Assessing Needs of the Synthetic Cell Community for Open Coordination

December 2025

RESEARCH REPORT

better synthetic cells together

b.next

letter to the community

We launched Nucleus in December 2023 as an open platform for synthetic cells, responding to the growing need for shared technologies to advance the field and realize the vision of engineerable biology built from scratch. What began as a focused effort with a few dedicated advocates has since grown into a global community of more than 30 academic, industry, and government groups—an exciting expansion that has naturally raised important questions about what Nucleus is and whom it serves.

By 2025, it was clear that the broader community required a stronger voice in shaping the direction of Nucleus. We commissioned Conscience, a nonprofit organization specializing in open scientific collaboration, to independently survey the synthetic cell ecosystem. Between July and November 2025, Conscience interviewed synthetic cell researchers across the US, EU, and Asia, as well as university technology transfer professionals, to identify the views and needs of researchers and their institutions. We asked Conscience to share their findings in this report so the community could develop a collective understanding of its perspectives and needs.

> "Collaboration and openness are scientific necessities for synthetic cell research"
> *— findings from Conscience survey, July-November 2025*

Conscience found broad agreement that collaboration and openness are essential for synthetic cell research, given its technical complexity, methodological diversity, and early stage of development. However, several barriers remain: existing academic incentives for publishing, funding, and priority constrain researchers to small, trusted networks; a lack of translation pathways other than patents creates friction around sharing; and limited time and resources make it challenging to disseminate results in a way that others can easily build upon.

We are encouraged that perceptions of Nucleus and b.next's roles in addressing these challenges are strongly positive. Still, the community expressed a need for greater clarity on topics such as:

- What are b.next's commercial plans as a for-profit entity?
- How will contributors be recognized and rewarded?
- How will shared governance and long-term sustainability of Nucleus be ensured?

We are grateful for the community's feedback across topics including reproducibility and integration, barriers to sharing, the role of technology transfer offices, and participation and trust in Nucleus. These perspectives serve as the substrate for developing community-derived operational principles for both b.next and Nucleus.

In the coming months, we will open new dialogues with the community to address the challenges and opportunities highlighted in this report. We invite you to read the findings, share your thoughts, and join us in shaping the future of Nucleus. The need for our field to come together has never been more evident; we look forward to continuing to work with the community to build the foundations of engineerable biology.

On behalf of the b.next team,

Akshay Maheshwari
CEO

Anton Molina
Head of Ecosystem

bnext.bio

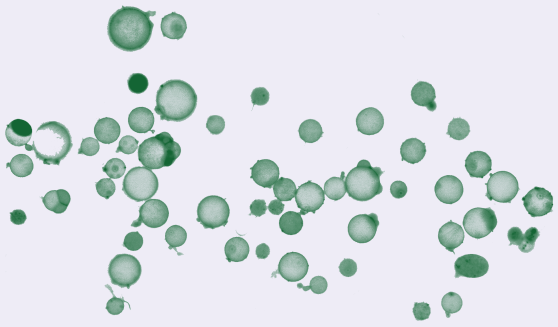
RESEARCH OVERVIEW

Our Mandate

This report presents findings from a qualitative research study examining the role of open science in the synthetic cell research community. In the study, we examined themes related to collaboration, open science/open source practices, intellectual property (IP) management, and perceptions of the Nucleus platform and b.next. Based on in-depth interviews with 16 synthetic cell researchers and three institutional technology transfer office (TTO) professionals conducted between July and November 2025, the study provides a detailed account of current practices, challenges and opportunities for strengthening open science/open source in this promising and scientifically-challenging field. This research was commissioned to begin the process of establishing community-derived Open Science Principles and operational practices that are rational and sustainable within the scientific, institutional and commercial realities of synthetic biology.

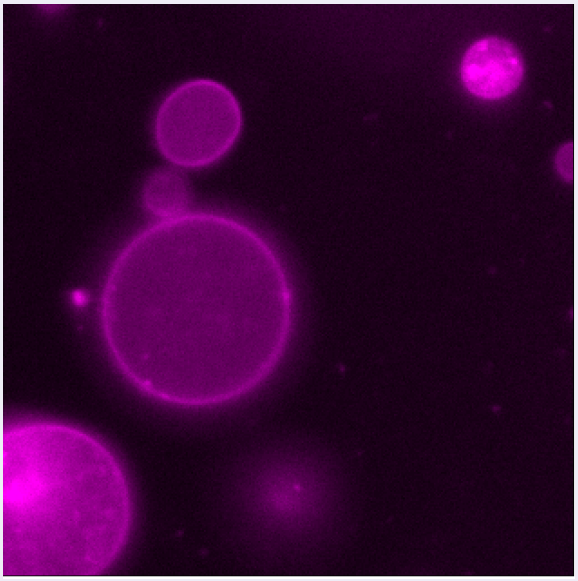
Findings and conclusions

Our analysis indicated a high level of agreement across the dataset despite geographical, research area, function, and seniority. Participants consistently emphasized that collaboration and openness are not optional but are scientific necessities in synthetic cell research. The field's technical complexity, diversity of systems and relatively early stage of development mean that no single lab can progress working alone. Researchers described a fragmented landscape characterized by limited interoperability of tools and protocols, poor reproducibility and insufficient standards. These challenges lead to widespread duplication of effort and slower-than-anticipated progress. Within this context, interviewees overwhelmingly viewed Nucleus as addressing a critical and currently unmet need by offering a centralized, open, and community-responsive platform for validated tools, protocols, data and know-how.



"Synthetic cells in green" — art derived from scientific data.
Anton Jackson-Smith / b.next, CC BY 4.0.

Despite strong normative support for open science driven primarily by a desire to advance knowledge and improve reproducibility, and because openness is seen as the 'right thing to do', this study



Synthetic cells expressing the self-inserting membrane protein Cx43. Yen-Yu Hsu / b.next, CC BY 4.0.

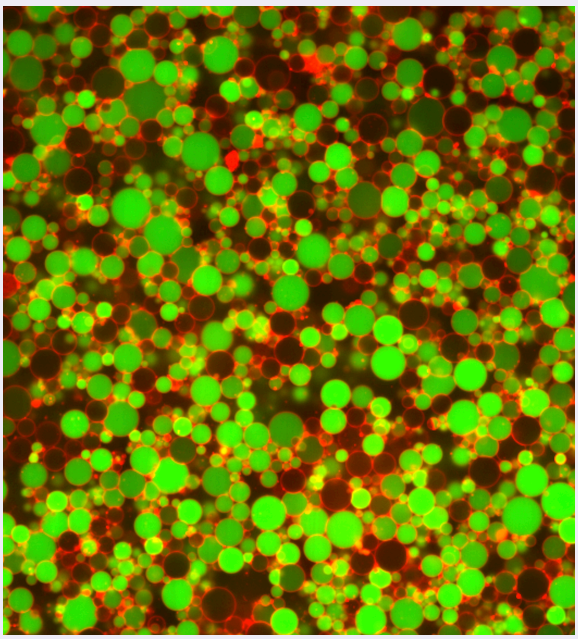
identifies a persistent gap between aspiration and practice. The findings reveal that much sharing occurs within trusted, closed networks — such as lab-to-lab partnerships and research consortia — rather than through open, 'distributed' models of open science collaboration. While researchers expressed strong ethical and scientific commitments to openness, their actual sharing practices are more contextual and strategic. Public sharing typically occurs only after publication or preprint, reflecting the need to secure academic priority, protect career advancement, and maintain competitiveness in an increasingly constrained funding environment. For many, participation in more expansive open practices is limited by practical concerns about time and resource allocation, and the potential to patent outputs.

Tensions between openness and IP protection emerged as a central theme of this research. Many researchers and TTO representatives underscored that public sharing compromises patentability, which remains the dominant pathway to translation, commercialization and impact within current innovation systems. While some participants expressed ambivalence about patents in principle, most viewed them as a pragmatic necessity for enabling scale, attracting investment and ensuring technologies reach real-world benefit. This dynamic gives rise to what could be described as 'pragmatic openness': a preference for being as 'open as possible while remaining as closed as necessary'. TTOs expressed, in particular, caution regarding permissive open licenses, citing institutional responsibilities to recoup investment, comply with funding obligations, and avoid enabling uncompensated commercial appropriation. A subset of interviewees, mostly closely involved with the Build-a-Cell Consortium, were less interested in patenting though again they saw this avenue as acceptable if it were the most viable path to benefit and impact. Large-scale and ongoing multi-stakeholder conversation is needed to explore the complexities of IP vs open source, and the risks, benefits and synergies of these mechanisms in biotech and in the syn cell space. Likewise, exploration of mechanisms to allow commercialization alongside open sourcing of outputs would allow researchers to contribute outputs of potentially greater scientific value and usefulness to Nucleus.

Despite these concerns, the study identifies an interest — among both

researchers and TTOs — for credible models that reconcile open science with sustainable funding, recognition, and impact. There is a critical need for evidence-based knowledge and educational materials around open-source pathways to inform decision-making and shift norms toward greater consideration of openness as a credible option. Likewise, participants repeatedly highlighted the importance of incentives, attribution, and tangible rewards for open contributions, including DOIs, 'open science' metrics, professional recognition, funding opportunities and clearer alignment with academic advancement criteria. Funders were widely regarded as a key lever for change: mandated openness, open science-targeted funding, and evaluation criteria tied to sharing and integration could quickly shift norms and practices across the field. Many pointed to the need for a fundamental cultural shift toward appreciation of the benefit to all of establishing high-quality open foundational resources – 'a rising tide lifts all ships'. Our analysis indicates that many researchers place a high value on openness – reducing risk and making these practices clearly individually rewarding would enable their fuller participation.

Perceptions of b.next and Nucleus were overwhelmingly positive, particularly with respect to the organization's technical competence, community ethos and responsiveness. However, important concerns emerged around b.next's 'for-profit' status, the potential for 'freeloading' of shared resources by other commercial entities, and ensuring that those who contribute are attributed and fairly recognized or benefitted. Likewise, there is a need to assuage concerns about the ongoing relevance and longevity of Nucleus. Our analysis indicates that scaling-up Nucleus critically rests on transparency, maintaining and demonstrating links to the community and 'giving back'. Researchers strongly emphasized that ongoing trust and participation will depend on clear rules of engagement, explicit communication about commercial activities, transparent community-responsive governance and demonstrable mechanisms for returning value to the community. Benefit-sharing — whether through reinvestment in shared infrastructure, community funding or other collective gains — was repeatedly identified as a critical condition for sustaining trust and engagement.



Synthetic cells expressing the fluorescent reporter protein plamGFP. Anton Molina / b.next, CC BY 4.0.

Taken together, our analysis suggests that strengthening open science in the synthetic cell space requires more than technical platforms or permissive licenses. It would be best served by deliberate alignment of infrastructure, incentives, governance and cultural norms across researchers, institutions, funders and other stakeholders. Nucleus is uniquely positioned to play a convening and enabling role in this process. However, its long-term success will depend on maintaining close community ties, addressing legitimate concerns around IP and commercialization, and demonstrating that openness can coexist with viable pathways to impact, sustainability and shared benefit.

About the author

Sarah Ali-Khan PhD is a Senior Fellow at Conscience with expertise in open science, genomics and biomedical innovation. She is interested in how we can shape policy to make it easy for stakeholders and communities to do good things, and support social justice and global-level flourishing. Sarah was previously a Research Associate at the Centre for Intellectual Property Policy and the Centre for Genomics and Policy at McGill University in Montreal. She holds a doctorate in Pharmacology and Therapeutics from McGill and did postdoctoral training in global health, ethics and innovation at the University of Toronto. After many years in Montreal she now lives on the Otago Peninsula in the far south of New Zealand. Alongside her academic career, she has contributed to governance and community initiatives in New Zealand and can often be found in the library, running forest trails, playing the violin or chasing her kids.

Conflicts of interest and role in research

This study was funded by b.next Inc. and actualized through the Conscience Medicines Network. b.next Inc. approached Richard Gold and Dylan Roskams-Edris (Chief Policy and Partnerships Officer and Advisory Services Lead respectively) at Conscience for support around business and governance planning in the open science innovation space. RG identified the need for this study and conceived it. Sarah Ali-Khan and RG designed the research. SA collected, analyzed, interpreted and wrote the report with research assistance from Jerod Miksza and Kevin Homsy BCL/JD candidates in the Faculty of Law, McGill University. SA is also affiliated with McGill Law.

RG received research support from Conscience and SA received a salary from Conscience Neither Conscience nor b.next Inc. was informed about who was interviewed and were presented only with non-attributable summaries of what interviewees said. There is no direct relationship between b.next, Inc. and either RG or SA. Interviewees were informed of the support given to both RG and SA through the informed consent process. Conscience is a non-profit corporation that imposes no restriction on research funding, advance approvals, or limitations on funding. b.next Inc. played no further role in the research other than to supply an initial list of key informants, provide feedback on the study interview guide and prepare the Nucleus White Paper (Appendix 1) for circulation to interviewees.

Table of Contents

INTRODUCTION

Background on open science and open source, syn cell research and b.next

Researchers and institutions, policy makers, journals, and others who fund and utilize scientific resources are increasingly recognizing the need to maximize the reproducibility, accessibility, usefulness, and re-usableness of these outputs, as well as reach greater efficiency in producing them. In an era of limited research funding, inequity, and an increasing need for innovative knowledge-based solutions to global challenges, these are particularly relevant from both an ethical and economic point of view. Open science approaches aim to address this ethical and economic need through structured and principle-based innovation.

Open science and open source are closely related concepts that build on the success of software's 'open access' model (Joly 2010). This concept of sharing research tools, methods, data and results (ie. 'source code'), eliminating barriers to collaboration (Ali-Khan et al. 2018, Build-a-Cell, Edwards 2016, Gold 2016, 2021, Ramachandran et al. 2021) and minimizing restrictive intellectual property (IP) (Gold 2016, 2021, Ali-Khan et al. 2017) is a founding premise of the synthetic cell and biology field (Endy 2005, Smolke 2009, Kahl et al. 2018, Build-a-Cell). These approaches have recently and successfully been championed by others in the biomedical realm (Morgan Jones et al. 2014, Ali-Khan et al. 2017, Neuro). Equally, Open source approaches to developing and sharing scientific hardware, software and reagents are also being trialed (reCLONE 2025, Open Hardware Foundation 2025). By sharing resources and coordinating efforts, synthetic cell developers aim at accelerating progress, rather than spend years duplicating basic set-up (Build-a-Cell). The vision is to advance faster where the field has promise including across health, medicine, bioremediation, environment, conservation, food and energy production, bioprinting and space exploration (Rothschild et al. 2024, Kahl et al. 2018, Powell 2018). While this potential is exciting, synthetic cell research remains at a fairly early stage (Giaveri et al 2025). There are significant scientific challenges to overcome, with some saying that progress has not been as rapid as expected since inception of the field (Rothschild et al. 2024).

b.next, Inc., a for-profit company based in San Francisco California is meeting these challenges by establishing an open source ecosystem aimed at energizing synthetic cell discovery and innovation. Its core, Nucleus, is a platform through which researchers share validated scientific resources including software, protocols, data, reagents, materials and know-how etc. (Nucleus (1)). While the contents of Nucleus will remain open, b.next hopes that innovative firms will build on Nucleus' knowledge to construct

and commercialize applications that spur a new wave of economic and public good. To this end, b.next is employing permissive 'open source' licenses that allow developers to reuse, remix, build out and patent derivatives of Nucleus resources (Appendix 1). Funded by a series of philanthropic grants and influenced by the open, community-based ethos of the Build-a-Cell consortium to which their founders belong, b.next has already carved out a singular presence in its less than two years of existence.

While b.next sees itself as 'of-the-community' and 'for-the-community', the company and Nucleus are still at an early stage in the development of their legal framework, sharing policy, and practices. At this point, b.next is in the process of building a viable and sustainable business model to support its founders' vision. With these goals in mind, b.next approached Conscience to carry-out qualitative research through a rigorous and transparent process to guide next steps. This report represents the first part of this work – the consultative engagement of synthetic cell researchers and institutional technology transfer office (TTOs) professionals through in-depth, open-ended interviews aimed to explore their experiences, preferences, their perceptions of the advantages and challenges around open science and collaboration, and on the aims, structure and workings of Nucleus. b.next will use these results as a starting point for community dialogue to derive guiding principles, best practices and detailed protocols to support engagement and ongoing trust.

Project goals

Engaging with key stakeholders through this study advances two aims; 1) it allows in-depth exploration of the current zeitgeist, perspectives and preferences that will lead to the development of Open Science Principles that are community-derived, fit-for-purpose and attuned to the synthetic biology context, and therefore more likely to be effective and sustainable; and 2) it works to strengthen a sense of co-development, ownership and community with key players in this research and innovation space. In addition, this work will eventually yield principles and knowledge that will guide management of open resources and commercialization across innovation contexts. As research and innovation gain in complexity, greater openness should be a central consideration shaping global scientific and technological development (Chesler and Baker 2010), yet cultural norms and practices remain nascent. Ultimately, this work aims to contribute to the development of insights and best practices not only for b.next and Nucleus, but beyond.

In this report, we use the terms synthetic cell developer and researcher interchangeably. The synthetic cell field is a sub-set of synthetic biology with much cross-over in techniques, materials and reagents and community members. We focused on speaking with researchers that work on synthetic cell and closely related cell-free

and synthetic biology activities. We differentiate between researcher and institutional technology transfer office professionals where relevant.

RESULTS

Overview

We interviewed 16 synthetic cell developers and three TTO professionals between July and mid-November 2025 (see Table 1), each lasting on average 75 minutes. We analyzed this data using standard qualitative thematic analysis techniques to examine collaboration, sharing and patenting practice, relevant challenges in the field, as well as views on b.next and Nucleus (see Appendix 2, Methods). To inform the latter, we sent all participants a White Paper prepared by b.next outlining Nucleus' goals, framework and open source licensing strategy to review well before the interview (Appendix 1). Interviews were semi-structured, meaning we used an interview guide, and questions were open-ended (see Appendix 3, 4) so that interviewees could focus on the topics they saw as most important. Consequently, we note that not every interviewee addressed every issue. In addition, two researchers limited conversation to 30 minutes due to scheduling constraints, so in these interviews we addressed only key points around patenting, sharing and Nucleus.

We found all interviewees responded positively and openly to the interview process with all saying they enjoyed it. Several expressed their appreciation that b.next has started what they said was an important conversation for the field, with many explicitly noting their interest in engaging with the findings. Many said this exercise has encouraged them to closely consider issues they had not had the opportunity to address previously. On the level of engagement, community consultation and awareness-building, this initiative was highly successful and communicated the sincere consideration that b.next has for this community. It also provoked deeper thinking around IP, publication, reward and sharing and encouraged familiarity toward, and appreciation of, Nucleus and b.next.

Our analysis yielded 10 major themes that we present in three parts with their sub-themes. These 10 themes are:

Part 1: Researcher collaboration and open science, open source and patenting practice

1. The importance of collaboration in syn cell research
2. An integration and reproducibility problem: Nucleus filling a critical need

3. Researcher collaborative practice
4. Researcher awareness of open science and open source
5. Researcher sharing and open science practice
6. Motivations and advantages to sharing
7. Barriers or challenges to sharing (including IP and patenting practice)

Part 2: Researcher collaboration and open science, open source and patenting practice

1. The impact of TTOs' policy and practice on sharing

Part 3: b.next and Nucleus

1. Views and concerns about b.next and Nucleus
2. Encouraging trust and participation in Nucleus

Table 1: Demographic breakdown of interviewees

Research area	**N 19**	**%**
Bottom up synthetic cell biologists	3	16
Top down synthetic cell biologists	2	11
Synthetic biology and cell-free expression systems	4	21
Cellular engineers	2	11
Trainees (Postdocs or PhD students - included in tally above)	2	11
Technology transfer office (TTO) professionals	2	11
Years in practice (post-PhD) (excludes trainees and TTOs)		
0-10 years	1	7
10-20 years	8	57
20-30 years	3	21
30+ years	2	14
Location		
USA (not CA)	7	37
California	4	21
UK	4	21

EU	1	5
Asia	13	13
Other	1	5
Institution type		
Academic	16	84
Government	1	5
Not-for-profit	2	11
Gender		
Male	12	63
Female	7	37
Involvement with Nucleus (excluding TTOs)		
Past or present exchange or collaboration	13	81

THEMES: PART 1

1 - The importance of collaboration in synthetic cell research and innovation

Almost every interviewee underlined the critical role of collaboration for the success of their practice and, more broadly, to the advance of synthetic cell research. Interviewees observed that the field is so complex that no group can master it all, meaning collaboration and openness are scientific necessities and, according to some, established cultural norms. A number of interviewees underlined that advances in the field have been slower than expected. Many said that large-scale collaboration and open conversation about standards, reliability, the development of routinized reliable protocols, and more strategic coordination of research activities are required (see Theme 2 and Theme 7). See Theme 3 for more on researchers' collaboration and sharing practice.

> “If everybody thinks that they’re going to build a synthetic cell on their own, they’re going to waste a lot of time and they’re not going to manage it. So we do need everybody involved.”
>
> — Researcher 1030

2 - Integration, reproducibility, standards and measurement: Nucleus filling a critical need

Almost every researcher at least touched on and in some cases talked at length about their concerns that the field of synthetic cell science is facing a profound integration, reproducibility, standardization and measurement crisis that is limiting collaboration and progress.

A fragmented field with a need for better integration

Nearly every researcher pointed to ‘fragmentation’ as a central and chronic challenge. They noted a number of underlying issues. Synthetic cell research is conducted using many different organisms, systems, materials and engineering approaches. Lessons learned in one system often do not translate to another. Reagents and protocols were said to be ‘super finicky’, at least partially due to poor standardization, reliability and quality control. For example, several interviewees spoke of shared plasmids that despite months of trying, failed to work. Upon re-sequencing, they turned out to contain mutations. Others said shared software sometimes only works for a limited time. Many said that the same reagent or protocol often performs differently across labs. Further, many reagents are either not available commercially at all or providers discontinue or change formulations, so consequently must be made by individual labs or ‘patched’ together from different sources. Thus, many bemoaned the fact that labs are continually ‘reinventing the wheel’ adapting or rebuilding their own version of reagents, protocols and workflows because shared and commercially available ones do not generalize or simply do not work in their hands. One researcher underlined that the difficulty of the science requires you to ‘use exactly the same stuff’ if you want to reproduce an experiment. Getting the ‘same stuff’ is currently challenging.

Tacit know-how and ‘lab magic’

Another issue mentioned by more than half of our interviewees was the limits of written methods and protocols. These often do not capture sufficient detail to allow outcomes to be reproduced. While some held that crucial details are omitted on purpose to maintain competitive advantage (see Theme 7), most underlined that it is impossible for

written materials to capture fine nuance such as the order of operations, timing, humidity, 'lab magic' and other tacit knowledge. Many specified that the delicate nature of the science means that the most effective learning occurs at the bench, in person. A few further added that using standard protocol formats alone would be a significant step forward.

A deeper standards and measurement problem

Several interviewees underscored a more fundamental barrier to progress: a lack of standards and meaningful measurement frameworks. Interviewees identified that standards will allow for effective data-sharing and optimized use of AI, both essential requirements for transitioning to 'Big Biology' and reaching the field's North Star goals. At present, it is unclear which parameters and data should be captured, at what resolution and under which conditions. Interviewees advocated for large-scale and ongoing conversation to this end.

> "Biology is really complicated and even if the thing works in this particular context and it works great and I've validated it and I've got a data sheet that says it and everything, does not mean you can grab it and pop it in your thing. We are lacking a deep intellectual framework of context - what context means in biology. And until we have that, large-scale efforts to modularize everything, I think they're fine to play around with. I'm not sure how successful they'll be"
>
> — Researcher 0819

Several interviewees identified poor incentives and funding gaps as key barriers to solving the issues described above. Academic grants and PhD projects favour individual differentiation, novelty and publication rather than development of community resources. The laborious and meticulous work needed to develop and validate standards, benchmark and implement these across labs, and maintain quality resources across time is 'not sexy' nor usually fundable by traditional academic grants. As one interviewee explained, without incentives and funding for integration and infrastructure, the field will continue producing 'small demos with a dozen engineered components' rather the scalable systems with thousands of useful modules. Equally, they underlined that focus on individual advance rather than seeking to 'raise the tide and lift all ships' is a culture issue, and one that needs work to be changed.

> "I think there's a general problem in that people prioritize getting things working for them over getting things working that others can use. And so it's often the case that there's a little bit of overhead in using somebody else's protocol. Rather than saying, well, it didn't work, so I worked with the group... to modify it so that we could all get something that worked that we could all use? That's a lot more work. And so that gets in the way of things"

— Researcher 0812

Nucleus is filling a critical need

Within this context, almost every researcher said that Nucleus is filling a critical and currently unmet need. Many underlined the value and practicality of having a centralized, open and community-responsive platform providing the infrastructure to streamline collaboration. Functions for Nucleus suggested by interviewees included: validate and integrate measurement frameworks and standards for protocols and research tools; establish principles for communication, data, tool and material sharing; make tacit knowledge more transferable; maintain accessibility and continuity of validated resources and knowledge; and serve as a 'library' or 'operating system' underlying the field (see Theme 10 for more suggested roles and ways for b.next to contribute).

Several interviewees cited analogies to Linux, the Arduino ecosystem and other open-source systems, where shared infrastructure eventually becomes the standard and accelerates innovation. They emphasized that critical mass — and sustainable funding — are needed to reach such ubiquity. In our dataset, Nucleus was viewed as the only entity currently positioned to serve this community-level purpose, since individual labs lack the time, incentives and appropriate resources.

"Something's not been working in synthetic biology. And I think it's clear because we haven't made as much progress in the last 20 years as we thought we would. How can Nucleus fix it? Well, I think it is fixing what's wrong. I think it's a big piece and I really hope this experiment of Nucleus can work. I don't know what Plan B would be for the field"

— Researcher 0804

Points to consider

- Many researchers said there is much room for improved collaboration in the field 'just because we still work in silos for the most part'.
- Most researchers said more, and more streamlined, collaboration would be desirable: 'more collaboration is beneficial to almost an unlimited extent'.
- A few researchers in the US noted there is poor connectivity between labs. Groups are geographically dispersed and there is often only one synthetic cell researcher

per institution despite regional clusters. Though not explicitly mentioned by interviewees, the same issue likely exists at the level of countries and continents.

- Several researchers with physics and engineering backgrounds suggested that biologists are not trained to be sufficiently quantitative. They said that this is a key contributor to current poor interoperability and reproducibility.
- One researcher said they envisage b.next as a centre of innovation in syn cell science analogous to Bell Labs of the 1950s (Gertner 2012), where many PIs would work closely in a culture of intellectual freedom, interdisciplinary collaboration, and discovery.

3 - Collaboration and collaboration sharing practice

Our analysis differentiated between sharing 'lab-to-lab' or 'on request' and within research consortia from 'open public sharing' or what could be called 'open distributed collaboration' which is aligned with notions of 'open science' (Fecher and Friesike 2014, Gold 2021). In this section we describe researchers' collaboration and sharing practice lab-to-lab and within consortia. We then outline researchers' awareness and understanding of 'open science and open source approaches' (Theme 4) before describing their open sharing practices in Theme 5.

Researcher collaboration practice

Researchers seek out collaborations to access complementary knowledge, expertise, scientific resources, and to secure funding. Several noted that collaborating is what makes their science practice fun. All interviewees participate in multiple lab-to-lab collaborations within small groups of individuals who know each other well. These relationships are usually based on close personal relationships and shared funding, with IP agreements and licenses in place to define boundaries and expectations. Researchers are mostly comfortable sharing ideas, unpublished data, reagents and other scientific resources within these groups because trust is high.

Almost all researchers are involved with collaborations within large national or international research consortia – the key example being Build-a-Cell – in which many interviewees take part. While Build-a-Cell was said by many to operate completely openly with all knowledge posted online, some researchers described these as semi-open spaces, where ideas, materials, protocols, and reagents are shared within groups but not beyond. Again, these relationships are formalized by consortia agreements that deal with publication, IP, non-disclosure, etc. Most interviewees said they do not share unpublished data within consortia because protocols, software, materials, and know-how are the most useful to others, and equally because these are 'non-competitive'

resources (see Theme 7). Some researchers noted that while consortia may be large, active collaboration usually occurs in smaller working clusters (i.e. 3–5 labs).

4 - Awareness, understanding and definition of open science and open source

All interviewees expressed generally positive attitudes toward open science, though their awareness and experiences varied. Several of the interviewees asked for a definition of open source or open science at the start of the interview stating that they did not have a clear understanding of the practices. Most other interviewees were familiar with the concepts through funder requirements, knowledge of the history of open source software development, their work with software, or through coming from an engineering background where preprint release is the predominant way of working. Several specified that 'open source' implies a collaborative approach to development and ownership of outputs, community-driven innovation, iterative contributions and being potentially comfortable with sharing outputs that may not yet be complete.

Conversely, most described open science as more constrained being about sharing outputs after they are published or shared as a preprint. Most said that open science means making the underlying tools and knowledge that led to a publication (what a few referred to as 'source code') public. Most mentioned the following as part of open science: software, sequence, protocol, workflow, methods, data, and reagent sharing; faster release of knowledge through preprints; Open Access publication; informal sharing of expertise and knowledge at meetings and conferences; sharing among labs 'on request'; and hosting or sending trainees to other labs to learn techniques.

One interviewee said that they consider regular academic research activity as equivalent to open science, including standard publication, providing detailed methods, sharing to Addgene and sharing directly to labs 'on request'. A few said that open science (and open source) are not something they routinely think about in connection with their work. Only two interviewees, whose research focusses on open source approaches, are involved in open source 'distributed' collaboration where they post outputs to public repositories, sometimes before preprints or publication, engage in collaborative development toward a particular output or product, and participate in fora where they freely share ideas and findings.

Overall, our analysis indicates that researcher understandings of open science and open source are overlapping and in practice qualified and context-dependant. Almost all researchers said that while they saw theoretical value in open science, their participation was limited because of practical considerations and the commercial or competitive potential of the output (see Theme 7).

Points to consider

- Build-a-Cell was mentioned by many as a 'wonderful community' exemplifying an open culture wherein ideas, protocols, tools, and materials are 'shared with anyone' and, at least aspirationally, 'no one has any secrets'.
- A good number of interviewees compared the open source software model to that of biotechnology saying that it does not neatly translate due to the patentable nature of biotech outputs, the high cost of equipment, materials and time to produce them, and regulatory requirements to bring a product to market.
- Many researchers noted that institutional or research field leaders and PIs play a definitive role in setting the open science culture in their particular contexts. In this light, many noted that the founding members of Build-a-Cell, and particularly Drew Endy, have established openness as a community norm in the synthetic cell space.
- Several researchers spoke of corrosive and counter-productive experiences in highly secretive labs as trainees. These experiences galvanized their commitment to open practice as PIs.

5 - Motivations for participation in Open Science/open source

Researchers described a number of motivations for their current practices around sharing of scientific resources, and by extension for their participation in Nucleus. Some of these motivations stem from moral and others from practical considerations.

Motivations for sharing and greater openness

Almost all researchers emphasized that sharing, transparency, and openness with outputs is the underlying tenet of the academic research model. Some noted that maximizing sharing is 'just the way it is done' and many underlined its important role in strengthening the collegial and collaborative ethos of the field. Almost all interviewees cited an ethical impetus to make knowledge publicly available to advance science more quickly. Several European and UK-based researchers further offered that as most research is publicly-funded, outputs by right belong to the public and should not be locked behind paywalls. Likewise, several others cited their belief that biological knowledge and its benefits belong to humanity. As such, placing knowledge in the public domain allows others to build on, make use of, and maximize the benefit of these advances.

"We're doing this for the good of everyone. Sharing knowledge will move everybody forward faster … our goal is to improve the state of human life, life on Earth… that we publish everything

and that we have no secrets and that we're all in this together. I mean in academia, our job is to publish, our job is to advance knowledge."

— Researcher 0721

To this end, almost all interviewees talked about improving the reproducibility and quality of science by making outputs more widely, quickly, and freely available (see also Theme 2) so they can be replicated and validated earlier and reduce duplication. Many subscribed to the belief that publication is not enough, rather all research products and 'source code' should ideally be released. A good number underlined the importance of releasing negative findings and more thorough and detailed protocols and methods. These were all framed as ways to maximize the value, efficiency, effectiveness and impact of research investments, as well as saving time and reducing costs.

Many cited professional benefits saying that sharing raises their professional visibility and stature, leading to increased citations, opens opportunities for research and philanthropic funding, and job opportunities. Likewise, some said openness has allowed them to build community and make new connections, leading to invitations to join new and different collaborations and expand their interests. Several researchers said that sharing to repositories like Addgene, Github, and NCBI is more efficient for their practice than responding to multiple individual requests. A few said they are compelled by funder requirements to publish in Open Access journals and publicly share data and other outputs. Finally, one cited the defensive benefits of sharing, saying that releasing to the public domain prevents others from unauthorized commercialization and blocking of access to their work. Similarly, a few noted that preprints allow them to release findings faster, with all the ethical and practical benefits cited above, and importantly, it preempts potential scooping.

Researchers' current sharing practice

Researchers in our dataset said they share a wide range of scientific resources. Sharing 'on request' or 'lab-to-lab' is standard practice, with most saying that they will share most outputs with collaborators and consortium colleagues. Researchers made a distinction between sharing with those they know and trust within these groups and open public sharing with the international scientific community. Thus, they are more guarded about publicly sharing outputs that may have competitive value, whether commercially or academically (see Theme 7).

Almost all researchers said they share ideas and sometimes unpublished data at conferences, noting that they feel comfortable doing so because these are closed

events, recording is prohibited, and sharing is oral. Some noted that they will share 'non-competitive outputs' such as methods, protocols, reagents and techniques that are of immediate benefit to collaborators and consortia members, and in some cases more broadly, before publication.

Almost all interviewees said that the fair and sustainable time to publicly share is after publication (or preprint). This timing allows them to complete and validate the findings of a scientific study, secure academic priority and the associated career benefits, and prevent scooping. One researcher said the main reason they share after publishing a preprint is that it allows them to easily and immediately provide an accessible and complete resource to interested parties. Many said that uploading outputs and sharing to Addgene, NCBI, and other repositories is part of their post-publication workflow.

There was some differentiation between demographic groups in their attitudes to sharing. Five researchers suggested that they 'share almost everything', had minimal concerns about being scooped, favoured maximizing the free public use and re-use of their work, expressed less interest in protecting their outputs with IP (Theme 6), and likewise said they do not seek to financially benefit from their output. In some situations these researchers suggested they may share publicly earlier than publication or preprint. Two of these were researchers with 30+ years of experience, two were researchers whose work focusses around open source approaches, and one was government-based. All five are attendees or members of Build-a-Cell.

> "It's important to me that we're all building the future together that we want to live in, but in fact we also have to live in it... I'm not in it for the glory, right? I want to enable work. I think, you know, success to us looks like - we would love nothing more than our stuff to go out there and change the world. Get it in somebody's hands, get it changing the world. Fantastic."
>
> — Researcher 0408

When these views were relayed to other interviewees during our interview process, some pointed out that researchers may 'say but not actually do'. Some also underlined that well-established senior researchers can afford to be less protective than those at earlier stages who are still actively building their careers.

Points to consider

- A few interviewees noted that even progress on the use of preprints in the biological fields is a huge step forward. They noted that publishing preprints, publicly sharing genetic constructs, source data, and software are not yet standard practice.

- Several interviewees said that sharing is streamlined when others, including collaborators, are working under the same culture, set of expectations, and technological framework.
- Some noted that a broad cultural change in science, emphasizing the benefit to all of sharing, is needed to optimize participation. They noted that there needs to be wider recognition that 'a rising tide raises all ships'.
- A few said that open science and especially open source (i.e. defined in this circumstance as sharing outputs before they are complete) approaches are often not a part of trainees' learning experiences. Thus, many are not familiar or confident with more open practice, nor know how to implement it.
- One said that sharing can enhance standardization of their own techniques, which is beneficial to their own research activities.
- The two open source-focussed researchers said that posting findings during development attracts valuable input from their scientific communities. Likewise, collaborating with end-users throughout the research process increases the value and utility of outputs.

6 - Barriers, caveats and qualifiers for sharing

While almost every researcher supported openness in theory, they all articulated concerns and caveats, and their participation is in many cases contingent and contextual.

Sharing needs to be meaningful and useful

Several researchers underlined that an important barrier to successful open science/ open source is securing community trust that shared resources are correct, validated, will work, and that they are properly annotated. They warned that, otherwise, sharing may be a waste of time and money because no one will be willing to use the resources. Several underlined the enormous and unpredictable costs of pursuing projects that will never work because the shared output was flawed.

Researchers strongly underscored the importance of sharing resources that are meaningful and useful. Thus, almost all share after publication when outputs are fully quality-controlled in order to protect their professional integrity and to obviate wasting others' time with erroneous resources. A few underlined that 'slow science is good science'. For example, one lamented the continual posting of cell-free 'optimizations', each of which is too quickly replaced by another. Furthermore, they added that pressure to prematurely 'feed the algorithm' with new outputs is counterproductive to researchers' mental health.

> “This open science idea is very, very difficult… It’s very difficult to ensure that people actually record all your data in a proper format. So I think that that is difficult, there’s too much data that you can’t trust”
>
> — Researcher 1030

A few researchers said they do not share data even after publication because while materials, software, and protocols are useful, they believe that the data are not. They sought to avoid ‘data dumping’ – saying these can be tantamount to meaningless if they lack details of how they were generated or are not in standardized formats. Again, it was reiterated that there is much work to do to understand what should be measured, why and how (see Theme 2).

Points to consider

- Many researchers underlined the importance of focussing sharing in areas where the needs and requirements have been defined by the community (see Theme 2).
- Researchers praised b.next for setting context and boundaries around what they aim to build and the definitive value of Nucleus’ in-house validation step.
- Biobricks and Addgene were mentioned as sources of materials that sometimes did not/do not work.
- One researcher highlighted the enormous maintenance costs of research data servers. They noted that these are currently disproportionately shouldered by the US, noting that if the US pulled back, science could face a crisis to the point of being unsustainable. They called for the establishment of guidelines for improved sharing of this burden.
- One researcher said b.next’s aim to validate all contributions to Nucleus is not realistic and may become quickly become untenable if the community shares as much as b.next hopes they will.

Protecting competitive advantage

Almost every researcher emphasized that they are working within a highly competitive research environment where funding is increasingly difficult to access. Key currency for academic advancement and winning grants is high impact publication. Researchers operating in the academic setting said that they prioritize capturing strong metrics to support these outcomes.

Almost all researchers said they are strategic about protecting novelty and exploiting the full benefit of their work before sharing it. Thus, it was suggested that pre-publication sharing of data or reagents could preclude publication in top-tier journals by reducing the novelty of findings or might lead to being scooped. Both of these outcomes would have adverse consequences on researchers' ability to secure future funding. Many said they determine whether and what they share on a case-by-case basis.

A few researchers felt their research is unique enough that others would not be able to scoop it (i.e. be the first to publicly announce a discovery and thus gain academic priority and associated recognition and career rewards). However, again, it was largely researchers with 30+ years experience, in the government setting, or those in open source-focussed research who said they were less concerned about being scooped.

Free-loaders and national security

Some interviewees raised related concerns about 'free-loaders', those who take advantage of shared resources but do not reciprocate. An extension of this was the potential for appropriation of their work by commercial entities without acknowledgement or compensation (see Themes 8, 9). Likewise, a few noted that an additional source of tension is competitiveness on a global scale where there is much at stake (NSCEB 2025). For example, some voiced concerns that 'Chinese science takes but does not give back'.

> "You know, I feel like China, for example, is going use whatever's out there in the open, but not give anything back... I don't know how everything that we do to try to build and be open and shared doesn't just also benefit other people who are not interested in sharing"
>
> — Researcher 0731

Points to consider

- Researchers underlined that protecting novelty, proper attribution, and their academic priority are absolutely critical and non-negotiable factors in determining the extent and timing of sharing.
- For this reason, almost every interviewee favoured post-publication (or post-preprint) sharing.
- A few researchers underlined the need for a larger conversation about the boundaries of openness in the current geo-political climate.

Intellectual property and researcher patenting practice

A major caveat discussed by every researcher was the tension between the potential to patent and open sharing. In this light, one researcher bluntly said 'sharing kills your IP' because sharing of outputs in the public domain before filing for IP compromises the novelty requirement of patents, invalidating a claim. Patents were said to be valuable to researchers because they allow the capture of venture capital investment so that the researchers can launch start-up companies and commercialize technology. Equally, researchers said patents can be licensed to companies, bringing collaborations and funding to support their programs. Researchers and TTO representatives repeatedly underlined the dwindling health of traditional academic funding and the growing importance of tapping alternative streams (see Theme 9). All but three researchers in our dataset hold or have applied for patents (of these, two were trainees and one was an 'open source-focussed' researcher).

Some researchers were agnostic about the absolute value of patenting. Instead, the critical goal emphasized by all was that their technology reach optimal dissemination and public impact. To almost all interviewees, patenting seemed to be the only credible, well-defined and proven pathway to achieve this.

> "I'm really interested in my technologies getting out into the world and somebody's going to have to license them and scale them up and produce them. And if I release something open source and they say, wish you didn't have done that because I really wanted to take your thing and get it out into the world. So, we IP everything just so we have a path to working in the current, you know, capitalistic infrastructure of scale, which I'm not necessarily happy about that, that's the way that things are, but then I operate within that system, at least currently"
>
> — Researcher 0819

Almost every researcher spoke of the appropriateness of protecting their outputs with patents in certain contexts, in particular for technologies in more advanced stages of development. However, some, including TTO reps, noted that it is sometimes difficult to judge the value of patenting a particular output, particularly in the syn cell field where productization and service potential are not yet clear. Many said that research tools and early-stage developments are less appropriate for patent protection. Nevertheless, a few pointed out that the patenting of Shimizu's PURE and licensing to New England Biolabs has made this key reagent broadly accessible to the scientific community in a standardized useable form, allowing for important advances in the field (Shimizu et al 2001). Again, many interviewees spoke of strained funding and the needs of university infrastructure, research and student support. In this light many researchers said they feel a responsibility to their institution to see if something is patentable (see Theme 9).

Many researchers were definitive about not sharing anything of commercial value to the public domain. Many interviewees and notably TTO representatives again noted the potential for commercial entities taking advantage of shared resources to their own benefit (Theme 9 and see Theme 11 for findings in the context of Nucleus).

> "I mean, OK, if you have an absolutely really blockbuster cool idea and you didn't protect it, then you know, big pharma companies would just take it for free and then they would make money off it. And then it's OK, great. So it entered the world ecosystem. But you know, a laborer deserves his wages"
>
> — Researcher 0730

Again, interviewees in the government setting, those with 30+ years of professional experience, those whose research focussed on 'open source' approaches and also female researcher interviewees tended to express less interest in patenting. Nevertheless, all but one said they would pursue patents if it was 'more enabling for the field' or, specified one researcher, if their student wanted to do a start-up. Many interviewees thus seemed to ascribe to the idea of 'pragmatic openness' or 'as open as possible, as closed as necessary' (Landi 2020).

> "I think overall it's whatever is moving the field forward, whatever is preventing start-ups from failing, whatever is de-risking technology so that it can be operationalized, that's what we want to do. And I think you need to take that on a case-by-case basis. And so sometimes we patent things, sometimes we don't bother"
>
> — Researcher 0408

A few interviewees spoke of commercialization pathways that do not use patents citing the importance of branding, reputation, and exemplary science for staying ahead. Likewise, many were interested in how 'open source pathways' leading to value and impact may work. They strongly underscored how little they and their TTOs understand about these models (see Theme 9), and called for evidence, case studies, and other credible information about risks and benefits to inform decision-making.

Points to consider

- One interviewee said that multi-institution patents had prevented them from sharing to open repositories because negotiating release of the technology with all these groups was too complex.

- Only one interviewee, an 'open source research-focussed' trainee, said they would not patent because of its potential to block community access to technologies and propagate monopolies.
- All researchers asked about the impact of using others patented technologies in their practice said this has never been a problem as free and unlimited academic use of patented technologies is standard in their settings (US, EU and UK researchers said this).
- A few researchers said there is too much focus on patenting everything under a false belief that this will lead to profits. They stated that in contrast, most patents cost more than they earn.

MTAs and legal agreements

Many researchers spoke of the burden and complexity inherent in the use of MTAs (and other legal agreements). Many noted that these are unnecessarily complicated and sometimes take a year or more of negotiation before they are approved and research can progress. Researchers suggested that TTOs are even more risk averse and stringent with material transfers than with patents. Like researchers, TTOs wish to pre-empt misuse and exploitation, as well as obviate liability and bio-security risks. Some researchers admitted that they sidestep TTOs and share materials under the radar. None of the researchers' institutions utilize the Open MTA because of its permissiveness concerning downstream commercial use (see Theme 9).

Infrastructure, financial, human resource (HR) and time allocation

Almost every researcher talked about time and cost as a major barrier to sharing. For example, researchers cited the time and human resources (HR) needed to verify, sequence, annotate, organize, write up, and upload or distribute resources. Others mentioned the effort inherent in setting up and managing an effective online sharing platform or website. Another said their team has a monthly documentation day, but noted that this is unusual in the field, is a big commitment, and still does not come anywhere close to doing as much as they could. Several noted the difficulty and time to navigate unfamiliar formats, platforms, and repository websites noting that staff to help implement openness would be highly desirable. One said they have a full-time data officer while others enlist the help of institutional information technology (IT) staff when necessity dictates. Many emphasized that researchers are typically over-committed, saying that they are currently sharing to the extent possible considering infrastructure, time, and financial and HR limitations (as well as the other issues mentioned in this section). In particular, early-stage researchers with smaller labs stated that although their philosophical commitment to openness is high, the reality is that they are limited in what they can do.

"It's definitely a balance … In the beginning, I really had this idea that anything we ever published would have that standard and I think I've since realized that that's not something I can live up to, simply for practical reasons. Students are not all equally good at essentially sharing protocols or writing things up etc. There's only so much time you have in a day. It is very time consuming to do it well"

— Researcher 0916

Making sharing worth it – the importance of incentives and rewards

As described above, there are important costs associated with the process of sharing. Similarly, there can be significant value in the outputs themselves, including the funding, time and effort invested in their creation. As such, researchers and universities want to maximize these investments for themselves and their stakeholders, and accrue clear and direct benefits from their work.

When asked if their open science practice was worth it, some researchers were less than certain. While it was said that advancing the field and doing excellent and complete science are important rewards in themselves, almost all said that more and more meaningful incentives are needed to make sharing worth it and optimize participation. Again, access to funding, opportunities for collaboration, achieving broad research impact, and raising professional prestige and profile in their institution and community (with associated career benefits) all emerged as key meaningful rewards. At this point, the rewards accessible through patenting pathways seem clearer to TTOs and some researchers.

"I think as soon as you have cost, cost drivers, you have big incentives to try to protect your resources… Let's just say you spent $2,000,000 coming out with a perfect CRISPR protein, then you go release it out and someone can launch. That means they're going to undercut whatever you can do. So I am not surprised that it is not a thing. The incentive structures are not there for people to just let loose. There's a lot of intellectual property complexities."
— Researcher 0819

De-risking openness: DOIs, credit, attribution, and tangible rewards

Researchers said that, at this point, many are uncomfortable with 'going out on a limb' to participate in more open research. As previously noted (see quote, Theme 2), many said that researchers – including trainees – would prefer to focus on personal

advancement rather than assist the community without tangible personal benefits. Researchers mentioned two key approaches to de-risking greater openness.

DOIs, credit, attribution, and tangible rewards

First, many favoured instilling a better system of open science metrics, credit and attribution and ensuring that this is recognized by academic advancement committees and granting agencies. Such metrics could extend to tracking the real-world impact of open contributions, as well as lead to awards, rewards and even research funding for achieving certain goals (see Theme 11). In this vein, some said being able to track influence and even garner feedback would be desirable.

The role of funders and foundations

Second, many noted that if funders mandated and policed sharing, and used sharing metrics to weigh grants, this would completely and rapidly change the open science landscape. Likewise, one researcher noted that foundations could de-risk stepping outside the current patent-based ecosystem by providing a guaranteed pathway to manufacturing, delivering and deploying technology in return for going open.

Points to consider

- Many researchers praised the inclusion of DOIs for outputs shared to Nucleus' DevNotes platform (Nucleus (2)). Some further underlined that DevNotes fills an important and unmet community need by providing an outlet and credit for publication of negative results.
- US interviewees said that open science metrics such as Addgene deposits or output downloads are merely asides for advancement and granting committees. In contrast, interviewees said that in Europe, open metrics are given more weight.
- Some researchers said patents and technology start-ups are also seen as valuable metrics by academic advancement and granting bodies.

THEMES: PART 2

1 - The role of TTO policy and practice on open source/open science sharing

Many researchers mentioned the role of TTOs in influencing their participation in open source/open science and more particularly in Nucleus. Based on this, we interviewed three TTO representatives – two at US and one at UK institutions from which our researcher interviewees were drawn. Their positions were a senior licensing manager, a business and innovation manager, and a director for innovation, patents and licensing.

All work with researchers in the syn cell space. A key goal of our questions was to understand TTO interest or otherwise in open source/open science, barriers, opportunities, and what drivers would induce institutions to support researchers in these practices.

TTO goals and roles

TTO representatives specified that the primary directive of their offices is to support innovation and translate technologies from the lab to societal benefit. A secondary but important goal, in particular underlined by our UK interviewee, is recouping revenue from their investment in researchers' work to support the institution – patents, licensing, equity in start-ups and industry partnerships were all mentioned. All three TTOs said the public is a key stakeholder in their practice. They also underlined that any revenue captured is not to 'line their pockets' but definitively to benefit students, infrastructure, and research at their institutions.

> "Ultimately our responsibility is to do the right thing by [institution name] and by the technology. But like I said, with an eye to being fairly deferential to the researchers as well. So yes, our responsibility is ultimately to the taxpayer to the extent that a good chunk of our research is federally-funded. So we're really balancing all those things"
>
> — TTO professional 1016

The work of TTOs – helping researchers manage outputs

Both TTO and researcher interviewees said TTOs partner with researchers to advise on best management of their outputs. Our interviews suggested that there is more focus on patenting in the US than in other countries. Many researchers said that TTOs are risk averse and suggested that their default is to patent. US TTO interviewees with whom we spoke were consistent in saying that they prefer to maximize 'shots on goal', particularly in the case of an early-stage field like syn cells where commercial potential

is exciting, but unclear. Our UK interviewee said their institution takes a more selective approach due to the high costs and time involved in patenting. For example, they consider the impact of embargoing research while a patent application is prepared and processed, and the effect of doing so on researchers' funding. Likewise, if financial gains may be outweighed by the benefits of 'putting the technology out there' they may advise publishing rather than patenting. They said without TTO input, many researchers would prefer to publish and simply target public funding. However, all three interviewees emphasized that public funding is becoming a less viable avenue.

Awareness and knowledge of open science/open source

Almost all researchers with whom we spoke were doubtful that their TTO was knowledgeable about open source/open science, many noting that their TTO had not discussed these approaches with them, except for those involved in the Schmidt Sciences-funded Developer Cells Program (DevCells Program). Many also said that if their TTOs were aware of open source, they were wary.

> "I don't think the concept of open science is particularly clear to them and the first response, at least verbally from [TTO institution name] - was a bit, was almost hostile, I would say, because it's the idea being that if there is potential IP involved in a project, they want to make sure that their institution is going to get a cut of the pie, right?"
>
> — Researcher 1029

Indeed, TTO interviewees expressed caution about the possibilities of the open science model. Two stated they have limited knowledge and experience with open source and open science. However, all three said they were familiar with the former concept through the software space but had never – before Nucleus – grappled with this in the context of biotech. All three noted the incongruity of directly mapping the software model into biotech because of the much larger investment involved in biotech research and commercialization, and the potential financial rewards at stake. However, all three said that as open science-based funding opportunities are starting to emerge, they are now drawn to think more about these approaches.

Barriers to participation in open source

The TTO interviewees raised three main concerns about participation in open source. First, they confirmed that none of their institutions use the Open MTA and that they are uncomfortable with open source licenses. The key barrier is the permissive nature of these agreements which allow commercial entities to use and potentially commercialize based on shared outputs, without financial benefits for the researcher or institution.

While they noted that sharing basic technologies, protocols etc. might be acceptable, a potentially lucrative therapeutic or an experimental set-up that has taken years to develop should rightly benefit the university and the researcher.

> "I guess the question comes down to how do we recoup on our investment if we've put five years of a researcher and funding into getting a cell-free system working – to just go, all right now anybody use this, build upon this, do whatever you want with this – is a difficult one to stomach when the research funding environment is so challenging at the minute"
>
> — TTO professional 1104

Second, US interviewees noted potential complications raised by the Bayh-Dole Legislation. They believed – incorrectly – that federally-funded researchers are required to file IP on everything that falls with the definition of an invention as defined by Bayh-Dole, or pass the rights to back to the government agency which theoretically then files a patent. In practice however, the invention almost always goes into the public domain because agencies rarely pursue the patent. They noted that compliance reporting relies on invention disclosure by the researcher, which may allow for some professional discretion in deciding whether to make a disclosure. Relatedly, one US interviewee underlined that tax dollars through federally-funded research must not be seen to go directly to benefit for-profit entities. As stewards of federal dollars, they noted that TTOs are beholden to act as responsible managers of these funds. Interviewees said they did not know the fine details of this legislation, thus it would be fruitful to investigate the full implications and conflicts between open source and the Bayh-Dole Act in more depth. Interviewees noted that commercial or foundation-funded research are free of these obligations. Likewise, our UK TTO said they have not come across any such requirement to patent in their setting.

Incentives and solutions for participation in open source

TTO representatives reiterated that researchers have the final decision on how to handle their technology. They underlined that their duty is ensuring researchers are aware that in releasing open source, they may be compromising potential commercialization. Several researchers said that a key question is to clarify how these two priorities can co-exist. Two noted they have side-stepped this issue in the current first stage of the DevCells Program by focussing on development of foundational research tools. These are potentially less patentable and can be more easily rationalized as pre-competitive enabling knowledge.

Dual licensing

We asked TTOs how we can best balance the competing priorities of accelerating syn cell progress and enabling innovation without shortchanging universities. US TTOs pointed to dual or hybrid academic and non-profit licensing models as a possible solution. Further, two researchers held that open source is not incompatible with patenting, pointing out that after a provisional patent is filed, knowledge can be shared under the CERN-OHL-P license (Linux Foundation Collaborative Project 2018). One TTO interviewee further speculated that earning revenues from syn cell patents on methods and early-stage technology may be limited anyway, given that reach-through rights are difficult to secure and that technologies may be incorporated into a development platform or the like, and not into final lucrative 'end-products'. Thus, the opportunity-cost for institutions may not actually be as large as anticipated.

Research funding and 'optics'

Access to funding emerged as the key lever for inducing participation of TTOs and researchers. In the case of the DevCells Program, one TTO representative said that their institution was willing to support researchers' participation (involving initial relatively small amounts of funding), because of the potential for more financially significant opportunities and partnerships in future possibly IP-orientated phases of the project. However, they noted that short funding cycles for traditional grants may make participation difficult to sustain if further open source funding takes longer to materialize. They said that most researchers only have funds for 6-18 months into the future, so support for open source projects would need to fit with these timeframes. They also pointed to important 'optics benefits' wherein involvement in open projects can be leveraged to enhance positive and altruistic perceptions of the institution. Interviewees further reiterated funding, innovation and collaboration metrics as key drivers for engaging with open science and open source.

> "So I think the most important thing to measure would be – if we are giving up our IP and putting it down in the domain – so what did the researcher get in return? How many research dollars did bring it to the lab and then were there opportunities for grad students or postdocs to take this IP themselves and form start-ups? So it would be primarily driven by how much research money came through these open science projects... if it's bringing in research dollars for the lab, then yes, I think the university will be open to it"
>
> — TTO professional 0908

One interviewee also nodded to existing precedents for forgoing IP and working together. They pointed out many universities have experience with industry consortia that fund pre-competitive research and agree not to file patents on outputs. Two of our three TTO interviewees underlined the consideration that their offices hold around

supporting public benefit – for example diligence licensing norms in US TTOs (Lexology 2023) and AUTM's 'Nine Points to Consider' (AUTM 2007). Thus, there may be arguments to be framed around the greater good inherent in supporting open source to enable the syn cell field and its downstream economic and real-world benefits.

Support for Nucleus

While TTOs expressed concerns about open source they also expressed some positive opinions. All three recognized the potential value of open foundational resources. One underlined the benefits with respect to sharing of biological materials, noting that it is already difficult navigating attribution and rights over plasmids that accumulate layers of additions by different users. Thus, the situation in the synthetic biology field, which is characterized by many 'bits and pieces' coming from different sources, may quickly lead to untenable transaction costs. They further underlined the sense in making basic technology open to allow for simplified processing, and praised Nucleus' use of permissive rather than copy-left licenses.

> "I know the researchers involved are super-excited. It's the classic research mentality of we're going to do some super cool science and we're going to get it out there and this is a great mechanism to do it and...there will be benefits to this ecosystem, to this community, I think. The institution and the tech transfer office just kind of has to wear that more cynical hat. We unfortunately have to look at it from a point of view of, OK, where could this go wrong? How could we suffer for this?"
>
> — TTO professional 1104

Points to consider

- Like researchers, TTO interviewees strongly emphasized the need for evidence-based knowledge, case studies, and educational materials around open source to inform decision-making, and build understanding and comfort about the credibility of these models.
- A good number of researchers called for large-scale multi-disciplinary conversation including legal experts, VCs, foundations, funders, regulatory bodies, government, developers and practitioners, social scientists, the public, and others to deeply explore these issues.
- One said that an AUTM webinar would be an excellent forum for levelling up TTO awareness and understanding of open source.

THEMES: PART 3

1 - Knowledge, opinions and concerns about b.next and Nucleus

Researchers unanimously held strong, positive opinions about b.next and its representatives. Many had had personal contact with b.next and expressed a high level of trust in the organization due to these interactions. Those who have interacted with b.next or used Nucleus resources said that these have been extremely helpful in advancing their work. They praised the open, knowledgeable, pragmatic and approachable qualities of the b.next team. All but three researchers (based in Asia and Europe) have engaged with or are collaborating with b.next. Every researcher we spoke with said they would potentially be interested in contributing to Nucleus or using its resources, however this was strongly contingent on proper attribution protections, transparency about the business model and 'who has skin in the game', governance, benefit-sharing (see below), and determining how commercially valuable outputs would be handled. As noted in Theme 2, every interviewee noted their belief in the value of the work that b.next is doing.

> "I am aware of b.next's activities, but since I have not been asked to contribute in any particular way, I am not involved in their work nor do I use Nucleus. Of course, if there are resources useful for my own research and they are available, I would have no problem making use of them in the future"
>
> — Researcher 0923

Limited knowledge and understanding of b.next and Nucleus

Despite all but two researchers knowing of or working with b.next, almost all said they have little knowledge or understanding of how the organization works, its business model, or how b.next plans to remain sustainable and maintain its longevity. A few were unaware that b.next is a for-profit entity and almost all said they had little understanding of the relationship between b.next and Nucleus. A few pointed out that there is minimal information on b.next's website.

Concerns about b.next being for-profit

Many interviewees underlined the importance of b.next developing a plan to stay viable and continue to provide value to the community. All were unsure of how b.next would

do this but expressed appreciation for the business reality they face in needing to move beyond grant-based funding to a more sustainable model. When asked about b.next patenting derivatives of shared technologies, some expressed serious concerns about how such activities would align with b.next's community-based and open source ethos. Many cautioned that great care was needed around managing and communicating around such activities as there is high potential for damage to b.next's strong existing reputation and community trust. Some underlined that b.next should take care not to 'pretend they are not-for-profit if they are'. A good number of interviewees underlined the easier 'optics' and perhaps practicality of establishing separate 'not-for-profit' and commercial entities to manage open source and commercial functions of Nucleus and b.next respectively. A few noted that b.next may be more positively perceived and garner more community trust if it were not-for-profit. Others spoke of models where open source was able to co-exist with for-profit services even if these were carried out by another company – for example Red Hat and Linux.

"Why? Why muck it up though? Like, why muck up Nucleus with a commercial company for a specific product? Why not just start a separate company to develop out those technologies?"

— Researcher 0804

Patenting of derivatives of shared resources

Most researchers said that community patenting of derivatives of contributions to Nucleus is theoretically acceptable. A few noted that it is a standard expectation in science that others will build on your work. Several others said they would be happy to see their work be developed and translated to impact even if they were not doing it (see Theme 5). Those researchers whose work focusses around open source approaches underlined that commercialization is fine so long as access for stakeholders to the technology does not end up blocked. These researchers noted that in the open hardware/open reagent space, the community can be extremely judgemental about potential conflicts of interest, but suggested that the syn cell space is likely more commercially-orientated and possibly less hard-line.

"So I would feel OK hypothetically speaking. If I make something that goes back to the Nucleus community that is used for commercializing, I will be OK with that as long as it's still open source. My issue wouldn't be with the commercialization of anything inspired or derived from this contribution, but it's more about the patenting. Then I wouldn't be OK with that because the contribution I made was intended to be accessible and replicable and appropriable by anyone"

— Researcher 0729

As previously noted (Theme 6) at least half of our interviewees said they would not share anything of potential commercial value to Nucleus. Others again underlined the lack of benefit to themselves and the tax-paying public.

> "It doesn't feel like a particularly good deal. So why would the taxpayers from around the world contribute to the science that then benefits a small number of companies or a large number of companies, but doesn't benefit the taxpayer who invested? That feels like a strange starting point, at least. There's no benefit to the researchers who make the knowledge freely available. So I will be out"
>
> — Researcher 1030

Similarly several researchers pointed out that if people only contribute what they do not think is valuable, the repository may end up being 'full of junk'.

b.next patenting of derivatives of shared resources

Many researchers were unsure about the acceptability of b.next itself building out and patenting based on openly contributed resources. Some said it would not make sense if others were permitted to do this but that b.next was not. However, a few noted that b.next will have privileged access to Nucleus resources. This could raise hackles, particularly if community access was then closed off. Interviewees mentioned Open AI and Makerbot as examples of open organizations that have changed tack unexpectedly to the consternation of community members.

> "It's trickier from a community perspective when you are the entity that has convened that community and it then financially benefits you individually that people are contributing these things. And that is I think, fine when the rules of engagement are clear from the start. So if it is clear to people, they should know that you too can make use of those open resources. You are a neutral entity and should communicate when you intend to not be that... it really annoyed the people that had kind of put stuff in because that wasn't the deal when they started. And so they kind of felt like they'd been taken advantage of. So I think there is a bit of a big risk on that front"
>
> — Researcher 0729

Optimized PURE

Every researcher expressed approval of the notion of b.next optimizing, standardizing, and making broadly available to the community the PURE system, in addition to

providing the open recipe for this. It was said that providing a reliable and affordable source of the system would be of great value. Researchers underlined the amount of work that would be involved in this endeavour, saying b.next would be deserving of profit from this project. A good number however, emphasized the importance of clearly articulating that this system is a community-developed resource that has benefited from the contributions of many, and attribute and possibly share benefits. A few questioned how an optimized version of a PURE-like system could be proven novel and therefore patentable, and likewise if the recipe were made open, how b.next would prevent others from under-cutting their market. Several researchers mentioned New England BioLabs as model for a community-responsive organization that provides reagents and high value to the community.

Other concerns and opinions about b.next or Nucleus

Here we note some further feedback about Nucleus or b.next that were not directly addressed above or in the more general sections about barriers to sharing and open science.

DevNotes

Many said they are not active users of DevNotes (nor the Nucleus Distribution or Hub) yet because it is so new that they have not had a chance to investigate. However many were enthusiastic about the concept, the format, and the DOIs offered. As noted in 'Barriers or challenges to sharing' (Theme 7), a good number said they would prefer to see if these platforms prove to be relevant and sustainable before they invest in contributing. One researcher underlined the need for user-friendly interfaces noting that navigating DevNotes was not intuitive. They called for training and information underlining that using new formats and platforms is always a barrier to participation, particularly for those who do not personally know or have experience with b.next or are more peripheral community members. A few researchers also called for more information about how publication in DevNotes may affect acceptance in high-impact journals and how DevNotes differs from standard publication, for example a 'Nature Methods' submission. Relatedly, one interviewee praised DevNotes and the Nucleus protocols saying these could aid standardization, streamlining and encouraging sharing.

Reaching critical mass

Many spoke of the need for Nucleus to gather a critical mass of users and contributors, such that it becomes ubiquitous and the unquestionable 'place to go' for sharing, accessing, and building syn cell technology. Again, researchers underlined the need for incentives. For example, one suggested offering grants to encourage collaboration, integration and contribution with the award scaling by the number of groups collaborating and modules added back to Nucleus. In this context, several researchers

also underlined the need to strengthen a culture of sharing and also to expand the number of labs working on synthetic cells.

Fellows and students visiting b.next

Some interviewees spoke about students and fellows visiting b.next. They emphasized that learning at the bench is incredibly valuable and the most efficient way to transfer knowledge. In this context all said that IP frameworks would need to be laid out preemptively. Some noted that such frameworks would be considered by themselves and their TTO the same as any other relationship with industry. One did note that outputs could potentially be 'open-sourced', but again this would have to be discussed in conjunction with their TTO. In this vein, another questioned whether those that teach techniques to b.next should be paid as consultants, analogous to other industrial lab situations. One underlined the need for sharing of IP and authorship between the visiting scholar and b.next. Another said that at least the basic science parts of any shared work should be made open. Finally, one suggested that running intensive paid sessions for trainees could be another revenue stream for b.next.

Industry involvement in Nucleus

There were a variety of views about industry involvement raised by interviewees. Overall, researchers saw the possibility for mutual benefits but, again, many were concerned about the potential for 'free-loading', appropriation, and closing-off of technologies. Some noted that this is currently the status quo, as industry already scouts the literature for anything interesting. Thus, they raised the question of the value-add for industry and for the academic/not-for-profit Nucleus community respectively. If companies were active and contributing members they might benefit by having access to expertise and influencing the research programs of top minds in the field. Likewise, there could be exchange of highly-trained personnel between settings with networking benefits for trainees. Industry could act as suppliers for labs by developing products responsive to researchers' needs. Contact with industry may lead to collaboration and funding opportunities, access to infrastructure, and possibly pathways to commercialize. One suggested industry involvement may help the field with standardization. Some noted that expanding the diversity and number of engaged stakeholders, including industry and VCs involved in the ecosystem, would be important to drive the field toward establishing innovative syn cell companies.

Some interviewees discussed rules of engagement. Many mused that if Nucleus were truly open then anyone should be able to access resources on the same terms. Nevertheless some went on to suggest ways to reduce the opportunities for companies to behave badly including: creating a strong framework of expectations and code of practice; requiring that if you take, you must give back (and monitoring and making this transparent to users); setting up a community fund that companies could

contribute into; requiring companies to pay a fee for access; and a minimal requirement for users to provide information about their identity, affiliation and how they plan to use the resources. One said they doubted industry involvement could be of value as industry is profit-motivated, while another doubted that they would want to freely share their knowledge.

"You just want to avoid any misconceptions that would then lead to people feeling that what they put in has been taken and used in a way they didn't anticipate. So as long as that's there at the start, I think, I think the ...greater the buy-in from different stakeholders, the better to be honest. I think it'll become a stronger community and hopefully you'll get cross-pollination of ideas, projects and people"

— Researcher 1029

Nucleus licenses

At least half of the researchers with whom we spoke said they were not knowledgeable about different types of licenses and that they leave this to their TTOs. Others who felt comfortable commenting said they thought the CERN-P-OHL-2.0 and other licenses in the Nucleus White Paper are appropriate and fit-for-purpose (Appendix 1). A few underlined the importance of using permissive licenses (see also Theme 9), saying that only such freedom to operate will allow the innovation landscape to diversify and advance. Some said that educational materials on the implications and details of open source licenses would be helpful.

"I think we're not going to get a synthetic cell unless you have something like that. Like you have to have the breathability for getting more people involved. So you can't be closed off about it. Nobody's going to build a synthetic cell"

— Researcher 0731

Points to consider

- A few researchers highlighted the need for consideration around bio-safety in the syn cell space. One called for establishment of a bio-safety sub-committee at Nucleus to monitor these issues.

2 - Encouraging participation and building trust in Nucleus

Benefit-sharing and staying connected to the community

As repeatedly noted in these results, almost all of our interviewees spoke extensively about concerns over the fairness or sustainability of open sharing in the absence of benefit to them. This view was further developed with respect to Nucleus and the potential for others and b.next to financially profit from the repository.

> "Are b.next going make money from those collaborations, based on the know-how they got from academic researchers whose time they didn't pay for? A lot of people are going to have shown them how to do things for free. While a lot of that sounds like it will be published in these DevNotes, there is a lot of know-how that is difficult to express in text and images. It will be important to know what b.next are going to do with the know-how and expertise they get. A conventional company would at least be paying consultant fees for things like that."
>
> — Researcher 0910

Our analysis very strongly indicates that assuaging doubts and strengthening trust and buy-in crucially turns on b.next staying closely connected and responsive to the community and being seen to be contributing back and adding value. Benefit-sharing emerged as a real game-changer in terms of how researchers felt about potential commercialization of shared assets by b.next (and others).

> "You have to get some place to the point of trust, right? .... You've got to somehow believe that b.next is going to continue to support that open ecosystem that you're contributing to and not simply draw from it and not give back to it. Obviously, you know, at the start, everything they're doing is contributing to that open ecosystem... they'll just have to be careful as they go forward to make sure that they continue to provide value to the people that are helping build the platform that they're commercializing or building commercial products on top of. I think it's possible".
>
> — Researcher 0812

A few described models where dividends or a cut of the profits could be distributed back to those who contributed. Others suggested community-level benefits. Asking how b.next could give back elicited a variety of ideas (see Table 2).

Contributor and user agreements and a governance body

Researchers strongly underscored the need to clearly and transparently lay out the company ethos and aspirations to stakeholders. Contributor and user agreements should include details of expectations, boundaries, possible outcomes from contributing, who will benefit, how and to what degree. Many said it is critical that a community-benefit plan be established preemptively. There was also almost a unanimous call for establishing a governance framework that is closely-connected with the community, for example involving a rotating board of researchers.

> "Definitely a strong connection to the scientific community that uses the platform and provides the information – that would be very, very necessary I think. Making that even somewhat formal in terms of an involvement in the governance body of Nucleus. That could be a good idea because it would also quite visibly send the message – we are there for the community. We are part of the community. The community is part of us. This link has to be very strong for people to trust it, I think".
>
> — Researcher 0916

Table 2: Suggested roles for b.next and ways to 'give back' and add value

Concern or knowledge gap raised by interviewee(s)	**Suggested activity to address the concern**
IP, open source and sharing practice	
Unquestioned reliance on patenting as the most effective pathway to commercialization, public impact and broad dissemination	• Prototype a new model to benefit based around open sourcing foundational knowledge
Lack of evidence on the relative risks and benefits of patenting vs open sourcing of scientific outputs	• Develop in-depth case studies and other comparative evidence around open source pathways to benefit through the life cycle of an output

Lack of awareness and deep understanding of IP vs open source pathways and open licensing practices	• Develop and deliver webinars and other educational materials for institutions and researchers to inform decision-making • Convene multi-stakeholder conversation to explore, deliberate and inform including researchers, government, funders, foundations, VCs, industry, science publishers, legal scholars and IP experts, sociologists etc. Could include online forums for community discussion and in-person workshops
Poor appreciation of the benefits of enhanced sharing of knowledge and scientific resources – tendency to focus on personal and lab goals over producing and sharing useful community resources	• Encourage cultural change to scale-up sharing (including to Nucleus), by promoting and educating on the benefits (for researchers and other stakeholders including the public) of building an eco-system where all can use, benefit and give back. For example, expand the Build-a-Cell ethos to the broader synthetic biology and related academic communities • Develop systems of reward and benefit wherein it becomes easy, standard and clearly advantageous for researchers to share (see box directly below)
Out-dated systems of credit and reward around science publishing and sharing, in particular to recognize and reward open sharing	• Help develop and instil a meaningful and open science-responsive system of metrics for openness • Ensure that these are recognized and weighed by academic advancement committees, funders, foundations and other relevant stakeholders
Translation challenges	

Poverty of pathways between academia and the start-up space to develop syn cell inventions	• Enhance start-up support for syn cell technologies • Lobby for relaxed regulatory requirements as companies are finding their feet • Establish seed funding and incubator space • Build links to mentors, lessons learned and repositories of knowledge to support and de-risk early-stage biotech ventures
Scientific challenges	
Significant scientific challenges to address in syn cell research	• Establish X-prize or similar competitions to target key scientific barriers
Integration and standardization	
Poor reliability and access to key reagents	• Standardize and make widely accessible at fair cost optimized reagents (and their recipes) including PURE
Poor transferability of detailed and tacit knowledge	• Run intensive in-lab training modules or 'Cold Spring Harbour'-like sessions for developers
Poor reproducibility and inter-operability of reagents, materials, tools and knowledge	• Quarter-back standard setting and cross-lab implementation, and the maintenance and quality control of reagents and materials etc.
Funding challenges	
Increasingly limited research funding available	• Provide research funding such as grants, student fellowships etc. • Develop avenues to provide more long-term funding solutions
Build-a-Cell funding expiring	• Provide support of Build-a-Cell
Research field alignment and coordination	

Poor alignment of field-wide research activities and goals, for example how projects might cross-pollinate and synergize (while acknowledging that the diversity of views about 'what a syn cell is for' makes broad agreement challenging)	• Create and promote more community-wide and global dialogue to move toward agreement and coordination of shared goals, standards and complementary activities (recognizing that these will always be dynamic and that productive exploration around the sidelines may likely emerge and is desirable)
Public awareness and responsibility	
Limited public awareness of syn cells and their promise	• Raise the profile of syn cell research and potential by instigating more open public conversations about the role of science and technology including syn cells in the US (and beyond) • Drive more public literacy and dialogue around these issues, about the world we would want to live in and how to makes choices consistent with creating it
Limited engagement of the field on what it is to be a responsible and ethical synthetic biologist	• Convene and promote more discourse in the field about the societal and environmental implications of syn bio and syn cell research • Establish a group to monitor, gather and disseminate knowledge

REFERENCES

1. Ali-Khan S, Harris L, Gold ER. 2017. Motivating Participation in Open Science by Examining Researcher Incentives. Elife Oct 30:6:e29319. doi: 10.7554/eLife.29319
2. Ali-Khan S, Jean A, MacDonald E, Gold ER. 2018. Defining Success in Open Science. [version 1; peer review: 2 approved]. MNI Open Res 2:2 https://doi.org/10.12688/mniopenres.12780.1
3. AUTM. 2007. In the Public Interest: Nine Points to Consider in Licensing University Technology. Available at: Nine Points to Consider in Licensing University Technology. https://autm.net/about-tech-transfer/principles-and-guidelines/nine-points-to-consider-when-licensing-university (accessed Dec 10, 2025)

4. Build-A-Cell. Open Collaboration supporting the science and engineering of building synthetic cells. https://www.buildacell.org (accessed Nov 15, 2025)
5. Chesler E, Baker E. 2010. The importance of open-source integrative genomics to drug discovery. Curr Opin Drug Discov Devel 13(3): 310-316.
6. Endy D. 2005. Foundations for engineering biology. Nature 438. 449-453. https://doi.org/10.1038/nature04342
7. Edwards A. 2016. Perspective: Science is still too closed. Nature 533: S70. https://doi.org/10.1038/533S70a
8. Fecher B, Friesike S. 2014. Open science: one term, five schools of thought. In: Bartling S, Friesike S (eds) Opening science. Springer, Cham, pp 17–47. https://doi.org/10.1007/978-3-319-00026-8_2
9. Gertner J. 2012. The idea factory: Bell Labs and the great age of American innovation. Penguin Press.
10. Giaveri S, Abil Z, Kohyama S et al. 2025. Building a Synthetic Cell Together. Nat Commun 16, 7488. https://doi.org/10.1038/s41467-025-62778-8
11. Gold ER. 2016. Accelerating Translational Research through Open Science: The Neuro Experiment. PLoS Biol 14(12): e2001259. doi: 10.1371/journal.pbio.2001259
12. Gold ER 2021. The fall of the innovation empire and its possible rise through open science. Res Policy 50:104226. https://doi.org/10.1016/j.respol.2021.104226
13. Joly Y. 2010. Open biotechnology: licenses needed. Nature 28, 417-419. https://doi.org/10.1038/nbt0510-417
14. Kahl L, Molloy J, Patron N et al. 2018. Opening options for material transfer. Nat Biotechnol 36, 923–927. https://doi.org/10.1038/nbt.4263
15. Landi A, Thompson M, Giannuzzi V et al. 2020. The 'A' of FAIR - As open as possible, as closed as necessary. Data Intelligence 2 (1-2): 47–55. https://doi.org/10.1162/dint_a_00027
16. McKenzie B. 2023. Life sciences licensing from US universities – six areas to consider. Leology https://www.lexology.com/library/detail.aspx?g=604f3386-0357-4a07-94c5-b4ddef8ca4d0 (accessed Dec 10, 2025)
17. Linux Foundation collaborative project. SPDX.2018. CERN Open Hardware License Version 2 – Permissive. SPDX Workgroup a Linux Foundation Project https://spdx.org/licenses/CERN-OHL-P-2.0.html (accessed Oct 15, 2025)
18. Montreal Neuro. What is Open Science? https://www.mcgill.ca/neuro/open-science (accessed Nov 15, 2025)
19. Morgan Jones M, Castle-Clarke S, Brooker D et al. 2014. The Structural Genomics Consortium: a knowledge platform for drug discovery. RAND Corporation, Santa

Monica, CA. https://www.rand.org/content/dam/rand/pubs/research_reports/RR500/RR512/RAND_RR512.pdf (accessed Oct 31, 2025)

20. National Security Commission on Emerging Biotechnology. 2025. Charting the Future of biotechnology. An action plan for American security and prosperity. https://www.biotech.senate.gov/final-report/chapters/ (accessed Nov 15, 2025)
21. Neuro.TOSI Alliance of Open Science Institutes. https://www.mcgill.ca/neuro/open-science/tanenbaum-open-science-institute-tosi/promoting-open-science-across-canada (accessed Nov 15, 2025)
22. Nucleus (1). Open Science. https://nucleus.bnext.bio (accessed Nov 15, 2025)
23. Nucleus (2). Developer Notes. Build synthetic cells that work. https://devnotes.nucleus.engineering (accessed Nov 15, 2025)
24. Open Science Hardware Foundation. Open Science hardware Foundation. Advancing open source instrumentation to accelerate science and benefit society. https://opensciencehardware.org (accessed Nov 15, 2025)
25. Powell K. 2018. How biologists are building life-like cells from scratch. Nature. 563. 172-175. DOI:10.1038/d41586-018-07289-x
26. Ramachandran R, Bugbee K, Murphy K. 2021. From open data to open science. Earth Space Sci. 8:e2020EA001562. https://doi.org/10.1029/2020EA001562
27. Reclone.org. Reclone reagent collaboration network. https://reclone.org (accessed Nov 15, 2025)
28. Rothschild L, Averesch N, Strychalski E et al. 2024. Building Synthetic Cells – from technological infrastructure to cellular entities. ASC Synth Biol 13, 4, 974-997. https://doi.org/10.1021/acssynbio.3c00724
29. Shimizu Y, Inoue Y, Tomari Y et al. 2001. Cell-free translation reconstituted with purified components. Nat Biotechnol 19, 751-755. https://doi.org/10.1038/90802
30. Smolke C. 2009. Building outside of the box. iGEM and the BioBricks Foundation. Nat Biotechnol 27, 1099-1102. https://doi.org/10.1038/nbt1209-1099

APPENDIX 1: NUCLEUS WHITEPAPER

Nucleus – a developer ecosystem building synthetic cells (July 11, 2025)

Mastering the engineering of biology will unlock new modes of technology that enable humanity to flourish. Yet, the inherent complexity and diversity of natural cells means that the best we can do today is develop an increasing number of bespoke engineering tools and solutions. Engineering efforts are now organized as small teams that must own the entire development "stack", from system design to DNA implementation, constraining progress to particular cellular systems with tens of engineered components that are rarely interoperable in new contexts. Making it easy to build integrated systems with hundreds to thousands of components will require new technical and social frameworks that move beyond natural systems and idiosyncratic engineering practices.

Nucleus is a platform for the collaborative development of synthetic cells—non-living, genetically-programmed biomolecular machines—that are entirely composed of well-understood, modular, components. **Synthetic cells are the most promising vehicle for systematically integrating and deploying thousands of components at scale for diverse contexts and applications.** Nucleus includes technical resources such as validated protocols, plasmids, and software code that allow engineers to focus on developing new capacities, rather than reinventing what has already been done. **Nucleus is an open source project built on open science practices where everyone is encouraged and free to use, modify, and build upon shared capabilities.** By providing an accessible and well-documented platform, Nucleus aims to be biology's Arduino.

Nucleus stands to operationalize the hundreds of foundational components and capabilities that are actively being developed by the frontier synthetic cell community. These components are now largely developed in isolation, without shared design principles or common features (e.g., buffer conditions or membrane compositions), and thus are slow and difficult to combine and build upon. **By developing components using the same underlying platform, integration and scale become possible.** Nucleus provides a technical framework built on pre-existing optimization and validation of basic cell-building components (cytosol, container, and content) and reference functional cell designs. It also provides the underlying documentation and protocols to use these

components, making it the most expedient means of creating baseline cells upon which to build new functionality.

Nucleus serves as the venue for the co-development, specification, and standardization of the means to build components, modules, and cells at increasing levels of sophistication. Collaboratively building and integrating at scale requires working in a way often at odds with the default means of working in academia. Nucleus includes data-sharing infrastructure that enables geographically distributed engineers to easily share and analyze datasets. This infrastructure includes integration with a publishing suite, enabling engineers to share ideas and results. Nucleus as a social framework acts to teach, incentivize, and build energy around rapid, open sharing to increase the velocity and scale of collaboration within the community.

b.next is the open core synthetic cell company based in San Francisco. b.next developed the Nucleus Ecosystem to support the development of a synthetic cell industry built on collaboration through open technology. As a company, it provides core services and reagents to deliver synthetic cell applications to the world. For example, the b.next Foundry is the manufacturing pipeline for producing key reagents, components, and physical development tools (e.g., Nucleus PURE, measurement standards, debugging kits, and DNA). b.next also hosts Nucleus Labs, the physical embodiment of the Nucleus Ecosystem, providing built-for-purpose laboratory space for developers from across institutions to perform integration.

Nucleus increases the capabilities of synthetic cells for all.

Nucleus consists of three core pillars that serve distinct functions. The **Nucleus Distribution** is an integrated knowledge base and collection of tools that enable the Developer Community to build with a shared foundation. **Nucleus Hub** is a collaboration platform that provides digital environments and tools that enable developers to work together. **Nucleus Developer Notes** (DevNotes) is a publishing platform for DevNotes, short-form scientific notes for rapidly communicating on-going work. DevNotes are how the developer community can contribute to the collaborative development of the Nucleus Distribution.

Developers start with the Nucleus Distribution; build with Nucleus Hub; and share progress and results with DevNotes. New capacities are validated and integrated back into the Nucleus Distribution for use by the Developer Community (Figure 1).

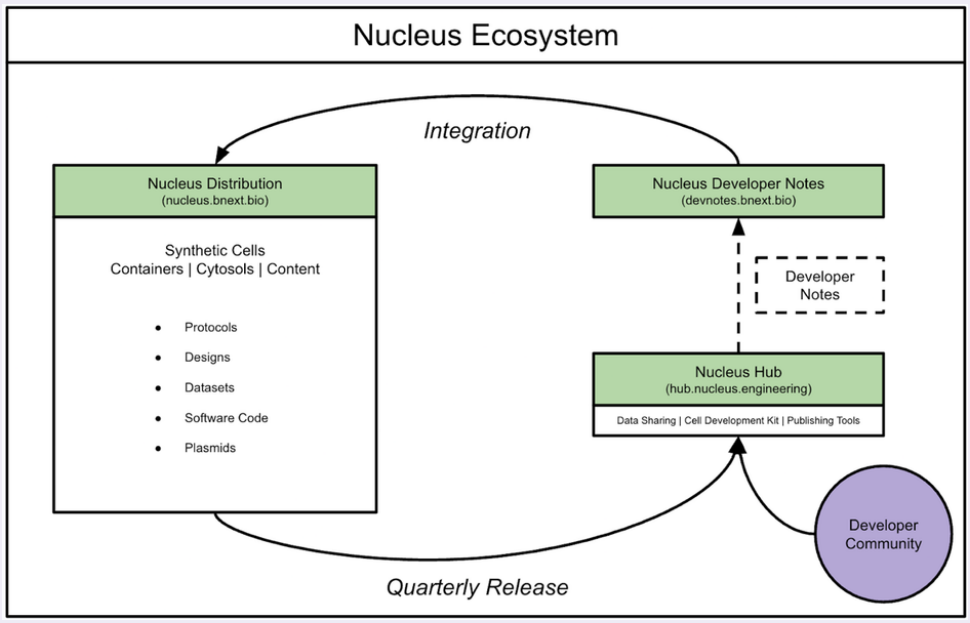


Figure 1: Overview of the Nucleus Ecosystem. Boxes represent distinct pillars of the Nucleus Ecosystem and arrows show the flow of information between them.

1 - Nucleus Distribution (nucleus.bnext.bio)

The Nucleus Distribution is an open-source collection of protocols, designs, datasets, software code, and biological materials that are designed for interoperability. The Developer Community collaborates to develop the Nucleus Distribution. The distribution supports PURE-based modules and synthetic cells. The Distribution is versioned and updated quarterly based on community contributions and integration work done by the Core Development Team at b.next. The key elements of the Distribution include:

- **Nucleus DNA Distribution.** The Nucleus DNA Distribution consists of genetic constructs that can be used to engineer synthetic cells. It contains plasmid DNA for making the PURE system, fluorescent reporter proteins, and a growing set of genetically encoded modules that expand the functionality and improve the performance of the underlying PURE system such as molecular logic, increased metabolism, and membrane-associated proteins. The constructs have been experimentally validated and datasets describing expected behavior are provided. The genetic constructs are open source (sequence information available on GitHub) and open access (available under OpenMTA). The Distribution is currently available by sending a request to build@bnext.bio.
- **Nucleus Protocols.** Nucleus Protocols are validated protocols that describe how to use the Nucleus DNA Distribution to make a variety of cytosols and synthetic cells

based on the PURE system. They include detailed lists of materials and reagents and provide step-by-step instructions that can be used directly at the lab bench.

- **Cell Development Kit (CDK).** The CDK provides supporting software code to work effectively with cells and cell components. At present, this particularly includes tools for standardized measurement of cytosol (plate reader) and cell (microscopy) data. Collection and analysis of such data in a way that is quantitatively comparable and shareable between collaborating laboratories is critical for co-development, integration, and to enable later uses of the data such as modeling or replication of a cell design. The CDK increasingly includes the means for specification of cell designs and automation of cell-building processes, and the CDK forms the first step of the process to share designs, experiments, data, and analysis by various means (GitHub, Nucleus Hub, Developer Notes, etc.).

2 - Nucleus Hub (hub.nucleus.engineering)

The Nucleus Hub is a shared environment pre-loaded with digital tools, such as the CDK and DevNote publishing suite, that helps facilitate collaboration between members of the ecosystem. Nucleus Hub is based on Jupyter Hub and obviates the need for users to manage complicated software environments. As such, it provides a way for developers to share and analyze data in the cloud using a common set of standard tools. Nucleus Hub is configured to accommodate expanding circles of trust. Developers can work individually, in small groups, or use the integrated publishing suite to make contributions to Nucleus Developer Notes that will be publicly available. Currently, access can be requested by sending an email to build@bnext.bio.

3 - Nucleus Developer Notes (devnotes.bnext.bio)

Nucleus Developer Notes is a publishing platform for rapidly sharing new developments with the Nucleus Ecosystem. The Core Development team at b.next integrates work shared as DevNotes into the Nucleus Distribution.

- **Developer Notes (DevNotes).** DevNotes are the mechanism by which contributions to the Nucleus Distribution are made. DevNotes resemble scientific publications but can be structured like a software project. The scope of a typical DevNote is a single claim. They are built on Jupyter Notebooks, providing integration with data, analysis, and a variety of other file types. They can be issued a DOI, enabling them to be easily found and cited. DevNotes come in a variety of flavors including new modules, proposed work, result replication, negative results, and technical notes. In general, DevNotes are regarded as preprints and not classified as published work.

Making a Contribution

What is a Developer Note (DevNote)?

DevNotes are a short form of scientific communication that can be described in one sentence. They provide the Nucleus community with a means to rapidly share useful results and insights. Since they are built on top of Jupyter Notebooks they can easily integrate code and a variety of file types, bundling an entire research workflow into a discrete package (Figure 2A). DevNotes are used to make contributions to the Nucleus Distribution and can be generated on Nucleus Hub (Figure 2B). Results and insights that are highly useful and/or relevant will be integrated into the Nucleus Distribution by the Core Development Team at b.next.

What can I contribute as a Nucleus Developer Note?

Anything related to PURE-based cytosols and synthetic cells is solidly within the scope of Nucleus. Ideally, contributions should build on existing components of the Nucleus Distribution in some way. There is no limitation on how long or short a DevNote should be. A good rule of thumb is that you should be able to describe your DevNote in one sentence. Some examples might include:

- **Experimental plans.** Even if you are just planning an experiment, feel free to submit it as a DevNote to let others know how you're thinking about approaching the problem and get feedback from others earlier. DevNotes can be updated so experimental data can be included along the way
- **Module development.** Experimental data showing that a genetically encoded module works in PURE. The corresponding DevNote should include data, a design file containing sequence information, and a protocol showing how to implement the module.
- **Experimental replication.** If you're planning to use a component from the existing Nucleus Distribution or from the literature as part of a larger experiment, sharing that the module works in PURE in your hands would be valuable to others.
- **Technical Notes.** If you have a trick you use for making routine lab work more efficient or more reliable, share it with others.
- **Open questions.** If there are questions that you feel are worth writing up and of interest to this community, others would probably love to know about them and might even have some answers!

If you're not sure where to start or have an idea for a new type of DevNote and want to get involved, don't hesitate to reach out to build@bnext.bio.

When should I contribute to Nucleus?

The small scale and flexibility of the DevNote format means that they can be shared at any time during the research process that the contributor thinks would be appropriate. DevNotes are considered preprints and therefore do not count as previously published material. DevNotes can be shared along the research journey and be used as building blocks for assembling longer format manuscripts. This strategy would provide a means to organize work while getting credit and feedback along the way.

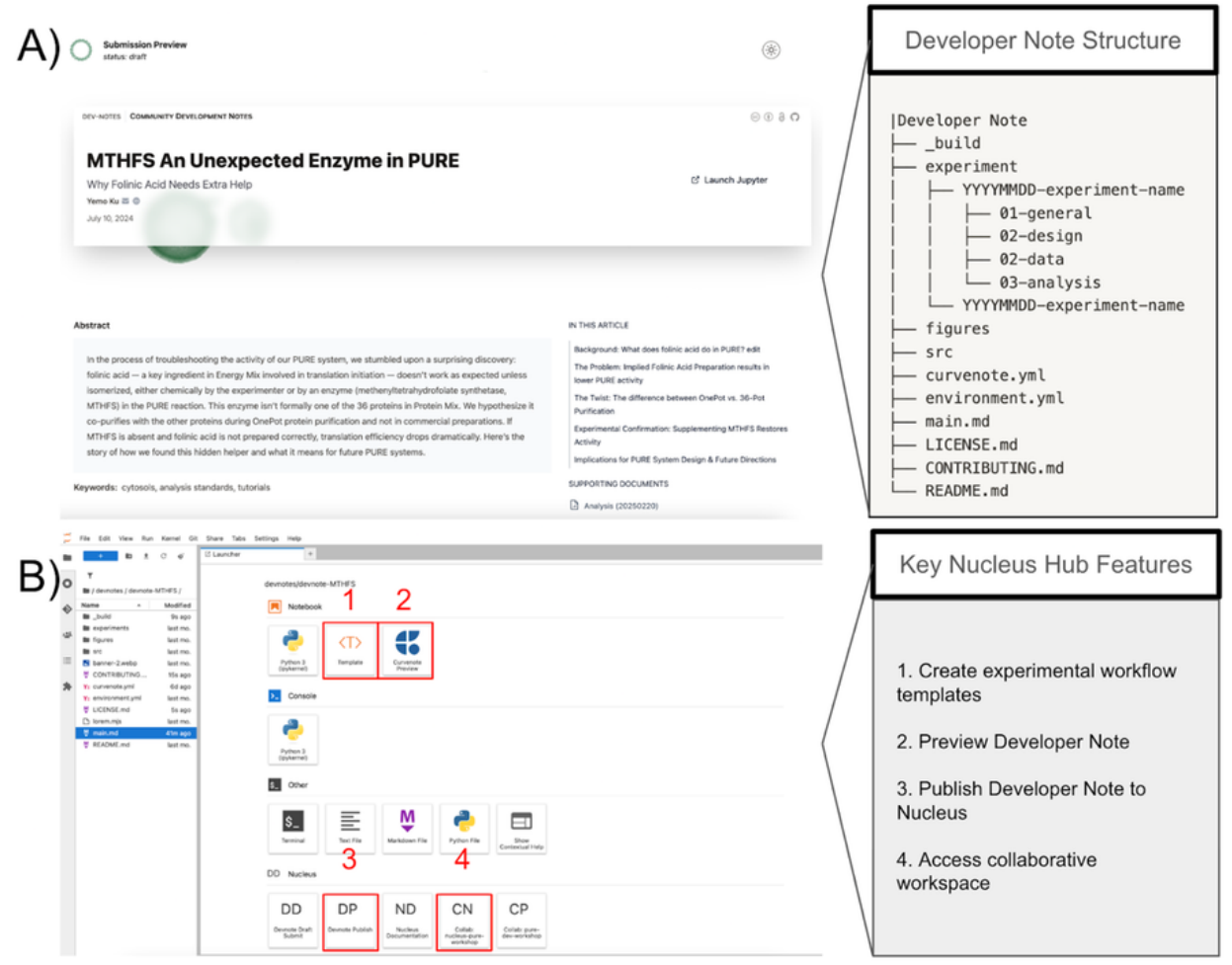


Figure 2: Developer Notes and Nucleus Hub. A) Human-readable view of a Nucleus Developer Note; inset shows the underlying file structure. B) View of default landing page for Nucleus Hub; inset shows key user features that work out of the box.

How exactly do I make a contribution?

1. **Request Access to Nucleus Hub** by navigating to hub.nucleus.engineering and making an account. Email build@bnext.bio to approve your account.

2. **Familiarize yourself with the DevNote template** by following the guide at nucleus.bnext.bio/devnote-tutorial.
3. **Build your project.** If your contribution includes experimental components, be sure to structure your project following the template structure. If these don't work for your particular project, let us know!
4. **Submit your DevNote** to be posted on devnotes.bnext.bio.
5. **Questions?** Don't hesitate to reach out to build@bnext.bio.

Open Source Licensing

Open source licensing refers to a practice pioneered by the software industry that made it possible to easily share, reuse, and modify software code. Open source licenses provide a clear signal for what others can legally do with contributed software code, reducing barriers to participation and making it straightforward to build on the work of others. This legal clarity has been critical to the success of collaborative software development, enabling software engineers to work together seamlessly across institutional and industry boundaries for decades.

Our goal is to create a similar culture and practice of sharing that enables Nucleus developers to collaborate across institutional and industry boundaries. Nucleus adheres to a **permissive open source licensing scheme** built on existing, well-established open source licenses appropriate for biotechnology. The Nucleus open source licensing scheme covers more than just software code, it includes protocols, designs, formulations, and materials needed for making synthetic cell modules.

Permissive means that contributions can be used, modified, manufactured, and distributed by anyone for any purpose, including commercial applications.

Nucleus licensing scheme

Table 1: Nucleus contribution component types and corresponding licenses. All contributions are "wrapped" by CERN-OHL-P-2.0.

Component Type	License
Formulations (e.g. cytosol, membrane, etc.), Protocols, Documentation, Jupyter Notebooks, Characterization datasets	CERN-OHL-P-2.0
DNA template designs	CERN-OHL-P-2.0
Biological materials (e.g. plasmids)	CERN-OHL-P-2.0 + OpenMTA

Software (e.g. CDK)	MIT
DevNotes	CC-BY-4.0

What rights and obligations do these licenses provide?

Contributions are licensed under the CERN Open Hardware License-Permissive version 2.0 (CERN-OHL-P-2.0), endorsed by the Open Source Initiative as meeting all requirements for being a true open source license. **This permissive license gives users the right to make and convey products manufactured or assembled from the licensed source material.** Contributors are encouraged to read and familiarize themselves with all of the licenses used in the Nucleus Ecosystem. This specific license was chosen because it includes provisions directed to the manufacture and assembly of physical products, including non-source code elements, such as designs, and includes terms for both copyright and patents, essential for working with biotechnology contributions. **Users are required to acknowledge contributors for their work and retain all notices and acknowledgements.** The CERN-OHL-P "wraps" the entire contribution, while individual components of a contribution such as datasets or protocols may also be licensed under a more specific, compatible license as described in Table 1. This is particularly useful if a contribution makes use of existing components that are available under existing, compatible licenses.

When is open source licensing appropriate? Open source licensing is appropriate when you want to allow others to freely use, modify, and distribute one's own contribution. It's ideal when you want to encourage community collaboration, build on existing projects, or make your contribution widely accessible.

Contributions that describe foundational or "low-level" capacities are ideally suited for an open source licensing approach. Foundational capacities such as molecular logic or energy generation modules stand to improve the utility of a significant number of other components if made accessible and interoperable. "Low-level" capacities such as basic sensing mechanisms or cellular machinery components are not particularly valuable in isolation; instead they become valuable when used in combination with many other components, most likely developed by third parties.

Contributions that describe capacities that are valuable in isolation may not be well suited for open source licensing. For example, a sensor for a specific therapeutic target or pathway for production of a valuable compound could serve as the basis for a successful company and should be evaluated for commercial viability as proprietary IP. Deployment of a proprietary sensor using an open source Nucleus synthetic cell as a deployment chassis would be possible under the Nucleus open source licensing scheme.

It is always possible to go open source first and take a proprietary approach later. Releasing early, foundational work as open source can benefit others and provide you with valuable feedback. Proprietary applications can be built on top of the open foundation and benefit from community improvements to the underlying platform.

How do I make an open source contribution?

The structure of Nucleus DevNotes makes it straightforward to release your contribution into the core open source distribution:

1. **Read the license.txt file contained in the root directory of the DevNote template**
2. Declare which files are considered Covered Source in the license.txt file. **The default declaration should cover most use cases.**
3. **Submit the DevNote.** By submitting the DevNote you acknowledge that you have the rights to license others to use your work.

Questions?

For guidance on licensing decisions or help implementing these practices, contact us at build@bnext.bio

APPENDIX 2: METHODS

For this study we used qualitative research methods: in-depth semi-structured interviews, followed by thematic data analysis.

Study sample and research design

We used a purposeful sample strategy to select an initial pool of participants. We used perspectives gained by Sarah Ali-Khan on her visit to Build-a-Cell and b.next in May 2025, a search of important literature in the field and lists of key stakeholders obtained from b.next to selectively invite research participants. We then followed up using a 'snow-ball' strategy to identify further interviewees. During interviews we asked participants to suggest the names of others they felt would be particularly informative to speak with. After triangulating with internet searches and their publications to check for suitability we invited these individuals to participate in the study. The key informant nature of our final interviewee group is underlined by the fact that all the researchers we spoke to were named by at least one and often several of the others we spoke with. We aimed as much as possible for balanced representation across gender, time in practice, research area and geography starting with those that had been identified as key informants by b.next.

Many interviewees said that the input of their institutional technology transfer offices (TTOs) is important is in making data and material sharing decisions. b.next also underlined their interest in exploring the views of TTO representatives. Thus, we also collected the contacts of institutional TTO representatives known to researchers during interviews. We subsequently invited and interviewed several to explore and verify these perspectives.

One of the key goals of this research was to understand the synthetic cell research community's preferences, concerns and opinions about the Nucleus open source eco-system to guide the further development of its structure, policy and practice. As Nucleus' framework and policy are nascent and therefore not well-known to researchers, b.next developed a White Paper (Appendix 1) that we sent to participants well in advance of their interview. In this way participants were able to reflect on this content and provide up-to-date and informed opinions.

Data collection

The first author Sarah Ali-Khan (with a research assistant (RA) and Richard Gold copied in) sent out 41 invitations to the study and multiple follow-up reminders by email. RA

Jerod Miksza scheduled twenty individuals for interviews, with one cancelling due to the US government shut-down. Seven invitees stated they were too busy to participate, the remainder did not respond. We quickly gathered positive responses from US interviewees, likely because b.next and their founders are better known in the US. Interviewees in the UK and Europe required multiple invitation letters and follow-ups to secure. The slow response time may also have been due to the summer holiday season and busy start of the academic year.

Sarah Ali-Khan who has a PhD in Pharmacology and Therapeutics and 15+ experience in the area of open science, ethics, innovation and social justice conducted the interviews over the McGill MSTeams Platform. Interviewees were situated at home or in their places of work across July to September 2025. Interviews were digitally-recorded and transcribed verbatim using MSTeams, then checked for accuracy by our RAs. Interviews length ranged between 30 and 120 minutes with the majority lasting between 60 and 90 minutes. We developed the interview guides based on our review of the open science and synthetic cell literature and our understanding of b.next's goals and business model, and in collaboration with b.next (see Appendix 3 and 4 for Interview Guides). The interview process was iterative, in that key issues raised by interviewees are fed into subsequent interviews.

Data collection

During the interview process we also collected demographic information from our research participants. Where required and where it was possible, these data were verified through internet searches. The information collected included: researcher field of practice (self-identified from a list of relevant areas complied by the research team and verified by b.next as meaningful categories); number of years of research experience post-PhD; gender; job title; region and country of institution. Researcher time in practice was recorded in one of four categories: trainee, < 10; 10 - 20; 20 - 30 and 30+ years. Job title captured whether researchers were Principal Investigators (PIs), group leaders or trainees. Research field included: bottom-up synthetic cell; cellular engineering; synthetic biology and cell-free; and top-down (and middle-out) synthetic cell research. These demographic profiles were used to examine if opinions and practice varied between groups.

Qualitative thematic analysis

We have used qualitative thematic analysis techniques to analyze the data we obtained (Braun and Clarke, 2006). This process consists of 7 key phases: (1) familiarization—in which we read interview data in-depth multiple times; (2) generation of initial codes and application of codes to the dataset — or indexing — in which we identify and tag pieces of data (passages of text) relating to a common theme or idea relevant to the

research question; (3) searching for and verification of themes across the entire dataset; (4) identification of relationships between codes and of distinct differences between subgroups of ideas; (5) definition and naming of themes; (6) re-reading of the interviews and modifying codes based on emerging themes; and finally (7) mapping and interpretation of the overall narrative identified from the data. We used NVivo 15 software (Luminero) to organize this process. Two RAs, Jerod Miksza and Kevin Homsey, Sarah Ali-Khan and Richard Gold conducted and/or supervised the data analysis.

Development of analytical categories

During the thematic analysis process we developed several analytic categories into which we coded the content of our interviews. These categories capture what we defined as substantive, auxiliary and key data or issues. Substantive categories capture interviewees' opinions, concerns, ideas and motivations regarding collaboration, sharing, patenting, the impact of TTO practice and policy on sharing; and concerns about and requirements for participation in Nucleus and b.next. Auxiliary categories capture contextual information that we used to further our understanding of the substantive categories, such as the types of resources, policy, research organism, models or examples that interviewees mentioned as relevant. For example, where a researcher expressed concern about b.next being a for-profit company and potentially blocking access to resources, the text would be coded into a substantive category and sub-category ('concerns and opinions about b.next and its activities' – b.next being for-profit – concerns may close access to resources) and an auxiliary category for an example of a company that interviewees noted as an example of this ('companies and policy' – Open AI, MakerBot) to give contextual information.

We developed substantive categories to distinguish between more traditional collaboration versus open science and open sharing practices. These included perspectives and experiences with collaboration; motivations and incentives to participate in open science and sharing; disincentives or concerns around open science participation; and researcher attitudes and experiences with patenting. Two further categories indexed opinions and concerns about b.next and Nucleus; and solutions offered by interviewees to overcome these concerns and optimize engagement and participation.

We classified interviewees' opinions and interactions with patents and material transfer agreements (in this study these were the only IP-types mentioned) into categories such as 'would not share commercially valuable outputs', 'patents are important for impact and wide dissemination', and 'researcher not in it for the money'. The remaining higher order substantive categories deal with specific issues including the reproducibility and measurement problem in synthetic cell research, the impact of TTOs on sharing and open science practice, and opinions on the current broader research

and innovation system in their setting. We integrated information from the latter category into the theme 'how b.next can give back' which included interviewees' suggestions on how b.next could contribute to the community including improving research and innovation systems. Consideration of these codes also helped contextualize the 'Barriers or challenges to sharing' and 'The impact of TTOs' policy and practice on sharing' themes (Theme 6, 8). For a full list of the categories and classifications developed through our analysis please refer to Appendix 5.

Inter-coder reliability

The research team undertook measures to ensure that the coding of the data was a reliable representation of interview content and that the coding framework was consistently applied across interview transcripts. The co-investigator and the two RAs familiarized themselves with the breadth of interview content and then collaboratively developed a preliminary coding framework. Throughout the interview coding process coders discussed changes to the code structure with each other to ensure uniformity and the research team met regularly to discuss emerging findings. The interview coders also undertook a formal inter-coder reliability analysis using NVivo 15 software (Lumivero), by both coding the same interview and measuring agreement between the two copies. Most inter-coder percentage agreement at each category varied from 80 to 100%, showing only minimal disagreement between coders. Categories at which agreement was lower were among the 'auxiliary' group. When we inspected discrepancies we observed that this was due to differences in the length of the text coders had selected for auxiliary categories. Sarah Ali-Khan carried out a final review of the entire dataset to ensure its consistency, and refined and derived the research themes from the coding categories.

Ethics consideration

This study was approved by the McGill REB I in May 2025. All interviewees provided written or verbal and recorded informed consent.

References

1. Ritchie J, Spencer L: Qualitative data analysis for applied policy research. In: Bryman A, Burgess RG, editors. Anaylzing qualitative data. London, Routledge. 1994: 173–94.
2. Patton M: Qualitative evaluation and research methods. Beverley Hills, CA: Sage, 1990.
3. Braun V, Clarke V: Using thematic analysis in psychology. Qualitative Research in Psychology. 2006, 3(2): 77-101. https://doi.org/10.1191/1478088706qp063oa
4. Lumivero. 2025. NVivo15. The most trusted qualitative analysis software is even better. https://lumivero.com/products/nvivo/ (accessed Oct 31, 2025)

APPENDIX 3: STUDY INTERVIEW GUIDE: RESEARCHERS

Project: 'Strengthening Open Science in Synthetic Biology: deriving Open Science Principles for b.next from key stakeholders – a qualitative research study'

Please note that during development of the report we adopted the more succinct name – 'Assessing Needs of the Synthetic Cell Community for Open Coordination'. We flag that we retain the original study titles in Appendix 3 and 4 as these were used through the research process and are the original documents sent to research participants.

Please note that question probes or follow-ups are denoted with bullet points.

Demographic and contextual questions:

To begin, I would like to ask you a few questions about yourself:

1 - First, what is your job title/position?

- Clinician-scientist
- Institutional technology transfer office representative
- Professor
- Research Associate
- Post-Doctoral researcher
- Graduate Student
- Research Manager

2 - Could you please briefly describe the kind of lab you work in?

- Bottom up syn cell
- Top down syn cell
- Cellular engineer
- Cell free and synthetic biology
- Other

3 - How many years have you been in practice?

- Less than 1 year
- 1 to 5 years
- 6 to 10 years
- 11 to 20 years
- More than 20 years

On open science in the field of synthetic biology

4 - In your view, what are open science and open source? Are they different? What does working in the 'open' mean to you?

- How well do you think open science/open source are functioning in your field?
- How important are these for advancing the field and benefitting society?

Openness, sharing and collaboration practice

5 - How do you feel that open sharing/open science relates to collaboration?

- What is the typical size and form of your research collaborations (if any)?
- What barriers and challenges have you experienced around your collaborations efforts and what were the outcomes?
- To what extent would more collaboration be beneficial to your practice?

6 - Have you had any experience publicly sharing data, research materials or software through open source repositories or in other ways? What was the context? What was the outcome?

- What motivated your participation?
- Which are your sharing channels of choice? Why?

    - For example, depositing materials on Addgene, sharing datasets on Zenodo, posting manuscripts on open access preprint servers?
- What problems or challenges did you experience or anticipate?
- What were the benefits or harms if any, to the research process and results?
- How did public sharing/ participating in open science affect collaboration in your practice?
- What challenges or benefits do you foresee in obtaining proper attribution or reward for and recognition of your shared work product? How could these challenges best be addressed?
- Are there considerations around the financial sustainability of open sharing? If so, what are the issues and how do you think they could be resolved?
- How have your institutional technology transfer office policies affected your participation in open sharing or other open source research hubs? If they have hindered participation is there a way to get around this?
- How could sharing, collaboration and 'working in the open' be incentivized for institutions?
- If a trainee would like to work in the 'open' but their Principal Investigator or supervisor does not, is there a way to get around this?

Openness, sharing and collaboration in the context of the Nucleus collaboration platform

7 - I am hoping that you had a chance to look over and reflect on the Nucleus White Paper that we sent out with this interview guide. Have you already had experience engaging with Nucleus online or based on the White Paper or your prior knowledge of the Nucleus Ecosystem do you plan to utilize Nucleus' offerings in the future ('Distribution' knowledge resources, 'Hub' collaboration platform or 'DevNotes' knowledge sharing)?

- Which offerings are appealing and why? Are there any you would not choose to participate in and why?
- How does Nucleus relate to other open source hubs? What could be done to maximize the benefits of contributing through Nucleus?
    - Nucleus uses a permissive open source licensing scheme building on existing and well-established open source licenses that are appropriate for biotechnology (CERN-OHL-P-2.0; CC-BY-4.0; MIT; and Open MTA). Do these seem fit-for-purpose to you or are there other supports, arrangements or licenses that would facilitate or otherwise encourage you to more freely share data, samples, software, materials, know-how or insights through DevNotes etc.?

- Is there anything you would add that would further inspire trust and optimize your participation in Nucleus?
- Do you have suggestions for a governance structure that could further build community trust in Nucleus?

- How do you think the quality of contributions to Nucleus should be maintained?
- What are your thoughts around ensuring bio-safety with respect to the Nucleus hub?

8 - What do you consider to be the appropriate boundaries of open science in the field of synthetic biology? Why?

- What scientific resources are you/would you be comfortable sharing and under what circumstances? With what limitations or caveats? Why?
  - Are different conditions required for different kinds of data or scientific resources? For example: primary and processed datasets and associated meta data; failed or negative experimental data. Scientific tools/materials: experimental protocols, reagents, cell-lines, primers/genetic sequences, antibodies, cell extracts etc.
- At which stage of the research process would it be appropriate to share these items? (eg. immediately upon collection, after processing, after manuscript submission, upon first publication?). What factors inform your answer?
- What are the attributes of projects that are appropriate to work on in the 'open'. Under what circumstances would you avoid working in the 'open'?
- What are your thoughts about a scenario where Nucleus users would work in a 'semi-open' environment where resources are shared only with a 'closed' smaller group of trusted members?

9 - Have you had any experiences with patents or other intellectual property rights (IPRs) held by others which affected your research? Have you had any experiences patenting (or asserting other IPRs) over your discoveries? Have you ever sought or do you anticipate asserting protections over discoveries, products or services you might derive from open resources (for example from Nucleus)?

- What motivated you to seek IP protection or to use materials or processes subject to IP protection?
- Have you experienced or do you anticipate problems or challenges around the use of IPRs in the synthetic biology field?
- Conversely, what are the benefits to the research process and results?
- Under what circumstances would it be appropriate to forgo/avoid intellectual property protection (like patents)? Under what circumstances would you consider IPRs important to seek? Why?

- Should contributors be able to share patented materials through Nucleus? If so, how do you see this working?
- What do you think is the best way to manage patenting or 'productization' of entities derived from open resources by users? For example should there be recognition or royalties from any profits fed back to the contributor of the base resource or profits fed back into the Nucleus Ecosystem to benefit the community?
- b.next is planning to sell a formulation of the PURE cell-free expression system that corresponds with the open source formulations they are making available through their open source platform. How do you think Nucleus participants would feel if improvements to PURE developed by users and contributed back to the hub were included in the marketed PURE product? How could this be handled fairly?
- What could be done to optimize the experience of users of Nucleus resources?

10 - How could the involvement of firms and industry as contributors or users of the Nucleus Ecosystem best be handled?

- What are the advantages and disadvantages of industry participation in the Nucleus Ecosystem?
- Should industry operate under the same set of requirements and expectations as academic users and contributors? If not, then what scenarios would be preferable?
- How could industry participation be optimized in a way that benefits all of the Nucleus community?
- How could Nucleus best motivate involvement of industry in the Ecosystem?

11 - Imagine there was a physical lab space to support the collaborative development of synthetic cells. For example, it could host 'Research Fellows' who may wish to move projects and discoveries between a Nucleus lab and their home institutional laboratories. How might this best work?

- How could bringing existing knowledge to the Nucleus labs be managed? Could fellows bring an IP protected entity to work on at Nucleus?
- How could management of new discoveries made at Nucleus Labs best function? For example, could a Fellow seek to patent and commercialize something they develop while at Nucleus? Equally, how do you see subsequent collaboration and publication working?

12 - What do you see as the relationship or what should be the boundary between Nucleus and b.next?

Broader research and innovation ecosystem

13 - In your view how well functioning is the research and innovation ecosystem in your country? If there are problems or barriers what are they? What solutions might work best? Could greater openness assist with improving these issues? How could the Nucleus Ecosystem or b.next as a developer and producer of reagents and tools assist? For example, could Nucleus help with mediating more effective interactions between industry and academia?

Please consider from the perspective of:

- Commercialization pathways
- Funding
- Reward and attribution
- Publishing
- Social and environmental justice

Key priorities and additional factors

14 - In your view, having reflected on the policy and practice outlined in the Nucleus White Paper, does this seem fit-for-purpose in facilitating collaboration, discovery and innovation in the synthetic cell field? Are there any key elements you would add or change?

- Are there any issues we haven't yet discussed that could make open science in synthetic biology or Nucleus function better or anything else you would like to mention?

Thank you for participating!

APPENDIX 4: STUDY INTERVIEW GUIDE: TECHNOLOGY TRANSFER PROFESSIONALS

Project: 'Strengthening Open Science in Synthetic Biology: deriving Open Science Principles for b.next from key stakeholders: a qualitative research study'

As noted at the top of Appendix 3 we adopted the more succinct name – 'Assessing Needs of the Synthetic Cell Community for Open Coordination' during writing of this report. We flag that we retain the original study titles in Appendix 3 and 4 as these were used through the research process and are the original documents sent to research participants.

Thank you for taking the time to speak with us today. This study aims to understand how we can best bootstrap the synthetic cell and biology innovation ecosystem by deploying an open source collaborative platform Nucleus, recently launched by b.next out of San Francisco. Greater openness through open source and open science approaches to dissemination of research outputs is one avenue aiming to accelerate discovery and translation to impact. So far in this study we have interviewed researchers working in academic, not-for-profit and governmental settings asking them about their interest and experience working with open source projects – in particular Nucleus. Many spoke about the definitive role that technology transfer offices (TTOs) play in how researchers are able to transfer their technologies to the world. We would like to ask you about your knowledge, experience and perspectives on open source approaches, particularly in the biology/ biotech space.

Please note that question probes or follow-ups are denoted with bullet points.

Demographic and contextual questions:

To begin, I would like to ask you a few quick questions about yourself:

1 - First, what is your job title/position and academic background?

2 - How many years have you been in practice?

On TTOs, open source and open science:

3 - Could you please tell us about the mandate and key goals of your institutional technology transfer office?

- Dissemination of knowledge; securing new sources of revenue for the institution through commercialization; ensuring researchers' outputs are not misused or exploited; raising the profile of the institution and its researchers to attract funding, collaborations and donations etc.?

4 - What do you see as the elements of a highly successful handling/dissemination/ translation of a research artifact from the view of your TTO?

- How do you measure the success of such a technology transfer?
- How successful do you consider current efforts to be?
- Do most outputs that are patented end up being licensed?
- Who do you see as the most important stakeholders in your endeavour and why?

5 - Open science and open source are becoming better known as ways to more rapidly share knowledge, accelerate discovery and innovation, allow for better replication and less duplication of research, and improve the economy of the scientific endeavour. This may also translate into quicker and more cost-effective options for public access when a product is developed. As well, open options offer an alternative business model that in some technology areas may be best suited to energize innovation. How is the awareness of open source and open science in your place of work and in your profession more broadly?

- How do see the difference between open source and open science?
- Do you find there is greater awareness of open approaches in recent times? How so? And if not why not?
- What is your understanding of how greater openness (open source and open science) could work for your institution? What do you see as the opportunities or risks?
- Can you see benefits for your stakeholders through the use of open source and open science avenues to tech transfer?

- How do you regard open source software contributions – how have they challenged or changed existing tech transfer practices? Do your institution and researchers always follow established policy and practice in (open source) software transfer or is there a discrepancy?
- Most examples may be in realm of software but please tell us about any open source biotechnology projects you have encountered? How did you navigate technology transfer? What are key points of difference between the software and the biotech paradigms? Are there transferable lessons learned?
- Please tell us about any open source or open science avenues you may offer to researchers or that you support them in pursuing? Eg. use of the Open MTA, permissive licenses such as the CERN-OHL-P-2.0 or Apache v2, commercialization in the absence of patents/open source business models, sharing to open repositories, placing inventions in the public domain etc.
- How do you help researchers decide what is the best approach to take in handling their outputs?
- Do you have public health, ethics or public benefit concessions in your technology transfer framework? Could you see these be deployed in navigating open source avenues?
- What are the key barriers to greater deployment of open source avenues?
- How do the requirements of the Bayh-Dole Act segue with open science and open source approaches?

6 - How does your office set its priorities and goals? How responsive are these to changes in the research and innovation landscape (government policy; funder requirements; what other institutions are doing; shifting cultural, societal or ethical norms and citizen expectations?).

- Have these goals and priorities shifted in response to there being an increase in open source projects?
- What incentives or different metrics could be deployed to encourage greater openness in technology transfer?
- Are open source approaches considered a viable tech transfer mechanism and if not, what kind of examples or demonstrations would be considered convincing?

7 - Have you come across Nucleus – an open source platform to enable the collaborative development of synthetic cells. We have also sent you a White Paper detailing the project which we hope you had a chance to take a quick look at.

- Do you have any feedback about this open source model?
- How comfortable would your office be in allowing researchers to contribute research outputs to the Nucleus repository?

- How comfortable would your office be in releasing patented research artifacts to Nucleus under a permissive license such as the CERN-OHL-P-2.0 or the Apache v2 that grant royalty-free, non-exclusive license to use the patented material to licensees? If you are not comfortable with such licenses what would be the key objections?

8 - Does your institution take measures to educate or highlight the concept of greater openness to researchers?

- Is your institution interested in knowing more about how greater openness could work for you and your community?
- What do you see as the best way to generate this knowledge or get this education? What is needed or who needs to bring their expertise?
- Some institutions have founded 'Open Source Program Offices' (OSPOs). What are your thoughts on these?
- What is the role of researcher funders and foundations in encouraging open science at your institutions and more broadly?

9 - Are there any issues we haven't yet discussed that could make open science in synthetic biology or Nucleus function better or anything else you would like to mention?

Thank you very much for participating!

APPENDIX 5: CODING AND ANALYTICAL CATEGORIES

Please note that as per our research ethics board (REB) commitment to protecting the confidentiality of participants we have included only the names of the major categories in the 'Miscellaneous background and demographics' theme of the coding framework. This is because some categories and sub-categories include the names of specific projects, institutions and researcher names that could allow for identification of interviewees.

Substantive themes:

1 - Opinions on patenting

- Concerns or drawbacks of patenting
- Positive effects or advantages of patenting
- Researchers' opinions and choices around patenting
- Alternative pathways to impact beyond patents

2 - Collaboration

- Importance of collaboration to researcher practice
- Importance of licenses, agreements and NDAs
- Importance of personal connections for building trust
- Importance of funding or shared funding
- Importance of shared goals
- Timing of sharing
- Types of collaboration
- Ways to share
- What collaboration involves

3 - Cultural or attitude aspects of openness and closed-ness

- Differing attitude to patenting in the US vs EU
- Comparisons between software and biotech Open Source
- Importance of responsible and ethical synthetic biologists

- Need for a cultural change to optimize sharing
- Research or institution leader or PI sets sharing culture
- Synthetic cell research and sharing culture

4 - Current sharing practice

- Definitions or understandings of open science and open source
- Does not participate in open sharing beyond std publication
- Does not share data
- Does not use the OpenMTA
- Has not patented anything
- Methodology and protocols easier to share
- Researcher has filed for patents or plans to
- Researcher side-stepping TTO to patent individually
- Researcher side-stepping TTO to share or access
- The default is to make things public
- The default is to patent
- We share almost everything
- Would not share commercially valuable knowledge to Nucleus

5 - Disincentives or challenges to sharing or open science

- Biosafety concerns
- Potential for mis-use of shared materials/knowledge
- Cost and logistics etc. challenges of sharing materials to distant locations
- Ensuring what is shared is meaningful, useful and validated
- In-person sharing is needed for optimal knowledge transfer
- MTAs and legal agreements
- National security concerns
- Need for staff to manage sharing
- Others may not reciprocate/ free-loaders
- Researcher time and money invested in resource creation
- Tension between open sharing and patenting
- Time and cost burden of sharing outputs
- Concerns about protecting competitive advantage
- Concerns about scooping

- Discomfort about breaking new ground to openly share

6 - Incentives and advantages to open science

- Importance of incentives to make sharing worth it
- Importance of a shared framework or set of expectations
- Incentives for institutions to participate in OS
- Motivations to share or go open
    - Academic credit and DOIs
    - Academic or ethical sharing ethos
    - Importance of sharing negative results
    - Improving scientific reproducibility, dissemination and impact
    - Increased prestige visibility and professional reward
    - Metrics for open science
    - More collaborations, community and connections
    - Personal reasons for doing open work
    - Sharing during research process can improve outcomes
    - Sharing mandated by funder
    - Sharing to repository for efficiency

7 - Concerns and opinions about b.next and their activities

- Researchers' relationship or history with b.next and use of Nucleus
- Positive sentiment toward Nucleus/b.next
- Perceived problems with Nucleus/b.next
- Limited understanding or familiarity with b.next/Nucleus
- Concerns about b.next being for-profit
- Attitude to patenting of derivatives of shared resources (permissive/ negative)
- Commercial entities will take advantage of openness
- DevNotes
- Fellows or students visiting b.next
- Needs to attain critical mass
- Industry involvement in Nucleus

8 - Requirements to encourage participation in Nucleus

- Building trust and encouraging participation

- Importance of a governance structure
- Importance of transparency and clear rules of engagement

- How b.next could give back or be profitable
  - b.next potential commercialization plan
  - benefit-sharing from commercialization
- Roles for b.next in improving the R&I system
  - Developing case studies and evidence around OS pathways
  - Education for TTOs and researchers around risks and benefits of OS pathways
  - In lab training modules for researchers
  - Instil system of meaningful metrics to encourage openness
  - Platform for discission of IP and OS pathways to impact
  - Prize or competition incentive
  - Prototyping new model and changing the culture
  - Quarterback multi-disciplinary conversation around OS pathways
  - Raising the profile of syn cell research and its promise
  - Quarterback setting of standards and the maintenance and QC of reagents and materials
  - Start-up support for syn cells
  - Research funding and student fellowships
  - Supplier or syn cells or PURE
  - Support of Build-a-Cell

9 - Opinions about the current research and innovation system

- Govt and funder policy for OS is supportive (UK)
- Growing interest in alternative funding beyond public grants
- Increased uni partnership with industry
- Innovation and commercialization is working well (US)
- Narrow focus on patents as the only path to impact
- Reproducibility of science concerns
- Research funding challenges
- Uncertainty about the productization of syn cells
- VC or start-up challenges

10 - Societal or scientific challenges for the synthetic cell field

- Importance of societal engagement with syn cells and their promise
- Integration and standards problem
- Lack of connectivity and coordination between researchers
- Need for deep intellectual inquiry into what is meaningful to measure
- Scientific challenges

11 - TTO Policy and practice

- Goals, stakeholders and measures of success
  - Metrics for impact and success
  - Stakeholders for TTO practice and outcomes
  - TTO role is to capture the value of researchers work
  - TTOs offering start-up support
- Implications of Bayh-Dole for OS practice
  - Federal funding should not go to directly benefit for-profit companies
- Licensing strategies and differential access
  - Academic vs commercial licensing
  - Diligence licensing for the public good
  - Non-exclusive licensing
  - Public domain licenses
- TTO Miscellaneous stats and history
- Researcher side-stepping TTO to share or access
- Researcher side-stepping TTO to patent individually
- TTO policy and practice around patenting and MTAs
  - Ownership of IP made by researchers
  - TTOs are there to partner and assist researchers
  - Differing attitude toward patenting across TTOs
  - TTOs patent pre-emptively without a licensee lined up
  - TTOs are selective about what they will patent
  - TTOs more stringent with material transfers
- TTOs understanding and acceptance of Open Source
  - TTO discomfort with open source licensing and the Open MTA
  - TTO acceptance or understanding of Open Source and open science

Auxiliary themes

1 - Companies and policy

- Lack of commercial companies in syn cell field
- Open source companies or non-profits
- Opinions on the kinds of technology patentable in syn cell field
- Policy or funders mentioned
- Syn cell companies

2 - Miscellaneous background and demographics

- Fields of research, labs, research organisms, meetings and projects
  - Organisms and labs
  - Organizations and meetings
  - Researcher fields of practice
  - Misc people, tech and projects
  - Professional position of participant
  - Researcher background
  - Time in practice

3 - NVivo codes and interesting quotes

- Free riders are part of the scenario
- I wouldn't begrudge them making money
- Pragmatic openness
- Sharing kills your IP
- Slow science is good science
- We IP everything

4 - Suggestions for additional interviewees

5 - Value of/ interest in this b.next study