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Research proposal [Part B2]

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Nano bubbles: how, when and why does science fail to correct itself?

Section a. State-of-the-art and objectives

a1. Overview and overall objective.

NanoBubbles investigates how occurrences of error and overstretched claims in research persist despite substantial contrary evidence. Three issues from nanobiology will be scrutinised to deepen our understanding of the social, cognitive and communicative processes that can prevent self-correction of science. These three cases involve widespread beliefs that inform considerable research efforts and public support, but that rest on disproven findings or overreaching assertions. The first involves the claim, originally made in a 1995 article,[1] that nanoparticles can uniquely cross the blood-brain barrier. Thousands of articles and reviews over 25 years followed, frequently linking this claim to the promise of new drug delivery strategies; yet translation remains distant and the proportion of particles reaching the brain (often not measured) is at best very small. The second case concerns the claim that the discovery of protein adsorption on nanoparticles, successfully dubbed the 'protein corona',[2] constitutes a paradigm change, when in fact research into protein adsorption on colloids predates the field of nanobiology by several decades. The third case concerns the highly-cited claim that nanoparticles harbour both great potential and risk because they can penetrate the cell membrane;[3] this claim was refuted in 2007.[4] All three claims persist widely and durably, even though objecting researchers have laboriously drawn attention to the refutations described above. These 'bubbles' raise uncomfortable questions about the behaviour of nanoparticles, but also about the conduct and organisation of scientists. All three bubbles are so entrenched that nanobiology research on these topics cannot advance without complementary humanities, social science, and informatics research showing how error is propagated; nor can nanobiologists advance their science without reflecting on error (non)correction. The NanoBubbles project aims to remove those barriers.

That researchers sometimes disregard contrary evidence was already observed by historian and philosopher of science Thomas Kuhn in 1962. For Kuhn, 'anomalies' accumulate without significantly undermining a paradigm because the paradigm that generated them is still otherwise productive. Only when anomalies become too prominent to ignore is a paradigm replaced. However, the current 'replication crisis' in many disciplines goes well beyond temporary neglect of anomalies characteristic of Kuhnian 'normal' research. Scientists and their publics are currently uncertain about the sciences' ability to acknowledge widespread error or even outright fraud. A fundamental reflection and reassessment of the organisation and practices of research has started, ranging from questions about the reliability of methods and research materials, to flaws in scientific communication and publishing, to dysfunctional systems of research evaluation and funding.

The currently dominant response (by critical scientists or in much of the 'meta-science' movement) is to address concerns about scientific error with stricter procedures that are meant to increase methodological rigour, improve statistics, or tighten publication standards. This research project asks the questions about deeper causes that should *precede* such solutions: we will investigate the dynamics that prevent or discourage self-correction in the first place. Rather than only insisting on stricter procedures, we investigate how self-correction processes falter, in spite of scientists' foundational commitment to self-correction as a guarantor of scientific progress. Through a rich and detailed study of three 'bubbles' in nanobiology, we will identify and challenge patterns in social interaction, in argumentation and in communication that reproduce error and overpromising and discourage error correction.

Drawing on the conceptual resources of Science and Technology Studies (STS) and innovative digital methods in scientometrics and text analysis, we will identify the processes that spread and reproduce error and create bubbles, and investigate new communication processes and tools to facilitate error correction. The combination of social science and humanities approaches in STS with digital methods from informatics is itself innovative; but NanoBubbles achieves even greater synergy by bringing critical nanobiologists fully into the collaboration, both in analysis of error (non)correction practices *and* in interventions to improve those practices. Our project will study how controversial claims in nanobiology originate, rise to prominence and are challenged in scientific debate, both in the past and present; and it examines the consequences of challenges that project members themselves will pose to the nanobiology community. Thus, NanoBubbles uniquely blends STS investigations and nanobiologist's attempts at error correction. The latter includes the first replication project in nanoscience, and one of the first replication projects fully embedded in a social science project. It also includes a ground-breaking attempt to systematically annotate the scientific literature (using Hypothes.is and PubPeer). We examine formal and informal scientific communications to understand how challenges to previous findings were and are received by the nanobiology community. These interwoven arms of the project cannot be carried out by separate disciplines, but rather emerge from intense cooperation among scholars from natural sciences (Lévy), informatics (Labbé) and STS (Mody, Halffman). The PIs will cooperatively supervise PhDs, postdocs and engineers, and work with senior staff who bring specific expertise to the project, including in philosophy of science, science ethics, and digital methods (Erden, Bordignon, Noël, Cabanac, Portet).

Our objective is to understand how, when and why science fails to correct itself, taking the three issues described above both as research fields (to which we also contribute) and as objects of study representative of other 'hot' interdisciplinary fields that experience sudden growth and massive investment (e.g. artificial intelligence, synthetic biology, etc). With this project, NanoBubbles will not only push the boundaries of each of the disciplines mentioned above, it also has the potential to inform policy and practices to improve the scientific enterprise.

a2. State-of-the-art and specific objectives

a2.1 Science and technology studies: controversy and agnotology.

In the 1970s, a new field of science and technology studies (STS) emerged, combining history, sociology, philosophy, anthropology, and other disciplines. Though STS has evolved in many directions, one early and still influential aim was to understand scientific knowledge-making as a social practice, without explaining incorrect knowledge differently than true knowledge, the so-called 'symmetry principle'.[5] This aim led to two novel approaches: 'controversy studies'[6] (historical and sociological studies of disagreements over scientific knowledge) and 'laboratory studies'[7] (historical and ethnographic accounts of social and embodied practices in laboratory settings). These approaches stimulated several fundamental insights, such as that scientists rely on 'tacit knowledge': knowledge that cannot be entirely put into words, but must be transferred by learning embodied skills face-to-face in order to reproduce experiments. Hence, scientists rely on social cues (not just on logic or textual description) to collectively determine whether experiments have worked and therefore whether experimental claims are correct. Those social cues are derived from the values and relationships of the society in which science is embedded. Thus, science's social dimension is made apparent by studying controversies, i.e., sites where scientists disagree as to whether particular experimental claims are correct.

STS scholars now instinctively search for controversial episodes in science, where the actors deconstruct each other's claims with reference to social processes. Since the early 2000s, however, controversy studies has moved away from the 'symmetry principle' that correct and incorrect knowledge should be explained in the same way. Attacks on climate researchers and other scientists by bad-faith actors – i.e., people, firms and think tanks that are not actually committed to the truth of the claims they make – make the symmetry principle morally suspect.[8] One strategy for replacing it has been to assert that STS has the expertise to identify whose claims are robust and whose are not.[9] Another has been to study the deliberate creation of scientific ignorance and misconception, rather than knowledge – an approach known as 'agnotology'.[10]

Agnotology studies are particularly salient for this project: e.g., European men erasing scientific knowledge produced by and about women and indigenous peoples,[11] cigarette companies creating doubt about knowledge of cancer,[12] or pressure from polluters leading to 'undone science.'[13] In recent years, agnotology research has led STS, both intellectually and in the public sphere.[14] *However, while agnotology offers new tools for understanding why and how some scientists and firms promote error, it has not fully investigated how scientists and scientific institutions facilitate the propagation of error and over-stretched claims, nor the practices and effects of the concerned scientists who seek to correct error. Our project will provide a deeper understanding of agnotology and identify processes that hamper correction, in order to facilitate improved scientific communication and deliberation.*

a2.2 Science and technology studies: conferences.

The other branch of STS, rooted in the 1970s ethnographic studies of laboratories, has become increasingly diffuse over time. Few ethnographies today are confined to the laboratory, but instead examine the field sciences,[15] citizen science,[16] or science in the courtroom[17] and other domains far from the lab.[18] Lab studies today include multi-species ethnographies in which interactions among human scientists are no longer the main focus.[19,20] Historical studies that aim for an ethnographic level of thick description do still frequently centre on the laboratory, but always situated in a larger social context populated mostly by non-scientists.[21,22]

This evolution in laboratory studies has offered a clearer understanding of how scientists are part of, and gain legitimacy from, society. However, it draws away attention from arenas of practice and communication *among scientists*. Clearly, scientists are 'co-present' in many places, not just the laboratory.[23] Agnotological processes operate through broad networks of scientific communication and exchange, some of which include or acknowledge societal actors (such as funder expectations of social impact). However, much communication among scientists is still confined to specialist forums. We will expand the laboratory studies approach not by looking beyond interactions among scientists, but by looking to specialist interactions beyond the laboratory. We propose a 'multi-sited'[24,25] ethnography and historical study that examines the variety of arenas – laboratories, journals, conferences, etc. – that are largely populated by scientists interacting with each other.

Of these, conference studies is a particularly fast-growing but still immature subfield where this project will make a major contribution. Despite STS' concern for the social construction of scientific knowledge, the places where scientists are at their most social with each other – conferences – have received limited attention. A few older studies looked at how scientists prepare for conferences,[26] and how conferences seed new fields.[27,28] *We know little about conferences as sites of embodied practice, interaction and knowledge construction, especially in the creation and reproduction of bubble claims. STS studies of conferences are slowly becoming more common, with a large cluster at Maastricht University.[29–33] Conference studies in STS also take advantage of related innovations in other fields, such as the emergence of 'meeting ethnography'[34] and scientometric research into social media*.[35]

In nanobiology, conferences have been a crucial site for debate over bubble claims, often in parallel with debates on social media (Twitter, Reddit). Whereas conflicting evidence in the literature may be ignored or simply listed without consequence, opposing claims about nanobiology are raised in a personalised manner at conferences, both in the 'front-stage' of presentations and discussion and in the 'back-stage' of conversations at dinners and coffee breaks. Examples include the debate "Nanotechnology is more hype than hope" at the 2016 World Biomaterials Congress (mentioned by Christine Allen[36]), the heated encounter between Raphaël Lévy and Chad Mirkin at the 2018 American Chemical Society meeting,[37] and the "Stars Collide Debate: Big-vs. Nano-Progress" at the Controlled Release Society's 2019 Annual Meeting.[38] *A systematic understanding of how communication at and around conferences occurs and whether conferences reinforce dominant conceptions in nanobiology will help show how they contribute to the reproduction or questioning of bubble claims. With this investigation, our project will lay the groundwork for improved conference deliberation processes.*

a2.3 Science and technology studies: scientific publishing

In addition to the laboratory and conferences, scientific publishing (journals in particular) provides a crucial arena for scientific debate, including in nanobiology. We consider journals as aggregates of ideas and functions located within the broader landscape of institutions and media that make up the social world of scientific practitioners. Journals have never been a passive vessel, but are rather sites where the rules of science themselves are debated and developed. The journal is both a set of copies and a 'collection' of articles, a material object (even when digital) with a prescribed format and number of pages or words imposed, and also a social organization or institution that creates that object. Journals also participate in a knowledge economy: they are purchased by university libraries and public and private R&D centres. There is therefore a large market for these publications, made up of several thousand well-resourced buyers. Journals are businesses and business considerations may prevent them from correcting errors as much as they should. They are also periodicals governed by their publishers' requirements and deadlines.

The contingency of the journal as a communication channel is especially clear in historical perspective. While scientific journals have acquired an essential status in contemporary scientific life, this was not always the case. At the end of the 18th century, elite academies and learned societies dominated the study of the natural world. Academic journals were relatively marginal, and sometimes even objects of suspicion. The journal was not a natural solution to the problem of communicating scientific discoveries. Rather, its domination is, as Alex Csiszar shows,[39] a hard-won compromise, born of political and trade demands, changing epistemic values, and debates about intellectual property. Many of the problems and tensions that affect scientific publishing today, Csiszar argues, are rooted in this long and complex historical process of compromise that continues into the present. In particular, *Nature*, as Melinda Baldwin demonstrates, has helped define what science is and what it means to be a scientist through editors-in-chief who are more than mere gatekeepers.[40]

Today, the journal, as it has come down to us through the accumulation and sedimentation of history, is both a gigantic publication infrastructure and a communication system that is increasingly questioned. New business models (such as Open Access) are emerging. Challenges are coming from alternative publication formats such as preprint servers, PubPeer and post-publication annotation, while new editorial procedures are tried out in specific niches.[41] While in most research fields journal articles remain tokens of recognition and achievement, they are becoming less exclusively the locus of written communication. In nanobiology too, understanding communication patterns and their role in the reproduction of error and over-stretched claims requires an analysis of how its journals have developed, how they respond to error, error correction and bubbles, and how they relate to new forms of debate and knowledge expression. *Our analysis will provide deeper understanding of how shifts in scientific publishing relate to the content and spread of controversial claims. Our findings will thereby help the emergence of improved communication platforms, in the form of journals and beyond.*

a2.4 Science and technology studies and meta-science: the sociology of error and promise

A fast-growing body of scholarship documents error and problematic research by combining quantitative and qualitative approaches. In response to the 'replication crisis' and concerns over research integrity and insufficient self-correction in research, the newly emerging field of 'meta-science' studies the spread of questionable research practices,[42–44] problems with statistics, and individual misconduct cases.[45] Meta science researchers tend to insist on stricter methods, tighter research guidelines, and increased transparency.

While such research has contributed considerably to our understanding of the incidence of problematic research, it is relatively disconnected from the conceptual understanding forged over many years in the STS tradition. In particular, STS sensitises us to the organisational context of research, to science as a social and human activity where authority, rhetoric, and trust, but also cost-cutting and politicking help determine what counts as knowledge. This redirects the focus from individual misconduct or sloppiness to collective processes to explain the persistence of error and failures of self-correction.

To understand (failed) error correction we need to examine the work setting of scientists in research organisations,[46,47] including power relations,[48] and productivist research conditions.[49] It is typically in the organisation that the tangle of social processes involving careers, hierarchies, funding and resources becomes concrete, including research organisations, university departments, journals, and professional societies and their conferences. The potential to address error or investigate problematic assumptions requires organisational conditions conducive to debate and reflection.[50] These topics were blazed by PI Halffman's PRINTEGER project (Promoting Integrity as an Integral Dimension of Excellence in Research, H2020 2015-18). Halffman's group is currently investigating failing validation of antibodies, circulation of misidentified research materials and the effects of journal guidelines on scientific quality.[51,52]

In contrast to most meta-science research, STS research starts from the observation that research operates in a variety of epistemic cultures,[53] with subtle differences in standards of evidence and appreciation of what counts as proof of validity. Especially in heated, multidisciplinary fields such as nano research, the interaction of a diverse range of research communities involves complex forms of uncertainty about scientific evidence, not only about which facts are correct, but also about which facts are relevant and about how they are salient (incongruous 'framing'[54]).

In nano research, uncertainty has been aggravated by breath-taking promises about expected scientific breakthroughs and technological potential. The 'generative' logic of technological promising has been analysed in earlier STS work, in particular for 'hard' nanotechnology.[55,56] As Van Lente points out, expectations about technological futures become performative, translating into incitements to pursue specific avenues of research or innovation ("this technology can…", "therefore we must…") so as to convince funders and investors[57] and obscure the risk of hype-disappointment cycles.[58] Anticipatory practices such as roadmapping, high-visibility publications and well-pitched success stories help create large-scale initiatives, such as the EU graphene flagship.[55] From the perspective of this 'sociology of expectations'[59], it is particularly interesting that claims about nano's potential are increasingly challenged from within nanobiology itself, raising interesting questions about how promises and hypes end, or are adjusted and corrected. Our research builds on work in STS analysing technological promises, asymmetric benefits,[60] (potential) risks, and the ethics of nanotechnology.[61] We also build on examples of citizen involvement in deliberation of these issues.[62]

The meta-science movement is justly proud to involve collaboration between social scientists and critical natural scientists. Such collaborations have a long history in STS too, for example in Harry Collins' critical engagement in the gravitation wave debate.[63] In controversial practices, under conditions of uncertainty, with opposing frames and varying standards of proof, the validity of factual claims cannot be restored merely with stricter research standards, but requires deeper deliberation. Such deliberation needs to account for the social nature of research, including where this deviates from ideal rational argumentation.

Using the nano bubbles identified in this project, our project will examine how concerns for correction or validation of research claims come together for researchers and research teams. Our objective is to investigate how the experiment, the lab, the research field and its wider funding and support network[64] interact in the reproduction of scientific error or over-stretched claims, and of nanobubbles in particular. While building on STS and metascience traditions, we break new ground by conducting both historical and real-time participant-observation studies – alongside critical nanoscientists – of how, when, and why replications of claims are attempted and (non)replications are challenged.

a2.5 Digital methods, including scientometrics and text analysis

Developments in scientometrics and text analysis offer exciting tools for analysing scientific debate, including error and correction. Specifically, these techniques can track scientific claims through large corpuses of communication, reaching beyond traditional journal articles. Meta-data (authors, citations, institutions) are now widely available and machine-readable, allowing even country-level scientometrics studies.[65] The next step beyond citation counting is to understand *why* a scientific paper is cited: to back up a claim, to point out a different problem, to explain a methodological point or, more rarely, to disagree with a claim (as reviewed by Tahamtan and Bornmann).[66] New tools are becoming available to classify citations based on context. For example, scite.ai classifies citations into three groups: mentioning, contradicting and supporting; negative citations are rare (less than 5%).[67] Citation studies also show that retraction or correction has almost no effect on citation counts.[68] These studies are early examples showing how scientometrics can provide system-wide insights into correction mechanisms (or their absence).

While there are many scientometric studies of nanobiology,[69–72] they concentrate on the interdisciplinary character and definition of emerging nanoscience. Classical information retrieval (often via on-line platforms) includes collection of a set of articles covering the discussed concepts, which are later combined with advanced visualization, network analysis and clustering tools. For example, CorText can analyse digital traces for detection of emerging domains of research, controversy analysis, mapping of publications, patents, and projects and social web analysis on scientific trends and dissemination (https://www.cortext.net/). Gargantext (https://gargantext.org/) helped analyze tweets and blog posts about the Plan S controversy.[73]

Since the automatic detection of meaningless scientific papers by Labbé and Labbé,[74] a family of new tools are emerging: the content of scientific publications is automatically screened to detect non-trustable or odd results. These semi-automatic approaches include: image analysis,[75] detection of flawed p-value[76], the Halffman team's tracing of misidentified research materials,[51] and identification of incorrect description and use of nucleotide sequence-based reagents by Labbé et al.[77] The latter employs natural language understanding to extract a claimed fact that can be checked against endorsed knowledge (using the blastn software). This approach can be seen as a knowledge-based (opposed to style-based, stance-based, propagation-based) fake news detection method,[78] taking scientometrics into a new, knowledge-critical direction.

Blog posts and comments are also a rich source of information regarding the diffusion or detection of errors in the literature. The concept of web-annotation,[79] with explicit machine-readable links between annotations and the annotated web documents, is emerging as an important approach to comment directly within the text of scientific publications.[80] In Nanobiology, Lévy has been pioneering these non-conventional approaches to science communication via a blog, Twitter, PubPeer and Hypothes.is annotations (Figure 1).

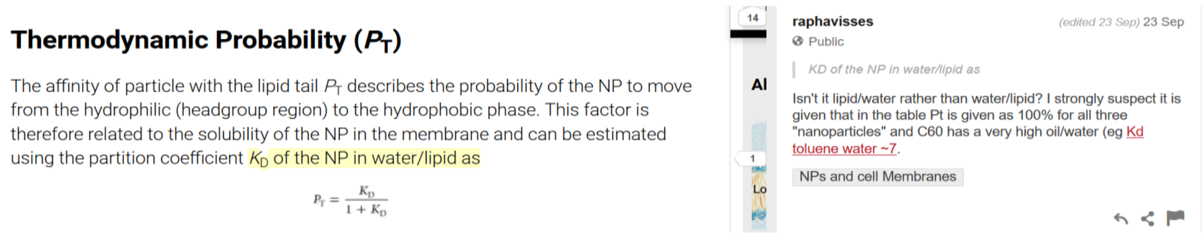


Figure 1: Example of an in-text annotation using Hypothes.is on an ACS Nano article about nanoparticle entry into cells.[81] "NPs and cell Membranes" is a tag. Link to the annotation: https://hyp.is/WLaw_t4OEemqm5eC5lBG5w/pubs.acs.org/doi/10.1021/acsnano.9b03434

Automatic citations analysis between scientific documents have proved useful but the new challenge is to build tools that enable organising and analysing the rich and rapidly evolving ecology of such online comments outside of well-established scientific records (tweets, web annotations, blogs, comments, PubPeer, Reddit, etc…). This means not only counting references to a document (cf. altmetrics[82]) but also assessing and leveraging the content of both cited and citing document.

Although these tools were developed independently of any sociological theory, they are now being harnessed by researchers (sociologists and non-sociologists alike) to produce knowledge of the social domain exploiting the massive volume of textual materials available.[83,84] These researchers work closely with computer scientists to elaborate on existing tools (natural language processing, clustering, network analysis, agent-based modelling, word embedding etc.) that are not common in sociology.[85–90] These methods offer the opportunity to identify strategies of individuals and organizations through analysis of diverse textual corpuses that go beyond journal communications to include social media and web-annotated documents.

We will develop tools to establish a corpus of nanobiology communication as a basic reference database for the project. From this corpus we can observe the circulation of nanobio claims, enabling closer qualitative study of crucial episodes. By combining digital and qualitative methods we then arrive at a socially thick understanding of how and where correction occurs. Our new digital tools will also help detect disagreement and promote post-publication discussions on forums in which critical nanobiologists participate.

a2.6 Nanobiology

NanoBubbles focuses on three contested issues in nanobiology briefly introduced below:

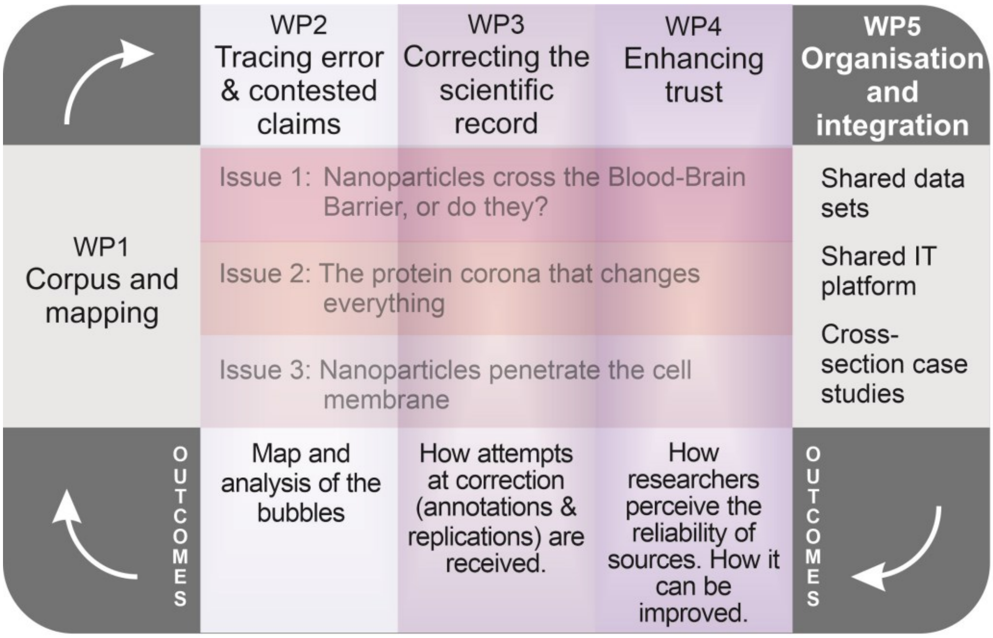
- **Issue 1: Nanoparticles cross the Blood-Brain Barrier, or do they?** The belief that nanoparticles are small enough to easily cross the blood-brain barrier is widespread, e.g. in scientific articles,[91–94] Wikipedia,[95] the general press and newspapers. It is the source of both hopes (for therapies) and concerns (about toxicity). Yet studies of blood-brain barrier physiology that predate the nano period show that only small hydrophobic molecules (i.e. much smaller than nanoparticles) can cross the blood brain barrier,[96,97] and also describe transport of proteins (and protein conjugates) via transcytosis.[98] A highly cited 1995 article[1] reporting nanoparticle-powered delivery of a therapeutic peptide to the brain marked the beginning of two decades of excitement, investment, and thousands of further studies. But 25 years later, translation remains distant[99] and the advantage of using nanoparticles (rather than other formulations) for drug delivery to the brain remain unclear.[100]
- **Issue 2: The protein corona that changes everything**. In 2007, Cederval et al introduced the expression "protein corona" to describe adsorption of proteins on nanoparticles[2] (over 2,000 citations). The introduction of this expression had a large and enduring impact: thousands of studies of the "protein corona" (continuing at a rapid pace). Yet, that very phenomenon had been a topic of research for decades (i.e., well before the emergence of nanobio) using different words: protein (or polymer) adsorption on colloids. The protein corona offers a lens onto practices few scientists find problematic (adopting fashionable terminology) yet which aid in the forgetting of past knowledge and may foster an embrace of misleading claims that hinders correction of more serious errors.
- **Issue 3: Nanoparticles penetrate the cell membrane.** An extremely highly cited (8,000 citations according to Google Scholar) review from 2006 claims that *some nanoparticles readily travel throughout the body, deposit in target organs, penetrate cell membranes* […].[3] This review is cited in key policy reports, e.g. UK Parliament[101] and Government[102], EU commission[103], US National Academy of Science[104] and the World Health Organization[105]. The claim made it to popular culture and is influencing emerging discussions of the risks of "nanoplastics".[106] It is also the basis for numerous research projects, e.g., in

computer modelling of nanoparticle movement across cell membranes. The 2006 review provided one reference for the claim that nanoparticles could cross cell membranes[107] (1230 citations). In 2007, Banerji and Hayes unambiguously demonstrated that the same nanoparticles did not diffuse through membranes[4]. However, that article garnered only 64 citations. Lévy published several articles on the interaction and fate of nanoparticles in living cells,[108–111] and his debut as a critical voice was when he challenged the evidence for "stripy nanoparticles"[112,113] which were claimed to have a special capacity to cross the cell membrane.[114–116] It has been known for more than 50 years that nanoparticles can enter cells, but not by penetrating the cell membrane. Instead, they enter by endocytosis, a process resulting in their entrapment in compartments inside the cell (endosomes) where they are isolated from the cell machinery. For this reason, Lévy also later questioned[37,117–119] the claimed detection of intracellular events with nanoparticles probes (reported in many high-profile articles).

Longstanding concerns about nano hype,[120–125] the slow translation of nano research into biomedical applications,[120,126] and lack of reproducibility in nanobiology research[127] show few signs of ameliorating. How much of the scientific record provides a solid foundation (the famous shoulders of giants) on which we can confidently build? How can we equip scientists, in particular younger scientists or those moving into highly interdisciplinary fields such as nanobiology, to make judgements about the validity of articles and claims? How, as a community of scientists, do we progress towards a shared understanding of contested issues? In this project we address these critically important questions via the STS and digital sciences approaches described above but also through two direct interventions: a) post-publication peer review and systematic public annotation of a large number of articles (issues 1-3), and, b) a replication project to experimentally test published claims (issue 3).

Section b. Methodology

b1. Work packages



The project is organised in five closely connected work packages, each involving all the PIs to guarantee maximum synergy. WP1 creates a corpus of sources mapping nanobiology and its community, on which WP2-4 can build their analysis. WP2 traces error and controversial claims in nanobiology over time. WP3 analyses attempts at correction and includes actual attempts at correction and improved communication to discourage error propagation and encourage correction in the future. WP4 analyses processes that impede or facilitate correction and investigates how scientists trust research results, as well as how this trust can be enhanced. A fifth work package is devoted to project organisation and integration. Each work package has ambitious objectives that require the synergy of research methods and disciplines brought together by the PIs and their teams. Whilst work packages have deliberately *not* been divided between PIs (to ensure that the project remains interdisciplinary and highly collaborative throughout), they have a WP lead whose role is to stimulate, monitor and report on progress. Below, we first describe each work package (sections b1.1 to b1.5), the methods that they draw upon (section b2), then the synergies and outcomes (section b3, reproduced from the extended synopsis B1), and finally present a simplified Gantt chart (section b4).

b1.1 Corpus and mapping (WP1) [lead PI: Cyril Labbé]

Shared IT platform. We will establish a shared IT platform providing support for data use and analysis, including for non-specialist project members. To empower synergies among the teams, the platform will:

- Assure the usability by non-IT specialists of advanced software developed by computer scientists,
- Foster harmonization, common usage and practices regarding concepts, datasets and procedures,
- Develop and curate the data management plan.

The platform team will be composed of two engineers with complementary skills (software development and digital humanities) under the supervision of Cyril Labbé and team member Frédérique Bordignon. The platform will provide access to a range of tools, from digital procedures that are relatively standard (for instance parsing or scraping tools, geolocalization or spatial activities, customized needs, etc.) to frontier research in computing sciences. The platform will define an explicit common vocabulary, particularly for nanobiosciences and technologies concepts. The team will coordinate the building of an ontology, co-elaborated with all PIs and their teams, to provide a hierarchy of concepts and define their semantic relations. This will facilitate many aspects of the project, particularly retrieval of articles and constitution of corpuses for scientometric studies, and for textual material analyses (evolution of concepts with natural language processing tools, discourse analysis and argumentative patterns recognition, tagging of interviews). A data management plan will be written as soon as the project starts and will be regularly updated. It will include information about what kinds of data are collected, processed and generated, what standards should be applied -if they exist-, and how and when they will be made available for reuse. The data management plan will be guided by the kinds of data generated in all the work packages; some of these, such as field observations (including visuals) and interviews, are not easily documented within widely-used protocols developed for quantitative data and will therefore require particular attention.

Shared data set. We will establish a shared data set that brings together texts, arguments, events, and the nanobio community relevant for the analyses in WP2-4. This will be both a foundation for the project and an evolving resource that will be progressively enriched throughout the project, creating synergy around data in NanoBubbles. This reference library will allow more detailed studies, in close collaboration between digital methods (scientometrics, textual analysis) and qualitative research (case studies, interviews, historical work, ethnography of conferences and scientific communication), in collaboration with critical nanobiologists.

The shared data sets include:

- A corpus of texts, ranging from research journals, to repositories, conference papers, social media communications and media publications (newspapers, magazines).
- An identification of key communication channels, including an overview of conferences, journals, social media, funding agencies.
- A set of key scientists and researchers in crucial positions, such as editors.
- An inventory of key terms, concepts, preparing further lexicographic work.
- Preparatory work for the annotation and replication projects.

<u>Main outcomes and synergies</u>: WP1 is highly collaborative. It draws on the expertise of all teams to build a shared vocabulary, tools, data sets and a data management plan that ensure synergy throughout the project.

<u>Risk assessment:</u> Given the PIs' different backgrounds, building a corpus and common language may be difficult and converge too slowly. This risk is handled by allocating particularly skilled human resources to this task (two engineers and a philosopher of language, Yasemin J Erden). Previous collaboration between team members will also help. Adopting an incremental and highly adaptive approach will allow a quick start and assure reactivity.

b1.2 Tracing error and contested claims (WP2) [lead PI: Cyrus Mody]

Using the corpus of data collected in WP1, this WP combines digital and qualitative methods to trace and analyse controversial claims and counter-claims. This multi-method analysis will investigate key arenas[57] of formal and informal scientific communication (including journals, conferences and social media), and their connections to research policy and wider media. Specific tasks are:

- Citation analysis, including a study of negative citation: an identification of landmark papers in nanobiology at the source of controversial claims, and following how these claims were cited. This task will elaborate novel methodologies that goes beyond citations positive vs negative citation.
- Case studies of controversial claims in nanobio based on qualitative interviews of key actors, informed by the citation analysis: deepening and triangulating the scientometric analysis, key scientists will be interviewed to assess how claims have spread and been received by the community. The qualitative study will elaborate on earlier patterns identified in nanotechnology.[55,56,58]
- A detailed study of crucial conferences in nanobio: analysis of how claims are presented and move between conferences and textual formats such as journals or social media, given the crucial importance of conferences as an arena where claims are articulated and challenged.
- Tracing concepts and claims textually across the scientific literature and other media: follow claims into wider media and the public arena, including newspapers and magazines; study changes and shifts in claims as they are passed on to these forums, building on earlier work about the presentation of uncertainty or metaphor in these wider forms of communication.[128,129]
- Tracing promises and claims as they inform research policy: study of how claims are presented in policy documents and research funding, in particular in the EU and US, including private funding.

Main outcomes and synergies: bibliometric *and* qualitative analysis of how nanobio claims spread, closer analysis of the hype and correction logic, including its discursive patterns.

Risk assessment: **(**1) We may find no traces or very few traces of errors' effects. That would be a result by itself. 2) Fail to understand the reasons for error propagation. This risk is limited because NanoBubbles will benefit from complementary skills (STS, Nano, CS) to reach a fine-grained understanding of the interaction of aspects of the error propagation process.

b1.3 Corrections (WP3) [lead PI: Raphaël Lévy]

This work package will study the effects of counter-challenges, corrections, or attempts at correction, both retrospectively (by historical actors) and contemporaneously with the project (by participating nanobio scientists). Specific tasks involved are:

- Study of the effects of annotation of published nanobio literature: as annotation of the literature is carried out, communication processes will be studied to investigate how annotation is received, and whether and how it can facilitate scientific deliberation on contested claims.
- Replication project: replication of crucial experiments that claim nanoparticles can cross the cell membrane or otherwise reach the interior of the cell. These experiments will be prepared following deliberation with researchers involved in the contested claims, and will be informed by STS analyses of the problems involved in successful replication/reproduction (such as the 'experimenters regress') and examples of replication projects in other fields.
- The editorial process: editorial reactions to attempts at correction, including a study of retractions in nanobio and a study of comments on PubPeer; with PubPeer's help, a study of moderation processes.
- Study of nanobio 'epistemic activists' and the backlash against them: analysis of scientists who campaign for improvements in the operation of science (nanobio science in particular), such as greater openness, tighter methodologies, better validation, or new forms of scientific review and communication. This will cover how their activism is received by other scientists in the institutional context of science, what contributes to the success of their campaigning, but also what drives these scientists and how they accommodate their activism within their scientific careers.

Outcomes and synergies: WP3 will stimulate debate about crucial nanobio claims; examine how correction attempts are received; and will clarify how a more productive setting for challenges and corrections could be created. The work package relies on close collaboration among researchers with expertise in nanobiology, in the technical operation of annotation systems and the skills to measure their effects, and in logical and social science analysis of communications under the agonistic conditions associated with controversial science.

Risk assessment: Risk (1) and (2) identified in WP2. A risk of the replication project is that colleagues in nanobiology do not accept the fairness of the experiments. This is in itself an object of study. The risk will be minimised by building on best practices from previous replications projects (we have and will continue to seek advice from Tim Errington, Cancer Replication Project and Alex Holcombe, replication project in psychology) including open science and seeking constant feedback from the original studies' authors.

b1.4 Enhancing trust (WP4) [lead PI: Willem Halffman]

In this work package, we will study how researchers perceive the reliability of knowledge claims and their sources, and how reliability and communication can be improved. WP4 is organised around three key questions that explore the conditions for improved deliberation in scientific communication.

- How are annotation systems (such as PubPeer) perceived? Study of how scientists perceive the reliability and quality of post-publication reviewing, the information offered through such channels, and the conditions for their reliability (such as the complications associated with anonymisation in light of the importance of scientific reputation).
- How do nanobio researchers assess the reliability of the literature, compared to more personalised forms of communication? We will analyse hierarchies of trust in the context of changes in the research system and research communication, building on earlier work in STS that examined how scientific authority derives from the reputations of prominent journals and researchers.[130,131]
- How can new forms of conference communication contribute to improved assessment of error? A study of scientific conferences can accommodate more dispassionate, less personal, and less biased forms of scientific dialogue, including new ways to organise scientific meetings and improved communications from those meetings, e.g., via related social media.
- Integration of results for an overall analysis of processes impeding or facilitating error correction in research: bring together key insights to demonstrate the logic of problematic claims, how they are challenged, and how scientific institutions more conducive to scientific self-correction could operate.

Outcomes and synergies: this WP provides overall integration of research results, identifying potential improvements in scientific communication and more realistic assessment of nanobiology's promise by bringing together Nanobubbles findings from STS, digital methods and nanobiological research.

Risk assessment: Fail to provide any effective propositions. Again, NanoBubbles will benefit from complementary skills (STS, Nano, CS) and so will provide propositions that are effective and fit today's scientific landscape. Because these propositions will be grounded by a technological and sociological understanding they will clarify the processes behind failed error correction even if our interventions fail.

b1.5 Project organisation and integration (WP5) [lead PI: Raphaël Lévy]

As noted above, synergies will operate among the first four WPs as all of them involve at least three PIs. WP5 is the organisational work package, containing project management (including ethics) and overall project integration tasks. Given the interdisciplinary character of the project, operating from four main locations in three countries, special efforts are required to guarantee that the considerable synergy potential of this project is realised. This involves regular contact among research project members, continued attention to project coherence, and care for shared data resources. While this WP contains integration on the level of project management, collaboration and synergy will be guaranteed throughout the teams involved. Synergy mechanisms will in particular benefit the project's junior researchers and we will pay particular attention to their intellectual as well as career development. To this end, synergy mechanisms include:

- A steering committee of the PIs, with regular conference calls (bi-monthly, increased if needed), as well as personal contact at least twice per year to discuss project management and collaboration options such as joint publications and further projects.
- Regular workshops: the entire project team will meet twice per year in an intensive workshop setting to discuss progress as well as stimulate collaboration and exchange. The PIs will host the workshops in turn. They will include training in our respective fields.
- To intensify interdisciplinary cooperation and synergy, all junior researchers will be co-supervised by two of the PIs, according to the requirements of the specific project.
- Discussion and joint principles for how to deal with the ethics of studying error, including how to deal with errors discovered in publications and conflict or opposition from nanobiologists.
- Minor activities to create a shared sense of mission and identification with the project. These will go beyond the social activities in the margin of the workshops.

While we address ethical issues in detail in the self-assessment document, we briefly highlight here our structure for ethics governance:

- NanoBubbles' Ethics Rapporteur, Yasemin J. Erden (an Independent Expert in Ethics for the EC since 2012) will undertake a number of tasks, including running sessions (attached to NanoBubbles regular workshops) to focus on ethics matters raised by the project. She will support PIs in the monitoring of ethical issues in their work for the lifetime of the project. This includes supporting PIs in proactive and timely engagement with university ethics monitoring processes at the appropriate institutions, and assisting with the successful completion of ethics applications, e.g. where there is any data gathering research involving human participants. Erden will act as a facilitator between PIs and the Ethics Advisory Board, as well as a confidential point of contact for any project participant more generally. Thus, we will maintain a regular dialogue on the topic of ethics, and ensure that it is a permanent feature of the project, rather than an afterthought, or a box-ticking exercise.

- NanoBubbles Ethics Advisory Board (EAB) is composed of Alfred Nordmann (Technische Universität Darmstadt, Institüt fur Philosophie, Germany), Katleen Gabriels (Department of Philosophy, Maastricht University, Netherlands), Hub Zwart (Dean of the philosophy faculty, Erasmus University Rotterdam, Netherlands), Ruth Chadwick (School of Social Sciences, Cardiff University, UK).

For independent advice on difficult issues and to quickly identify new opportunities, we will consult our interdisciplinary advisory board (IAB) composed of Catherine Murphy (Nanobiology; University of Illinois at Urbana-Champaign, USA), Wolfgang Parak (Nanobiology; Centre for Hybrid Nanostructures, University of Hamburg, Germany), Kornelia Konrad (STS; University of Twente, Netherland), Mario Biagioli (STS, UCLA, USA), Boris Barbour (Neurobiologist and founder of PubPeer; École Normale Supérieure, Paris, France), Elisabeth Bik (Science consultant, PhD, ex-Stanford) and Cassidy R Sugimoto (Scientometrics, Indiana University Bloomington). The board will meet annually alongside one of NanoBubbles biannual meetings.

<u>Risk assessment:</u> Risk related to four different locations and highly interdisciplinary project. The WP5 is by itself a way to manage this risk.

Gender balance. NanoBubbles' PIs are four men. We are conscious that this lack of diversity has consequences. We are committed to work actively to redress this issue and make NanoBubbles a welcoming and diverse group (e.g. gender-balanced line up of speakers at NanoBubbles events). This includes recognising the important work of all project members, both future recruits and academic colleagues already involved. In particular, Marianne Noël (Ph.D. degree in Physical Chemistry in 1992; Master's degree in the History of Science, Technology and Society, 2012; currently a CNRS Research Engineer at LISIS, Université Paris-Est) will work with Lévy, helping bridge the gap between STS and nanobio. Noël's intellectual journey from physical chemistry to sociology has paralleled (and regularly intersected with/supported) Lévy's journey from nanobio scientist to "epistemic activist". In April 2019, Lévy and Noël organized a seed meeting funded by the French Embassy in the UK where some of the NanoBubbles participants met for the first time.[132] Frédérique Bordignon (linguist, librarian, and head of the service for scientific information of École des Ponts ParisTech) will work with Labbé to establish the IT and information shared infrastructure central to the project's success. Yasemin J. Erden (philosopher, trained in philosophy of language, logic, and ethical theory; St Mary's University, London) working with Lévy, will support all aspects of the project in her role as ethics rapporteur and will bring her expertise in logic and critical thinking to the annotation project. The project will also remain mindful of gender as a contributing factor to academic structures generally and scientific debate in particular. This includes taking into account how gender plays a role in publication citations (e.g. 'The Gender Citation Gap'[133]), and taking care not to perpetuate these practices.

b2. Methods

Each of the work packages above draws on methods specific to the various disciplines within NanoBubbles:

b2.1 Digital methods, including scientometrics and text analysis

We first employ existing scientometric tools (e.g., citation analysis) to build corpuses (WP1). Studying corpuses and the citation graph is the basis for understanding how ideas or disagreements diffuse in the nanobiology community (WP2,3). The study of the citation context will contribute to tracing erroneous claims (WP2) and understanding the effects of corrections (WP3). Starting from current methods that define the citation context as either *positive*, *neutral* or *negative*, we will develop an extended citation theory that goes beyond this simple classification.

In addition to scientometrics, we will use natural language analysis of raw texts and web annotations. This will allow interrogation of the whole text of scientific publications, as opposed to the limited amount of text used in citation analysis. Natural language analysis is also a means for gathering information from non-traditional sources (e.g., blog posts and comments). Thus tailored text analysis tools will allow the detection of points of disagreement. Examples of such conflicting stances could be:

-"This suggests that TiO_2 nano-aerosol did not gain access in quantifiable amount to the CNS either across the BBB or through axonal translocation from the nasal mucosa".[134]

-"TiO_2 NPs could not only pass through the BBB but also disrupt the integrity of the BBB."[135]

Detecting such stances will contribute to both WP2 (tracing error) and WP4 (automatically detect disagreement and stimulate post web-annotations and post-publication discussions).

b2.2 History and Ethnography

Historical and ethnographic methods will be used for tracing the co-evolution of scientific conferences and practices of error propagation and correction in the sciences (WP1, WP2). Historical methods relying on archival (unpublished) and published textual sources are necessary for two reasons. First, controversies surrounding scientific errors do not commonly become publicly known, so it is difficult to use ethnography alone to catch a currently unfolding controversy to analyse. By taking a longer view through history it is possible to identify controversies and follow them over time. And second, the conference form has evolved; there is nothing natural or given about how conferences are organized today. An historical perspective allows us to see the contingency of the system and thereby offers a foothold for reform.

Four main types of sources lend themselves to historical study of older conferences. First, many conferences generate published proceedings. We propose to draw on the digital methods developed in the other subprojects to assist in review of such proceedings. Second, a significant number of scientists have written memoirs and (semi)fictional accounts of scientific life that include descriptions of conferences. Third, and probably most important, a few scientific organizations have placed records of their associated conferences in archival collections. The Science History Institute and the American Institute of Physics possess extensive collections of this sort. Finally, where published and unpublished contemporary documents provide an inadequate or partial picture, we will supplement with interviews with people who participated in past nanobio conferences. In addition, newer conferences often have a social media presence; digital methods (see b2.1) will be developed to allow these to be gathered. The historical method then proceeds by triangulating all of these sources and using them to interrogate each other – i.e., to provide context as to how and why each source was created and what its original intent and later effect were. By interpreting sources in this way, the historian is able to construct a narrative of change-over-time that is robust to new information.

However, historical methods do not suffice. Everyday practices are often not preserved in historical sources, especially practices relating to settings such as conferences that are rich in interpersonal interaction. Ethnographic methods are necessary to understand how conferences work and are experienced. Members of this subproject will accompany members of the other subprojects to the conferences they regularly attend to observe and experience contemporary attempts to correct the scientific record (WP3). We will also use ethnographic interactions to experiment with participatory forums within scientific conferences where scientists can discuss ways to make the correction of errors less fraught and personally-charged (WP4).

There are many forms of ethnographic method, but the general variant we will employ is ‘participant observation’. Here, the ethnographer participates in the practices evident in the ethnographic site. The ethnographer is perhaps not a fully-ratified participant, but usually attains the recognition and skill of other newcomers to the site such as children, students and migrants. While participating, the ethnographer engages other participants to understand the world and their actions as they understand them. The ethnographer also continually reflects on her own actions, laying bare the assumptions supporting them.

The ethnographic ‘site’ where the participant-observer locates herself is a contested concept. Ethnographers once spoke of going into ‘the field’ as though fields were self-evident and natural. However, this way of speaking creates a space between field and non-field that affords (post)colonial inequalities. We follow most contemporary ethnographers in viewing the site as a construction that the ethnographer plays an active role in creating. In most cases, actions taken in any one setting affect and are affected by actions elsewhere, so it is usually necessary to undertake ‘multi-sited’ ethnography to understand complex interactions among settings. This is obviously the case here, since error correction/propagation practices in conferences are coordinated with journals, laboratories, firms, etc. One of our first tasks will be to map a site encompassing these various domains within the nanobio community that will be amenable to participant observation.

b2.3 Article-level annotations and post-publication peer review

Understanding and analysing the scientific literature – particularly where there is significant hype and/or vague concepts and claims – can be challenging, especially for researchers who are new to a field. Annotations offer a way to distribute and discuss expertise. We will use annotations to provide detailed in-text comments on specific arguments or claims in scientific articles. For this purpose, we will harness the power of Hypothes.is,[80] an open platform that effectively implements a "knowledge layer on top of the web". Whilst commenting happens at the level of a sentence or a figure (Figure 1), the corpus of annotations can be searched and organised via keywords (tags), and thus statements, arguments and critiques that run across articles published at different times and in different journals can be pulled together according to different criteria. Each annotation is also an invitation to the authors of the publication and the broader community to engage in a public discussion (comments are open on each public annotation).[136]

We will:

- Develop best practice on how to annotate scientific articles. This includes training in philosophy, logic, critical thinking and will cover technical aspects such as the best way of using tags as well as scientific writing, and skills in peer review (including the logical analysis of text). This work will result in formal guidance in the first instance for NanoBubble's own team. It will then be shared online as a collaborative document and will progressively develop into a training programme accessible to all researchers (WP4).
- Annotate 1,000 articles (corresponding to the three issues) to generate a critical mass that will significantly affect understanding of the field (WP3). One objective is that researchers (in particular students) feel that they need to consult and expand this resource as they browse the literature.
- Creating tools to present, search, organise these annotations and allow others to do their own investigations (WP1).
- For each article annotated, a review, summarising the conclusions from the annotations (and linking to them) will be published in three virtual journals or Peeriodicals, one dedicated to each issue. Peeriodicals (**https://peeriodicals.com/**) is a platform set up by, and linked to, PubPeer (therefore those reviews will also automatically appear at PubPeer) (WP1).

At the point where a review is ready to be published in the Peeriodical, we will contact the authors (email) and then the broader community (social media, targeted emails) to invite further discussions. It is possible that our critical stance may provoke offence or resentment, or could put reputations at risk, and we will give extra attention for a fair, respectful and ethically sound attitude. We will develop guidelines to address that latter point and seek advice from our Ethics Rapporteur and Ethics advisory both on the principles and on the best way of handling specific cases if disputes arise. A similarly careful and caring approach will apply to the replication initiative.

b2.4 Replications

The NanoBubble replication project will be the first replication project in nanoscience, and one of the first replication projects fully embedded in a social science project. It builds on the lessons from previous and ongoing initiatives such as The Reproducibility Project: Cancer Biology,[137] the Brazilian Reproducibility Initiative (which seeks to assess the reproducibility of findings in biomedical science published by researchers based in Brazil),[138] and the Psychology Reproducibility project.[139] The project is a partnership with the *Beilstein Journal of Nanotechnology*, an international, peer-reviewed, Open Access journal free for author *and* reader (completely funded by the Beilstein-Institut, a non-profit foundation located in Frankfurt am Main, Germany). The focus of the replication effort will be on articles that report applications of imaging or sensing inside live cells using nanoparticles. Such applications require that a large proportion of the nanoparticles reach the cell cytosol. The aim is to evaluate the reproducibility of articles in that field. The tight scientific focus ensures that a good coverage of publications can be achieved by a relatively small-scale replication effort. It also helps with the feasibility since all required equipment is available in the world-class Matter and Soft Matter laboratory (UMR7057 CNRS & Paris Diderot, Paris France; Lévy's NanoBubbles' host institution). We aim to have at least two replications for each experiment, one carried out in Lévy's team and one subcontracted to an independent platform for both synthesis and imaging (see below for more details). Typically, the experimental techniques will include cell culture, optical and electron microscopy, nanoparticles synthesis and nanomaterials/sensor characterisation.

Choice of articles/experiments. The strategy for the selection of articles is inspired in particular by the Brazilian initiative.[138] Thus, we will not aim to reproduce entire studies, but specific experiments that respond to a set of criteria including the fact that they represent one of the key findings of the study. The exact criteria for inclusion will be determined during the first 12 months of the project and they will be open for public consultation. They will include practical considerations such as feasibility (e.g. accessibility of materials, cells, etc.) and cost (no single experiment/article should require more than 10% of the replication project budget). As the overarching question is whether nanoparticles can cross the cell membrane and access the cytosol, experiments that involve physical delivery of the nanoparticles (e.g. microinjection) will be excluded.

Pre-registration. Once an experiment (or series of experiments within an article) has been selected, a detailed protocol based on the published materials and methods will be written. As in the Psychology and Cancer replication efforts, we will seek inputs from the original authors to supplement any details that may be missing from the published work. The study will then be pre-registered, in a new format of publication that the *Beilstein Journal of Nanotechnology* will introduce in its workflow as part of this project. The pre-registration will include the details of the planned experiments and analyses.

Materials synthesis and characterization. An often suggested cause for the lack of progress in nanobiology is the variability in the synthesis and characterization of the nanomaterials.[127] This poses also a serious risk for any replication effort: a failure to replicate could be blamed on inability to prepare suitable nanomaterials. We will address this concern via a multipronged strategy: 1) we will characterize any nanomaterials in the project beyond the minimum reporting guidelines[127]; 2) we will use the network of laboratories that constitute the EU Nanomedicine Characterisation Laboratory to procure independent characterization; 3) in addition to nanomaterials prepared by the team, we will seek to procure samples from specialised companies whenever that is possible; 4) we will invite the authors of the original publication, and the community more broadly, to send samples for evaluation. Thus, we anticipate that each experiment will be reproduced with several batches of nanomaterials of different provenance. This will allow us to determine whether any difficulty in reproducing a particular study may be attributed to sample preparation.

Imaging of nanoparticles in living cells. A routine investigation provides tens or hundreds of images. Yet a major limitation of most publications in this field is that only one representative image is shown, often in a highly compressed format leading to a serious loss of information and potential for bias. We will share entire datasets using the open microscopy environment (OMERO) so that bias can ascertained independently and quantitative analyses reproduced. In addition to imaging studies done in the Lévy lab, we will use the Euro-BioImaging research infrastructure to procure independent replication of the imaging studies.

b2.5 Qualitative interviews and cases studies

Each of the nanobubbles will be investigated with a qualitative case study, relying on document analysis and interviews with scientists, both key actors and nanobiologists not directly involved in the controversy. This will include specific studies of research teams working on these issues, involving a representative range of researchers (gender, career age). Selection of crucial episodes, researchers, and research teams to study in more detail will occur on the basis of the corpus established in WP1. Interview protocols will be designed in collaboration between the scholars performing this research to safeguard comparability. Transcribed and anonymised interviews based on due prior consent will be circulated no further than the project team to maximise anonymity. Further restrictions may apply at request of informants.

b3. Synergy and outcomes

To better understand the complex ecosystem of science, NanoBubbles draws upon a wide cross-section of human knowledge to analyse how one part of the ecosystem, the field of nanobiology, works. This allows us to address our overarching research question: how, when and why does science fail to correct itself? NanoBubbles' approach blending the human sciences, informatics and nanobiology is unique, although it builds on earlier collaborations. That blending gives the project the potential for a major long-term impact on the research system (across all disciplines), through its investigation of ways to improve the reliability and efficiency of the scientific process. But that blending also allows all the project's participants to make transformative contributions to their own disciplines that would be impossible otherwise. Historians of science will gain new digital methods for collecting and analysing sources; conversely, computer scientists will gain new expertise in tracing not just metadata and citations but even the content of science across multiple channels of scientific communication. Computer scientists will also see the tools developed in this project integrated into the regular practice of critical nanobiologists, historians and sociologists – with potential for uptake in many other fields as well. Sociologists of science will gain true participant-observation experience of scientific experiments and conferences through collaboration with critical nanobiologists. Critical nanobiologists will gain an understanding of how their claims are entangled with the social organization and practices of their field. Thus this wide-ranging interdisciplinary collaboration makes possible methodological innovation and substantive basic science discovery in *each* of NanoBubbles' constituent disciplines as well as academically and societally relevant knowledge across our interdisciplinary cluster and potentially across all of science.

b4. Simplified Gantt chart

Work packages	Year 1	Year 2	Year 3	Year 4	Year 5	Staff
1. Corpus & mapping Shared IT platform						All senior staff RL: PD1-2, 5 CM: PD & PhD **CL**: PD1-2 & RE2 (IT)
2. Tracing error & contested claims						RL: MN, PD6 **CM**: PD CL: FB, PD1-2, RE1-2 WH: PhD1-2
3. Correcting the scientific record						**RL**: MN, YE, PD1-4, 6 CM: PD & PhD CL: FB, FP, PD1-2, RE1 WH: PD1
4. Enhancing trust Training						RL: MN, YE CM: PD CL: FP, GC, PhD1-2, RE1 **WH:** PD2
5. Organisation and integration						**RL**. All PIs, PD support. Advisory boards. YE: Ethics rapporteur

The simplified Gantt chart of NanoBubbles shows staff collaborating across teams within each work package. It is a rough periodization: not all sub-tasks are depicted separately because of space limitations.

PIs: RL: Raphaël Lévy; CM: Cyrus Mody; CL: Cyril Labbé; WH: Willem Halffman. The PI indicated in bold is the lead for the corresponding work package.

Senior staff: MN: Marianne Noël; FB: Frédérique Bordignon; FP: François Portet ; YE : Yasemin Erden ; GC : Guillaume Cabanac.

RE (Research Engineer), **PD** (PostDoc**)** and **PhD**; see tables in section c for more details.

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