction. No or few spelling or grammatical errors. Good balance between each required element. Consistent referencing.</td>
</tr>
<tr>
<td>40-49%</td>
<td>A good introduction to the technology. Describes the specific research area and a brief overview of the broad research area. Some discussion of the potential impact of the technology.</td>
<td>A good and realistic analysis of the technology readiness level of the product. A good discussion of the rationale for the decision supported by appropriate references.</td>
<td>A good discussion on the gap between the research and product. Some critical analysis supported by appropriate references.</td>
<td>Well written. Appropriate language for the lay audience in majority of the introduction. No or few spelling or grammatical errors. Good balance between each required element. Minor referencing mistakes.</td>
</tr>
<tr>
<td>50-59%</td>
<td>An adequate introduction to the technology. Describes the broad research area. Generally flows well, but some sections may not be clear. Gives indication of the potential impact of the technology.</td>
<td>A reasonable analysis of the technology readiness level of the product. Decision is supported by some references from a few sources.</td>
<td>A reasonable attempt at critical analysis.</td>
<td>Clearly written. Introduction not clear in places, or some explanations not suitable for the target audience. Minor spelling or grammatical errors. Some referencing mistakes.</td>
</tr>
<tr>
<td>60-69%</td>
<td>A reasonable introduction to the technology. Describes the specific research area and the broad area of the technology.</td>
<td>A reasonable analysis of the technology readiness level of the product. Decision is supported by references from a wide range of sources.</td>
<td>A reasonable attempt at critical analysis.</td>
<td>Clearly written. Least explanations are less complicated for lay audience or in an academic style. Report not well balanced between sections and/or numerous formatting mistakes. Some spelling or grammatical errors. Inconsistent referencing.</td>
</tr>
<tr>
<td>70-79%</td>
<td>A very good, clear and concise introduction to the technology. Describes the broad area of the technology. A very good and realistic analysis of the technology readiness level of the product. A detailed discussion of the rationale for the decision supported by appropriate references from a range of sources.</td>
<td>A good and realistic analysis of the technology readiness level of the product. A detailed discussion of the rationale for the decision supported by appropriate references from a range of sources.</td>
<td>A good discussion on the gap between the research and product. Some critical comments made.</td>
<td>Clearly written, but the introduction is less clear in places, or some explanations not suitable for the target audience. Minor spelling or grammatical errors. Some referencing mistakes.</td>
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<tr>
<td>80-89%</td>
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<td>A good discussion on the gap between the research and product. Some critical comments made.</td>
<td>Clearly written, but the introduction is less clear in places, or some explanations not suitable for the target audience. Minor spelling or grammatical errors. Some referencing mistakes.</td>
</tr>
<tr>
<td>90-99%</td>
<td>An excellent, clear and concise introduction to the technology. Describes the broad area of the technology, gradually narrowing to the specific research area. Clearly describes the potential impact of the technology.</td>
<td>An excellent and realistic analysis of the technology readiness level of the product. A complete discussion of the rationale for the decision supported by appropriate references from a wide range of sources.</td>
<td>A reasonable attempt at critical analysis.</td>
<td>Clearly written, but the introduction is less clear in places, or some explanations not suitable for the target audience. Minor spelling or grammatical errors. Some referencing mistakes.</td>
</tr>
<tr>
<td>100%</td>
<td>An excellent, clear and concise introduction to the technology. Describes the broad area of the technology, gradually narrowing to the specific research area. Clearly describes the potential impact of the technology.</td>
<td>An excellent and realistic analysis of the technology readiness level of the product. A complete discussion of the rationale for the decision supported by appropriate references from a wide range of sources.</td>
<td>A reasonable attempt at critical analysis.</td>
<td>Clearly written, but the introduction is less clear in places, or some explanations not suitable for the target audience. Minor spelling or grammatical errors. Some referencing mistakes.</td>
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