How to set up collaborations between academia and industrial biotech companies

To the Editor:

Much has been written about academic-industry collaborations in the biopharmaceutical sector; however, relatively little has been published in your pages concerning such interactions in the industrial biotech sector. In this Correspondence, we synthesize our collective experiences to discuss the possibilities and challenges that come with academic-industry collaborations in metabolic and biochemical engineering.

Industrial biotech has the potential to contribute to economic prosperity, to underpin a more resource-efficient, sustainable global economy, and to prevent or remediate environmental damages. These potential societal and economic benefits make it important to mobilize and align intellectual resources for advancing the field. Interaction of industries with the knowledge base of academic science is an important aspect of this effort. However, not all academic and industrial organizations and scientists are aware of the possibilities and pitfalls of industrial-academic collaboration. By sharing our opinions and experiences, we hope to contribute to successful interactions.

Any academic-industrial collaboration should start by acknowledging the different primary objectives of the partners. Academia's core mission is to educate highly trained, independent scientists and to carefully align and integrate their education with ground-breaking fundamental research. Industry's primary objective is to generate profit for shareholders, often through innovation and practical use of advanced technologies. Failure to recognize and accommodate these different objectives will, at best, cause friction and wasted time. At worst, it may result in a complete failure to meet objectives and withdrawal from further collaboration.

In the following text, we discuss four different modes of collaboration between academia and industry—consulting, contract research, bilateral partnerships and public-private partnerships (PPPs)—that faculty commonly encounter in the industrial biotech setting, together with pros and cons for both parties (summarized in **Table 1**). Compared to the biopharmaceutical sector, industrial biotech has fewer small-to-medium-sized enterprises (SMEs), and collaborations with these entities (rather than with large multinational corporations) involve challenges all in themselves (**Box 1**).

Industry consulting arrangements usually begin when a company invites an academic scientist (usually a tenured staff member) to participate as a consultant in internal discussions on research strategy, planning and progress. Contracts usually specify that ideas contributed by academic consultants become the exclusive property of the company. Although there are several advantages to faculty in these interactions (**Table 2**), consultancy also involves risks. Too broad a definition of the scope of consultancy contracts can impede academics in their research and freedom to interact with peers. A particular risk of consultancy is contamination with confidential knowledge. For example, a consultancy arrangement may provide a university professor with knowledge that could tremendously benefit a PhD student working under his or her supervision, but contractual obligations mean that the principal investigator cannot share the information with the student. If academic scientists feel that such strict confidentiality is not 'in their genes', they should think twice

Box 1 Collaboration with small and medium enterprises

In comparison with large, multinational companies, SMEs generally have only a few, specialized scientists. Collaboration with academia provides them with the opportunity to expand the scope and quality of their research. For academic scientists, collaboration with SMEs provides interesting scientific challenges as well as a chance to directly affect the success of a small company. In addition to these incentives, several aspects of collaboration with SMEs require special consideration.

Many large companies have clear procedures in place for engaging with academia and can mobilize internal specialists to deal with contracts and IP issues. However, the small number of in-house specialists employed by SMEs makes it difficult for these companies to allocate time for setting up and managing successful collaborations with academia. Young SMEs may find it particularly difficult to define their priorities and requirements in interactions with academia, and financial constraints may prevent them from engaging in projects with a longer time horizon. Open discussions between SMEs and potential academic partners about mutual expectations and obligations, involving scientists as well as contract experts, are essential to prevent disappointment.

Most universities see stimulation of science-based start-up companies as an integral part of their mission. 'Embedding' such start-ups in university research groups or 'incubator' facilities not only provides access to research infrastructures but also stimulates contact with academic scientists. Moreover, such on-campus enterprises provide invaluable inspiration to students. However, enthusiasm and good intentions are not a sufficient basis for a healthy long-term relationship between academia and start-ups. Especially when start-up SMEs operate within the context of academic research groups, it is essential to have clear, transparent agreements in place on IP ownership, fees for access to academic infrastructures, liability and confidentiality. Even when the SME is unable to disclose specific targets and strategies, sharing information on its mission and operations helps to maintain open communication channels with academic colleagues. Finally, academic hosts and embedded SMEs should be clear on 'exit plans' in case of success or, as will inevitably happen with some SMEs, failure to grow into a blossoming, fully independent company.

Table 1 Pros and cons of industry-academia collaborations

Benefit or risk	Industry partner	Academic partner
Pros	Access to specialized, world-leading skills and resources	Inspiration of academic research by application-derived questions
	Ability to develop and screen new talent for hire	Career opportunities for students
	Cost-effectiveness of research	Funding for research; consulting income
	Out-of-box thinking	Launch pad for young, rising professors
	Training in fundamentals	Awareness of trends in industry
	Access to extended networks	Options to build centers and consortia
	Informed consulting and Science Advisory Board contributions	Practical application of academic research and skills
Cons	Lack of IP protection	Restricted freedom to share IP
	Incompatible priorities (e.g., immediate applicability vs. fundamental understanding)	Incompatible priorities (e.g., education vs. commercial interests)
	Partners at different locations with different management cultures	Partners at different locations with different management cultures
	Typical length of PhD and postdoc projects reduces flexibility	Restricted ability to collaborate with other partners

about engaging in consultancy. Academic scientists for whom the advantages of consultancy outweigh the risks should carefully define the field of their activities and, for each industrial partner, aim to define this as narrowly as possible. In addition, confidential disclosures should be made or confirmed in writing, and within a defined period of time, to avoid misunderstandings. If you are considering entering one of these arrangements, then expert advice (e.g., from university tech-transfer offices and skilled colleagues) is essential for writing and reviewing contracts for consultancy, as well as for other modes of collaboration of academic scientists with industry.

In view of its limitation to a single person and comparatively low costs, consultancy is a popular interaction model in industrial biotech. For most companies, the intrinsic risk of providing confidential information to someone outside the company can normally be mitigated by strict confidentiality clauses in consultancy contracts. Academic consultants as well as their industrial counterparts need to be mindful that their typically enthusiastic exchanges do not exceed the boundaries defined in their contracts.

A second type of interaction involves contractual services. In such an arrangement, a company identifies an academic lab whose infrastructure and/or expertise matches its requirements and then contracts out research to that lab. Contract research typically addresses short-term, urgent and confidential topics. Consequently, publication of results may be restricted or even precluded, and academics should be aware of such restrictions before engaging in contract research.

Table 2 lists the advantages and risks associated with contract research. Evaluation of academic research groups by universities and funding agencies is often strongly based on their publication record and the publication records of the scientists they train. Some engineering departments, however, have a tradition of also considering collaboration with industry in their evaluations. Even if funding is scarce, the sole criterion for academics to engage in contract research should be that it contributes to their core academic mission, either directly (e.g., through industrial investments in infrastructure) or indirectly (e.g., by financially enabling fundamental research or providing advanced training to students and postdocs interested in industry).

As with consultancy work, a business-like approach should be adopted when negotiating terms for contract research. Contracts should include clear agreements on intellectual property (IP) ownership, rights to publish, financial issues, project term, grounds for termination and confidentiality. Transparency on these issues is typically high on the priority list of corporate representatives. Senior academic scientists should realize that confidentiality clauses involve not only themselves and their colleagues and students directly working on the project, but also other members of the research group and guest researchers with access to the project. Guaranteeing that all members of rapidly changing academic research groups are, and remain, aware of relevant confidentiality issues is not trivial.

A third type of interaction—(bilateral) industrial funding—differs from contract research in that the academic partner covers a substantial part of the total project costs (e.g., supervision costs of a PhD project and/or use of infrastructure). Furthermore, results can be published in scientific journals and PhD theses. Depending on its financial contribution, the industrial partner can *a priori* acquire the IP generated in the project or obtain a first right of refusal to license such IP. Alternatively, research contracts can define how IP from a project will be shared with, or acquired from, the academic partner.

Bilateral funding shares many of the advantages of contract research (**Table 2**). Additionally, it provides industry with direct access to focused research on topics that are relevant for innovation but that involve a need for prolonged fundamental exploration, a degree of risk and/or a requirement for expert knowledge that make them difficult to tackle in house within a company. For academia, bilateral projects enable research on application-inspired topics, often in close collaboration with industrial colleagues who are expert in research translation, which can be inspiring for students and staff alike.

Bilateral collaboration helps academic groups to align their long-term research strategy with challenges in industry. Although closer to 'pure' academic research than contract research, bilateral collaboration is not risk free. In particular, academic and industrial partners may easily develop different perceptions of the true project targets. For a successful collaboration, issues such as the relative importance of 'deep academic understanding' versus 'multi-gram-product-per-liter'-type targets should be openly and explicitly discussed and agreed upon during the project definition phase. We have had positive experiences with bilateral projects in which academic and industrial targets were specifically and separately defined at the outset and used to monitor progress throughout projects. Investing in a trust relationship and working towards a mutual understanding of the different and complementary roles of industrial and academic partners are paramount for success; window-dressing is no basis for long-term, productive collaboration.

Contracts covering all issues related to IP,

Table 2 Advantages of different collaboration models.

Model	Advantages for industry	Advantages for academia
Consultancy	Outside ideas: industrial projects are typically staffed to execute on a defined plan. Outside domain experts add new ideas to improve on the plan, rigor to the assessment of progress, and insights to overcome hurdles. Networking: good consultants know their limits and identify colleagues with strong knowledge in fields outside their own. Independent expert evaluation of internal research programs and strategy. Intellectual property ownership: clear, predefined rules give comfort that technology rights will be protected. This comfort is enhanced when dealing with consultants who have a strong track record of respecting client IP.	Scientific discussions: consultancy offers a wonderful 'playground' to escape academic management and sharpen academic minds on new, challenging commercial projects as well as understand commercial realities of translating research. Networking: consultancy often leads to other forms of collaboration, such as direct industrial funding of academic research in the consultant's group, joint application for government-funded programs, etc. Financial: provision of financial flexibility in financially challenged academic research groups. Alignment of long-term academic research strategies with industrial interests.
Contract research	Outside expertise and infrastructure to selectively and globally leverage advanced capabilities to benefit industry projects and technology platform building. Cost savings: no need to invest in fixed-cost in-house facilities, particularly for non-core technologies. Speed of research: answers can often be found more quickly by engaging established experts to solve specialized problems. Flexibility: multiple collaborations can be started and stopped as needed according to business priorities.	Networking: contract research can sometimes lead to follow-ups in more open settings. Financial: confidential contract research is generally well paid, and proceeds can be reinvested in infrastructure or fundamental research. In some situations, contract research can serve as 'matching' industrial funding in grant applications for government funding aimed at more open, fundamental research. Alignment of research strategy: enables academics to orient their research to be industrially relevant. Training: contract research sometimes offers unique possibilities to train students in 'industry-like' project settings. Critical mass: if contracts are designed well, highly qualified academics and technicians working on contract research projects can contribute to a group's infrastructure.
PPPs	Networking: successful PPPs also evolve into popular meeting grounds for industrial scientists from different companies. Critical mass projects: access to and involvement in high-quality, focused industrial-academic research programs with a considerable critical mass (10–100 scientists and PhD students) Recruitment possibilities: observing work offers the advantage of seeing first-hand how students and postdocs perform. Early access to novel techniques and concepts: blue-sky and cutting-edge research originating from academia often spurs applied research. Clear and uniform procedures for acquiring IP rights: may have advantages over a myriad of bilateral collaborations.	Networking for PhD students and postdocs: participating young researchers are frequently exposed to leading academic and industrial scientists. Critical mass projects: the critical mass of PPPs enables academic teams to take on challenges that would exceed the possibilities of any individual group. Alignment of resources and shared infrastructures: especially in larger PPPs, activities of different academic partners can be optimally aligned, thus fostering collaboration rather than unproductive competition. Funding: successful PPPs can secure a basal funding of research in a group, allowing continuity in major research lines.

confidentiality, screening of manuscripts and conference contributions—including maximum delays for screening and patenting—should be written and signed before research is initiated. Clear agreements on use and sharing of research materials generated during the project, such as cell lines and microbial strains, may require special attention. Many scientific journals now explicitly require that microbial strains and genetic materials used in published studies be made available, upon request, for academic research. Especially in projects that involve strains and/or DNA constructs provided by the industrial partner, addressing this issue can be challenging.

For academic researchers, it may be difficult but is nonetheless essential to accept that 'business' aspects of projects cannot be left undefined. In particular, it is naive to expect that emerging conflicts of interest on highly valuable research outputs—be it patents or journal publications—can be amicably settled in the absence of clear written agreements. People and priorities change in industry as well as in academia. Furthermore, in industry, decisions on business issues are rarely made by the scientists with whom the academic scientists interact but, instead, by their managers and by company lawyers. As with contract research, academic partners should be fully aware of confidentiality issues, including the requirement that students who leave their group after contributing to a bilateral collaboration project remain bound to confidentiality until the industrial partner has cleared its work for public disclosure.

The swift decision-making processes of industrial sponsors are appreciated by academic researchers accustomed to the sometimes slow and uncertain mechanisms of funding by governments and other granting agencies. However, a large and sustained dependency on industrial funding may blunt their engagement with research foundations and other sources of funding. We therefore recommend that, even in periods when industrial funding is plentiful, academic groups remain active in the 'rat race' to obtain research funding from granting agencies and foundations.

A final type of academic-industrial relationships is the PPP—a research consortium that typically involves multiple academic and industrial partners who, together, execute a multiyear research program. These have several interesting advantages over bilateral collaboration (**Table 2**) and, especially in Europe, have been gaining popularity in industrial biotech research. However, for many academic groups and industries, PPPs are new.

Most PPPs are financially supported by a 'blend' of (inter)national or regional government funding and contributions by the industrial partners. Industrial participation and funding of PPPs can be arranged in different ways. Some PPPs use public funding to finance a core fundamental research program, to which all academic and industrial partners have full access. Other projects, for which tailor-made agreements on confidentiality and IP rights can be drawn up, are funded by participating industries. An attractive feature of this 'two-compartment' model for industry is that

Box 2 Six recommendations to facilitate collaboration

When embarking on an industrial collaboration, it is wise to seek counsel from seasoned faculty who already have experience interacting with the private sector as well as legal and technology transfer professionals who are familiar with common pitfalls. Below we list six key factors to bear in mind before commencing work with a company:

- Openly discuss intended benefits, requirements and risks for both partners
- Consider which mode of collaboration optimally fits joint objectives
- Negotiate professional contracts on IP, confidentiality and publication procedures
- Retain full transparency within the academic research group about the terms and conditions of the collaboration, and instruct scientists and students on the importance of confidentiality and IP rules
- Monitor progress in the project frequently, and communicate about alignment with joint and individual objectives
- Build relationships grounded in mutual trust and respect; acknowledge and celebrate successes, learn from mistakes

it combines access to a broad, fundamental research program with the option to explore more competitive, confidential research. In other PPPs, a single research program, with uniform IP regulations for all projects, is funded from a homogeneous blend of public and private funding. This model, in which all research projects are accessible to all academic and industrial partners of the PPP, requires a great deal of trust and may be particularly suitable for fundamental research programs with a relatively large government contribution. In a third model, research in a PPP is organized in thematic subprograms, which are funded from blends of public and private funding. IP ownership in each subprogram is then based on the relative contributions of the participating partners. In large PPPs, this 'intermediate' model enables industries to focus their financial contribution and monitoring of the research on subprograms that are of special relevance to them.

Success of a PPP requires a strong sense of common purpose. Excellent communication, via regular 'live' meetings, and sufficient funding for each of the academic partners are two key prerequisites. If resources are spread too thinly (e.g., a single active researcher per participating group for a 5-year funding period), commitment is generally weaker than when at least 3–4 active researchers are funded in each participating group. A clear, joint vision on the future that is embodied by aligned, committed project leadership further strengthens collaboration. Government funding of PPPs generally has a finite lifespan but, with adequate industrial support, some PPPs use it to build a critical mass and performance level that allow them to become financially self-supporting through patenting and licensing incomes.

Irrespective of how industrial participation is arranged, a key challenge for PPPs is to maximize synergy by bringing together competing industries around their research programs. Not all industries, however, are inclined toward this mode of collaboration with academia.

In many industrialized countries, industrial funding of academic research is a fact of life. Interactions between industry and academia offer many advantages and increase possibilities for advanced training and education, but also come with downsides. **Box 2** summarizes six recommendations for successful initiation and execution of collaborations. However, the most important requirement for mitigating risks and reaping mutual benefits is a willingness of industrial and academic collaborators to understand and respect each other's core objectives and to actively seek options to optimally align these in joint research activities.

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Quality score compression improves genotyping accuracy

To the Editor:

Most next-generation sequencing (NGS) quality scores are space intensive, redundant and often misleading. In this Correspondence, we recover quality information directly from sequence data using a compression tool named Quartz, rendering such scores redundant and yielding substantially better space and time efficiencies for storage and analysis. Quartz is designed to operate on NGS reads in FASTQ format, but it can be trivially modified to discard quality scores in other formats for which scores are paired with sequence information. Discarding 95% of quality scores resulted, counterintuitively, in improved SNP calling, implying that compression need not come at the expense of accuracy.

Advances in next-generation sequencing (NGS) technologies have produced a deluge of genomic information, outpacing increases in our computational resources[1,2]. This avalanche of data enables large-scale population studies (such as maps of human genetic variation[3], reconstruction of human population history[4] and uncovering of cell lineage relationships[5]), but to fully capitalize on these advances, we must develop better technologies to store, transmit and process genomic data.

The bulk of NGS data typically consists of read sequences, in which each base call is associated with a corresponding quality score that consumes at least as much storage space as the base call itself[6]. Quality scores are often essential for assessing sequence quality (their main use), filtering low-quality reads, assembling genomic sequences, mapping reads to a reference sequence and performing accurate genotyping. Because quality scores require considerable space to store and transmit, they are a major bottleneck in