Comment

Supplementary information to:

The strategy behind one of the most successful labs in the world

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Luka Gebel, Chander Velu & Antonio Vidal-Puig

This Supplementary information comprises:

SUPPLEMENTARY INFORMATION GUIDE TO:

The strategy behind one of the most successful labs in the world

Luka Gebel[1,2], Chander Velu[3], Antonio Vidal Puig[4]

Affiliations:
[1]King's Business School, King's College London, London, United Kingdom
[2]Global Business School for Health, University College London, London, United Kingdom
[3]Institute for Manufacturing, Department of Engineering, University of Cambridge, Cambridge, United Kingdom
[4]Institute of Metabolic Science, University of Cambridge, Cambridge, United Kingdom

luka.gebel@kcl.ac.uk[1,2], c.velu*@eng.cam.ac.uk*[3], *ajv22@medschl.cam.ac.uk*[4]

Our general principle was to look for problems which were of very wide biological significance and yet at first sight appeared to defy explanation. It is exactly such problems which, if solved, produce major revolutions in our wider understanding of nature. Moreover, the fact that they are universal makes one hope that there may be an underlying simplicity

– Francis Crick and Sydney Brenner, 1971

SUPPLEMENTARY FIGURES

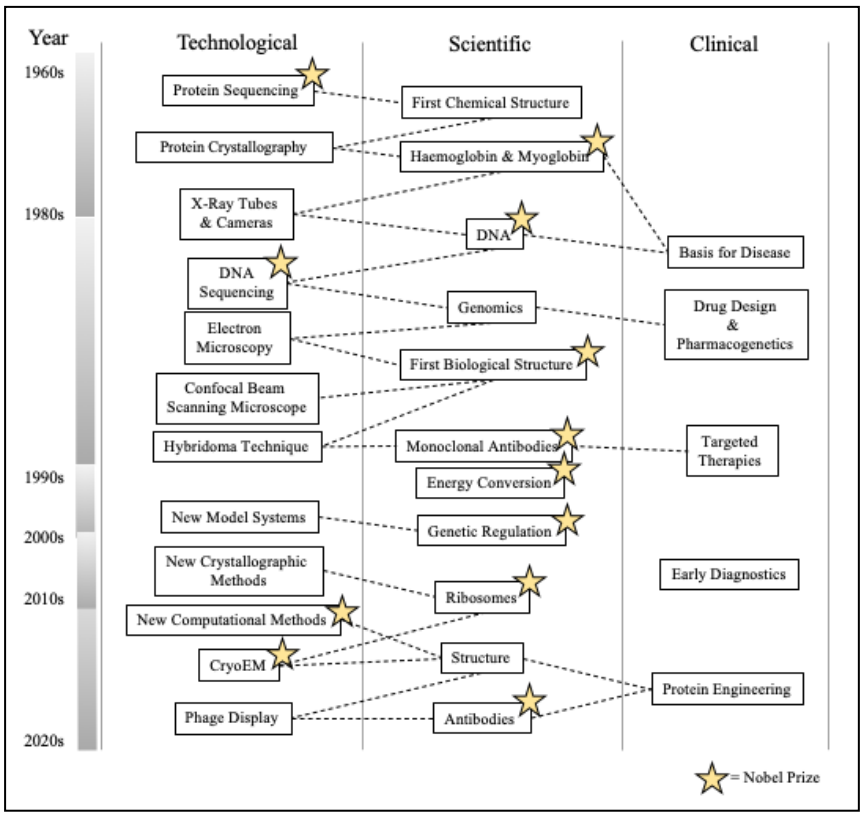

Figure S1: Historical View of Technology Development, Scientific Research and Clinical Applications at the LMB

This figure highlights the dynamic feedback between technological development and scientific questions. It categorises technological, scientific and clinical developments that can be traced back to the LMB from the 1960s to the 2020s. Stars highlight developments that received a Nobel prize. Dotted lines show how technological tools informed scientific findings and vice versa and how these were translated into clinical applications.

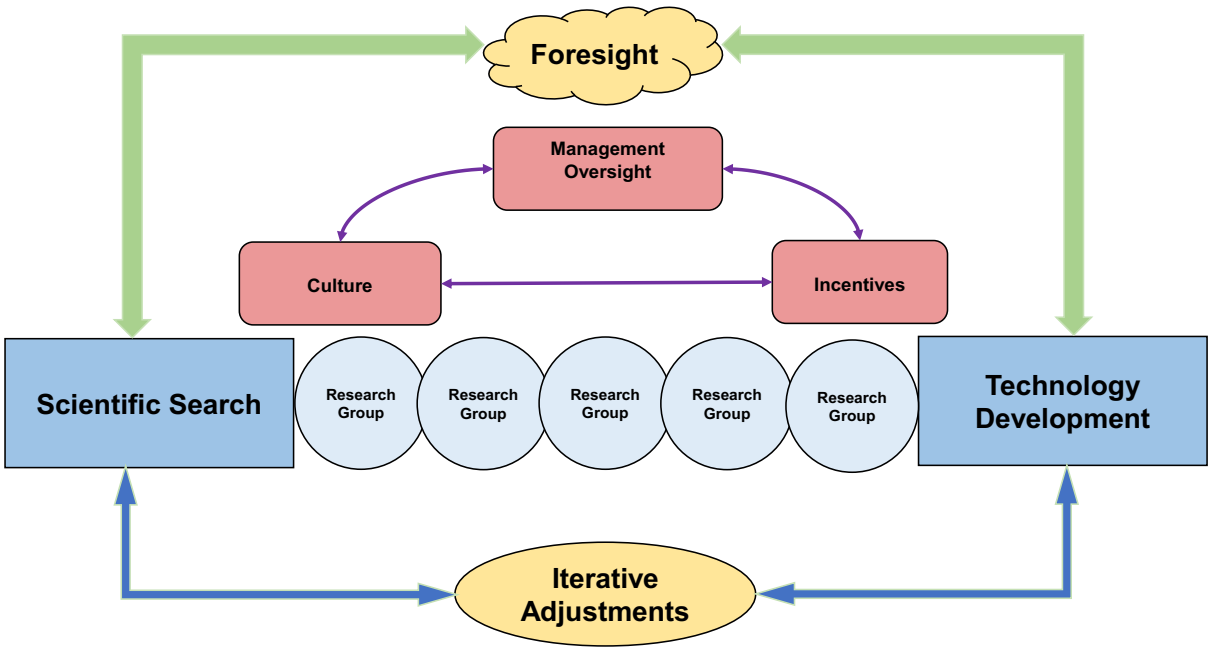

Figure S2: Management of Basic Science Discovery at the LMB
LMB's integrated management strategy prioritises three elements: culture, incentives and management oversight. LMB tackles basic scientific questions, necessitating the development of new technologies. While each group may request specific equipment, overlaps between the groups are prioritised by management for funding, which incentivises collaboration. The utilisation of shared equipment enables new insights, often resulting in the development of foresight through the identification of new scientific questions. This perpetuates a positive feedback loop, driving ongoing advancements and reinforcing LMB's position at the forefront of scientific research.

3. SUPPLEMENTARY METHODS

We conducted an inductive study based on 60 years of archival data (including research publications, meeting minutes, external assessment reports and internal management reports) and 12 semi-structured interviews with LMB and external scientists. The data analysis consisted of four stages (Miles and Huberman, 1994; Corbin and Strauss, 2014):

(i) Stage 1: Reconstructed historical timeline. We triangulated the data to create a timeline of central events in basic science, technology development and their clinical applications;

(ii) Stage 2: Verification of key events. We identified key events and matched them with micro-activities leading up to it (Krabbe & Grodal, 2023). We grouped all the key events in scientific discovery, usually marked by the recognition of a Nobel Prize and major science publications. As a result of stage 1 and 2, consistent feedback between scientific questions and technology development emerged. This prompted us to examine the literature from "science of science", "innovation management" and "strategy" as a lens to better understand the phenomenon;

(iii) Stage 3: Identified management processes. We mapped the management processes that support the feedback loop between science and technology development. We conducted qualitative coding by grouping themes that emerged from the archival and interview data. As a result, theoretical concepts of "culture", "incentives", and "management oversight" emerged;

(iv) Stage 4: Theorising and deriving a conceptual model. Based on the theoretical coding and extant literature we derived an integrated management strategy consistent with the data that provided theoretical insights.

Supplementary References

Corbin, J. and Strauss, A. (2014). *Basics of Qualitative Research: Techniques and Procedures for Developing Grounded Theory*. Sage Publications, Thousand Oaks, CA, USA.

Krabbe, A. D. and Grodal, S. (2023). The aesthetic evolution of product categories. *Administrative Science Quarterly*, 68(3), 734-780.

Miles, M. B. and Huberman, A. M. (1994*). Qualitative Data Analysis: An Expanded Sourcebook*. Sage Publications, Thousand Oaks, CA, USA.

4. SUPPLEMENTARY QUOTES/CITATIONS FROM REPORTS

Quote 1: The role of engineering tools is pertinent:

> *"New methods have always been at the heart of the rapid progress in molecular biology. It is thus pertinent to emphasise that the Laboratory, since 1962, has been at the forefront of development of methods and apparatus for molecular biology. Past examples are the method of isomorphous replacement, which made the solution of protein structures possible; protein and DNA sequencing; the construction of new types of powerful X-ray tubes and cameras, which made it possible to work on large weakly diffracting systems like viruses; low dose, high high-resolution imaging and image reconstruction methods in electron microscopy, which opened the structure determination of macromolecular assemblies in three dimensions; monoclonal antibodies; time-resolved X-ray diffraction of dynamical systems; protein engineering, and so on. A recent example is the confocal scanning microscope, which is a powerful new tool in studying cellular structure, and which has been successfully commercialised"* – LMB Quinquennial Review [1996].

Quote 2: The LMB encourages the recruitment of groups with complementary interests:

> *This cooperative atmosphere is encouraged by the recruitment of groups with overlapping interests, ensuring a critical mass in certain areas and providing a breadth of expertise that no one group could achieve. By this means, our strengths are maintained and developed over time* – LMB Quinquennial Review [2010].

Quote 3: The importance of the LMB's scientific diversity:

> *The LMB was founded by physicists and chemists: this physical view of biology persists, but the now much larger laboratory has a broad mix of talented individuals from very different backgrounds, including mathematics, engineering, and zoology. This means that it is usually possible to find someone in the laboratory to help you understand any problem that might arise in basic physics, chemistry, or biology* – LMB Quinquennial Review [2001].

Quote 4: Recruitment can affect the strategy as a whole:

> *"The strategy was specifically to move towards understanding and curing disease, which required staff able to undertake clinical research, in this case putting vectors into patients to achieve long term expression...such an appointment could affect the culture of the Laboratory hence impacting on the strategic direction of the Divisions and LMB as a whole."* – LMB Executive Committee Minutes [1997]

Quote 5: An example of the lab pressing forward with new technology to work on problems at the edge of what is possible – but in complementary directions:

> *In Cell Biology the major aim at the last review had been to expand into mammalian biology and this remained the vision. But it was also important not to suggest that cell biology only took place in that Division, since this reduced the case for the institute as a whole, and there was real attraction in presenting cross-divisional strategies.{…} Creating a sense of cross-divisional strategies had the added benefit of enabling group leaders to see their work as part of a larger umbrella programme, which might inspire individual programmes to aim at bolder goals* – LMB Executive Committee Minutes [2008].

Quote 6: LMB uses an incentive structure to align the organisation's culture with the goals of its people:

> *The LMB has always had a non-hierarchical structure – one in which emphasis lies in the quality of the argument, rather than in the status of the proponent. To foster such a freely intellectual forum, the Laboratory is (now) divided into four Divisions, each having its own scientific policy and subculture; within each Division, virtually all career scientists have their own, independent scientific programmes. It might be thought that this wide distribution of scientific control would lead to fragmentation, but the opposite tends to be true."* – LMB Quinquennial Review [2001].

Quote 7: The importance of small groups sharing expertise:

> *It is an important feature of the Laboratory that the permanent staff represent a broad spectrum of expertise which ranges from biology through biochemistry, chemistry, and physics to mathematics. The research is carried out by many small groups, mostly of three to four people and none larger than about a dozen, each under the leadership of a tenured member of staff. The absence of a rigid organisational structure and the lack of a rigid hierarchy ensures that expertise is shared and encourages extensive collaborations between the divisions at all levels. There are also close collaborations with other academic laboratories in the UK and overseas and with industry. Resources for the support of the scientific programmes are organised so that maximum flexibility of deployment can be achieved and maintained throughout the financial year. {…} This in itself is a great encouragement to the staff since it is clear that the response to scientific need is paramount* – LMB Quinquennial Review [1996].

Quote 8: The importance of technology developers with distinct specialisms is illustrated by a memo from the cell biology subcommittee in 2020:

> *Developments such as Bessel beam plane illumination will allow acquisition of detailed three-dimensional images of cells and tissues with minimal damage. To keep at the cutting edge, such microscopes are best built in-house (our skilled workshop facilities make this possible). As recommended by the Cell Biology subcommittee, this will require strengthening of our optical microscopy facility with an optical physicist dedicated to machine building and optimisation. As was also acknowledged, the mass of data that is produced is very challenging to analyse efficiently, and we would also like to expand our software and computational support to address this issue* – LMB Quinquennial Review [2020].

Quote 9: Expanding projects into the translational sphere risks LMB losing its core identity:

> *The work on protein engineering [and] antibody engineering, as pioneered at LMB, has acquired such dimension and importance that the Laboratory finds itself in a dilemma. To allow it to expand as much as it deserves endangers the very essence of our long-term strategy. To restrict it is to let pass a unique opportunity for strategic research, with great repercussions for British biotechnology. The IRC is an excellent solution to this dilemma. It will allow us to focus and expand our interest in areas which we consider most suitable to the Laboratory. Projects which are important for other reasons can now be diverted to the IRC [Interdisciplinary Research Centre, later renamed MRC Centre for Protein Engineering]* – LMB Quinquennial Review [1996].

5. ACKNOWLEDGEMENTS

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