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Noémie Merleau-Ponty

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## Chapter 8

# Sociology as Technology: A Toolkit for Studying *In Vitro* Gametogenesis

Noémie Merleau-Ponty ORCID ID 0000-0003-0340-9816

### Abstract

*In vitro* gametogenesis (IVG) is an in-progress laboratory technique for studying the biological development of oocytes and spermatozoa. Biologists face a number of technical challenges to building this “in vitro system,” acknowledging that reproductive and regenerative biomedical applications remain “quite a long way off.” In the context of the contemporary focus on “translation” in the biosciences—i.e., the expectation that basic science has impact on society through technological and biomedical innovation—various reproductive imaginaries based on IVG have emerged. This chapter, based on fieldwork and a review of scholarship on IVG and artificial gametes, asks the following question: What does the gap between laboratory research and its media representations say about developing a new biotechnology? Efforts to address this question have yielded diverse understandings of IVG, some surprising, thus offering feminist social sciences an opportunity to contribute to this unfolding technology by deploying its methodological toolkit.

**Key words:** in vitro gametogenesis; reproduction; artificial gametes; technology; translation; interdisciplinarity; participatory science; cyborgs; techno-sapiens

### Introduction: Attempting In Vitro Gametogenesis

A “gamete” is a mature sexual reproductive cell—a sperm or egg—that unites with another cell to form a new organism. The terms “in vitro gametogenesis (IVG),” “stem cell derived gametes,” and “artificial or synthetic gametes” refer to the use of embryonic or adult cells to make spermatozoa and eggs. A “germ cell” is the sexual reproductive cell before it matures into a gamete. Academic IVG research in various countries uses undifferentiated cells known as stem cells from either embryos or somatic cells to focus on “germline” (the lineage of cells culminating in the germ cells) development. In vitro human germline development faces two constraints: (1) Because they form early in fetal development, *in vivo* germ cells are inaccessible to researchers. In vitro cultures of embryos end after 14 days, precisely when germ cells begin to develop and germ cell formation in donated aborted fetuses is nearly complete. (2) No robust experimental platform for the study of human germ cell formation exists.

In 2011, following fertilization of artificial gametes, mouse pups were born in a Japanese laboratory (Hayashi et al. 2011). In 2015, Naoko Irie, a Japanese researcher in the laboratory of Azim Surani at the Gurdon Institute in Cambridge, UK, published an important article about human germ cell biology in the influential journal *Cell* (Irie et al. 2015). Irie showed that the SOX17 gene is specific to humans, who turn out to be quite different from mice (which were until recently the primary model of study). Unsurprisingly, the article attracted worldwide attention, even outside of the academic community, because of the reproductive potential of creating human artificial gametes and perhaps even curing a number of infertilities.

From 2017-2019, I worked with biologists at the Gurdon Institute in Cambridge UK, conducting interviews with biologists and attending biological and bioethical talks on gamete development. I spent 5 months in Professor Azim Surani's laboratory, working with Dr. Naoko Irie and observing experiments by other researchers in the lab. I also participated in team activities such as lab meetings and meals. My mentor for the project was Professor Sarah Franklin, whose research on in vitro fertilization nurtures contemporary studies of reproductive technologies and fertility.

"After IVF" (Franklin 2013), the findings of studies of primordial germ cells fuel applicative projections, as well as a broad range of reproductive hopes, including same-sex reproduction (i.e., having a baby with a same-sex partner), solo reproduction, multi-reproduction, post-chemotherapy reproduction, post-sterilization reproduction, and post-menopausal reproduction, to name only a few.

Nothing is publicly known about Naoko Irie's routine work. After I forwarded a TED talk to her video about *in vitro* gametogenesis that cited her article, she told me "They should see how it's done in the lab." She is not a fan of American-style, over-enthusiastic speculation about future innovations, and she reminded me once again about the painfully dull experimental routine that involves years of successive failures before it eventually may allow the publication of a single article. The arduous process of "crafting" biology is a standard feature of the culture of everyday research (Meskus 2018), although it simultaneously energizes the imaginaries of rapid technological breakthroughs. What does this broad gulf between the dogged pace of research and the rapid spread of imaginaries teach us about making reproductive technologies and creating techno-sapiens?

Unlike a linear view of the translation of scientific work into technological applications, the practice of biotechnological research and online representations coexist and are thought of by biologists *as not working together*. Colleagues warn about misrepresentations of their research in the media or bioethical publications—a layer of complexity often expressed as the dialectics between "scientific hype and reproductive hope." This gap is one of the significant challenges to translating stem cell research into biomedical practices (Gardner et al. 2015). Still, discourses about in vitro gametogenesis are "good to think with," because they weave the notion that "biology is a technology" of sex and social reproduction into various social media (Franklin 2013).

My work emphasizes the importance of nurturing alternative narratives that might otherwise be silenced by dominant expectations. Far from offering linear, easy-going translations based on scientific authority, biologists express doubts, questions, difficulties and wonder, some of which are described in this chapter. In a laboratory in which academic labor constructs in vitro gametogenesis, my presence was enacted as an interdisciplinary experiment. I attempted to culture stems cells alternatively with Irie to create one of these alternative narratives. I brought some tools from my own petri dish, or culture medium, where at the time I held a position as a research associate in the Reproductive Sociology Research Group based in the Sociology Department at the University of Cambridge.

I close the chapter by proposing "sociology as technology" as an alternative to linear translational thinking. This conceptual tool, built through my ethnographic practice with the biologists whom I had come to study, is also a response to the gap between slowness and rapidity, as well as an invitation to think in novel ways about the future of technology-making.

## **Relating Kin or Forgetting Progenitors?**

After 8 years of research in a Japanese laboratory, mice pups were born following the fertilization of artificial gametes that were induced from stem cells (Hayashi 2011). This technique is also being used with human cells in laboratories around the world, and primordial germ cells have been successfully produced in a British laboratory (Irie 2015). The technical challenges to creating an “in vitro system” based on human cells led one biologist to observe that “the question of future potentials, it’s quite a long way off.” Still, given the emphasis on “translating” the biosciences into technologies, scientific publications using mice nourished the imagination of artificial gametes for humans.

With the exception of Japan, where IVG is banned from producing human embryos for research, no other countries have implemented regulations for this research field (Ishii, Pera, and Greely 2013). In a translational atmosphere in which the media assume that applications of basic science are imminent (López and Lunau 2012), despite the many challenges to actually making IVG work, biologists and bioethicists nevertheless continue to write, albeit cautiously, about the social implications and value of this research. Two intersecting topics emerge from their thinking: (1) IVG as a technology for curing infertility by using biology to make artificial gametes and relating kin; (2) IVG as a model for the study of gamete development as “cell memory loss,” or the erasure of certain biological traces of the progenitor’s past life embedded in their cells.

### **IVG as Making Artificial Gametes: Relating Kin**

The possibility of making artificial gametes is linked to the well-known cultural value of genetic substance as the matter of kinship (Schneider 1980; Carsten 2011; Porqueres i Gené 2015; Merleau-Ponty 2017). Body parts, particularly gametes, carry relational capacities. They not only make new bodies through biological mechanisms, but they also identify people and relate them to each other as kin. They thus reproduce not only biology, but also social relations, embodied as “blood.” In 2015, a group of biologists in the Netherlands published a review of IVG that interpreted the development of this technique as a reproductive technology:

Although they are currently still at an experimental stage (...) deciding to introduce artificial gametes in clinical practice. . . requires a point of view that goes beyond biologic parameters. First, artificial gametes could change the field of MAR [Medically Assisted Reproduction] dramatically by discarding the entire concept of infertility, and potentially allowing new groups of patients (e.g. heterosexual couples without functional gametes, post-menopausal women and gay couples) to have genetically related children. Second, we are unable to acquire informed consent from the children that will be conceived. (Hendriks et al. 2015)

Additionally, because chemotherapy often affects fertility, cancer survivors are frequently seen as potential beneficiaries of IVG (see Chapter 3). Concerns with these applications include not only the lack of consent from potential future children, but also the prospect of the mass production, screening, and selection of embryos (Palacios-González, Harris, and Testa 2014; Cohen, Daley and Adashi 2017).

IVG also extends the value of genetics to sustain kinship relations beyond naturalistic and heteronormative reproduction to the possibility of the “democratization of reproduction.” It could thus theoretically become possible for every human--regardless of their fertility status or sexuality--to conceive genetically related children (Testa and Harris 2005, 165). In that

spirit, writing for the Nuffield Council of Bioethics (UK), the ethicist Anna Smajdor observed that:

Artificial gametes (AGs) might enable anyone to produce gametes regardless of whether they ever had ‘natural’ gametes, and irrespective of their age, sex, relationship status, or sexuality. The prospect of creating sperm from women’s cells and eggs from men’s cells might also democratize reproduction in enabling same sex couples to have children that are the offspring of both partners, something which has never before been feasible. Thus AGs offer the possibility of genetic reproduction to people who are not typically regarded as being infertile. (Smajdor 2015)

There are two principal representations of artificial gametes with regard to reproduction and kinship: (1) a classical interpretation of reproductive technology as an enabler of genetically-based parenthood; and (2) a tool for questioning the heteronormativity of these reproductive patterns. However, when the focus is not on future applications of IVG but on how it is currently used in scientific articles, it becomes apparent that IVG is not perceived as a reproductive technology for making artificial gametes but as a system for studying gametes’ biological development and, more specifically, for advancing understanding of a single critical event: epigenetic reprogramming.

### **Forgetting Progenitor Memory: IVG as a Model for Studying Primordial Germ Cells and Epigenetic Reprogramming**

“Epigenetics” is a common biological term that describes the molecular phenomena surrounding genes and the ways in which they are expressed and/or modified by environmental influences or other mechanisms. Epigenetic marks help determine how genes are made (un)available for transcription in RNA and proteins in cells. Some social science publications emphasize the fact that “epigenetics” introduce environmental factors into reproduction, blurring the boundaries between biology with health and politics (Lamoreaux 2016; Meloni; 2016; Lappé, Jeffries Hein, and Landecker 2019). In primordial germ cell formation, biologists point to the fact that some information from progenitors’ cells must be “erased” or “forgotten” for a new organism to initiate a life cycle afresh.

During an interview, a Gurdon Institute (Cambridge, UK) biologist claimed:

The big event [in gametogenesis] is epigenetic reorganization including DNA demethylation, which is extremely rare to see in the other cell types. So, this is the way to reset all the information for the next generation. (Interview 2, 2018)

“DNA demethylation” is the erasure of epigenetic marks located on DNA. These marks are known to induce the expressions of genes (i.e., by turning them on or off). Epigenetic reprogramming in gamete development was first described in mice (Hackett et al. 2013; Seisenberger et al. 2012). It is said to allow “primordial germ cells” to gain “totipotency”—the potential to develop into various specialized tissues in response to external or internal stimuli—within the fetus. Whereas every other cell type specializes during gestation, gametes alone retain the capacity to build every cell type (on condition that they mature and encounter another gamete in order to co-fertilize). Epigenetic reprogramming of cell information is thus represented as a critical event in the constant remaking of life through never-ending generations of new cells and individual organisms.

Epigenetic reprogramming is associated with the idea that “cellular memory” is “erased” (von Meyenn and Reik 2015). In the same vein, a stem cell biologist whom I interviewed argued that gamete development and epigenetic reprogramming are “a bit like a computer disk. [You] wipe out everything [and put] new information on.”

This approach may contradict the interpretation of IVG as a model for creating artificial gametes and relating people through reproduction and kinship. One approach values genetic substance as a kinship maker, initiating a discussion about democratizing reproduction by offering universal access to fertility. The alternative approach introduces ideas of cell memory loss and forgetting genitor—i.e., “parental”—embodiment. These two approaches to reproduction—kinship and relatedness—are not contradictory, however. Amander Clark’s laboratory, for example, promotes its research as both studying epigenetic reprogramming and attempting to offer solutions for patients rendered infertile by cancer treatments (see Chapter 3).

The differences between these two ways of writing about in vitro gametogenesis and gamete development also suggest a gap in translating basic science into viable reproductive technologies.

## **Benchwork in Translational Times**

Biological translation is often described as “bench to bed,” (from the laboratory to the clinic). Because it suggests that the process is short and smooth, this frequent expression can be misleading. Indeed, scientists often stress the laborious nature of benchwork. In the summer of 2019, Professor Azim Surani invited me to present my research on in vitro gametogenesis to his team at the Gurdon Institute in Cambridge (UK). I described my past work on in vitro fertilization, briefly summarized and analyzed the “relate and forget” dialectic described above and mentioned my plans to spend time in their lab. A stunned silence followed the presentation. Azim Surani had assured me that lab meetings were generally lively, but no one reacted. Probably to alleviate this awkward moment, he briefly remarked that media representations and benchwork were two very different things. The notion of artificial gametes was obviously out of place when referring to what biologists actually do in the laboratory with germ cells. I tried to avoid revealing my distress by taking notes about these remarks, firmly believing that we were experiencing a powerful ethnographic event.

A few months later, I discussed this initial encounter in an interview with a doctoral candidate in the same lab. While I was describing one of my principal findings—that it would be a long time before artificial gametes would be functional—we also reminisced about my audience’s stunned faces. My interviewee replied:

Artificial gametes: What? Are you serious? Let’s just think about the fact that this cell lineage dedicated to reproduction is specified in the early weeks of fetal development, and then stops for 12 to 15 years, until puberty eventually starts the process of making fully functional gametes. Would biologists be able to remake the very first steps? What about those years of dormancy and what about all the mechanisms involved during puberty?

In her characteristically direct way, she added: “We need to be very careful. [...] For example, when a journalist is interviewing Azim and then he over-inflates everything, that’s such a pity. [...] Because it’s a big lie, it’s not true that we are creating artificial [human] gametes, this is not true.” Naoko Irie specifically asked me to emphasize this statement after seeing a draft of this chapter, arguing that this “is critical when one talks about IVG, which

may also take 13 years to get gametes in vitro.” So, what is it that the laboratory is currently creating if not artificial human gametes?

Simply put, the team’s core contribution to germ cell development is *biological knowledge*—more specifically, an understanding of the molecular pathways involved in the specification of reproductive cells. In fact, medically assisted reproduction is not even cited in discussions of biomedical translational horizons and possibilities, while developmental knowledge and heritable diseases feature prominently. It is not so much *reproductive* medicine per se that is emphasized, but *regenerative* medicine that encapsulates the place of the lab’s research within the far broader spectrum of stem cell research. Azim Surani (2015) stated for *The Conversation*:

Imagine combining the procedures in one patient, for example a woman with a disease-causing mutation who does not wish to pass this mutation to her child. Starting with a cell taken from her skin, this is reprogrammed to a primordial germ cell, in which the DNA is then edited to remove the mutated gene. The primordial germ cell is developed into an egg and used to create an embryo for IVF, to be screened and transplanted back into her womb. The child and its subsequent descendants would be free of the mutated gene.

This scientist’s approach focuses on biological regeneration as a source of applicative imagination. This approach, however, is closely connected to existing “selective reproductive technologies” such as prenatal and pre-implantation diagnoses (Gammeltoft and Wahlberg 2014). Recent debates about germline editing have also inspired social scientists to investigate what potential users think of such technologies. These studies have shown us that regeneration is less of a concern than the recognition of disability rights, which are potentially challenged by the implication that living with mutated genes is inherently negative (Boardman and Hale 2018; Boardman 2020). At the bench, meanwhile, considerations of the future significance of such technologies for patients with mutated genes seem to be absent. Instead, the interest of the laboratory is whether biological mechanisms associated with disease and health can be unraveled and potentially modified.

Biology is a discipline, both as a human endeavor to create new knowledge and as a set of behaviors guided by values like “effort,” “diligence,” and the kinds of repetitive and hyper-structured labor that involve long periods of time and frequent failures. Indeed, ethnographic fieldwork in these labs reveals not only the kinds of biology actually undertaken in them, but also the sociological context in which they are undertaken. The short history of the stem cell field is built around numerous unknowns that researchers explore, using experimentation and exchange, within a highly competitive environment (Eriksson and Webster 2008). Human germ cell biology is especially “disciplined” because no prior knowledge exists on which to base new research. Naoko once told me that this work is like “walking in the dark.” Not only is there no previous literature, but before 28 days of human development—when abortion clinics, pending patient permission, donate fetuses--in vivo comparison is impossible. Indeed, as Naoko added, “it’s a new way of doing biology and you have to be extremely resilient.” Beyond testing different culture conditions, there are no guidelines, no protocols, and no grounds for comparison--just pure research. At the beginning, it took Naoko 4 years to recapitulate the first event of human germ cell development. In summarizing this blend of psychology, technology, and science making, Naoko illustrates how basic science is a process of discovery and application that is far from linear:

This project requires [you] to be optimistic and to be sure that you will get something. It is very risky because if you get nothing, you get nothing. After trying so

many things, you build some kind of instinct. (...) If you doubt your technique you cannot be sure of anything. If your tool is not right, you bring a lot of anxiety. It takes time and effort to build your tools. Even published papers—you are not entirely sure. I can wonder and go back to the first step again. But, at some point, you have to rely on something. Other groups will publish another way: is it the real way? With mouse models, it is less difficult because you can test in vivo. With human models you cannot. It also depends on how you set the goals and if you know what you want to see.

She portrays her project as a back and forth process involving failure, doubt, rethinking, and persistence in an uncertain environment. This quote also suggests that an important aspect of basic research requires letting go of one's assertiveness and accepting the unknown for what it teaches us: the humility to be able to repeatedly start all over again. As Naoko summarizes the process, "You cannot control everything. Not all of it is in your hands."

Not all researchers are as cautious as the two discussed here. I met one postdoctoral researcher from Japan who was less reserved about predicting the successful development of artificial gametes. "I don't think it's so far away," he said. While remaining cautious about the biology involved, he stressed the ethics of scientific practice, what Charis Thompson (2013) would call "good science." He told me that it took "just five years" between the first paper on mice gamete development and the development of functional gametes.

One important difference between mice and humans, however, remains the in vivo timing. Mice gametes develop in vivo in 20 days, but human gametes follow a different developmental calendar. First, infant oocytes are fully developed at the time of birth and remain dormant until puberty when, in males, spermatozoa start to be produced. According to my interviewee, another major difference between mouse and human models that presents an even greater challenge is that mice can be "used" and "sacrificed," "but you cannot do that with women." This researcher made it clear that his research field is helpful because it contributes to our understanding of how human gametes develop, but that it should not be used to conceive an actual human baby. Similar ethical concerns about the biological risks of IVG-conceived offspring have appeared in the journal *Science* (Lippman and Newman 2005).

No single point of view is more pertinent than another, but ethnographic work does tend to reveal unexpected narratives. Building on the bioethical idea of "the democratization of reproduction" (Smajdor 2015)—i.e., universal access to biological reproduction—I would like to discuss *the democratization of biotechnology conception*, which would entail two objectives: (1) the interdisciplinary creation of tools that (2) could be used to include a wider range of perspectives in the conception of biotechnologies. In this sense, I firmly believe that ethnographic, feminist-oriented social science is especially well-suited because of its bottom-up, qualitative approach and its inclusive, intersectional political agenda. *Sociology can be practiced as a technology for the democratization of biotechnology*, and from my personal perspective, it should be. (Let's start a debate!)

## **Sociology as Technology: A Toolkit for Democratizing Biotechnology**

"Flow Cytometry" is a biotechnique to identify the physical and chemical characteristics of cells. It is a decisive step in a biological experiment because results can be "seen" in the form of specific diagrams that indicate the presence or absence of the characteristics being sought through culture conditions. On August 21, 2019, I sat with Naoko looking at the charts on the screen in front of us. By contrast with cell culturing, this aspect of biological work lends itself to informal conversation because once the tube is placed under the needle, it is simply a



matter of time before the chart appears on the screen. This is Naoko's "favorite time" because she is able to see the answers to her question. In the short term, she says, she would like to see "a double positive" in her cells (whatever that means!). In the long run, though, she wonders about making artificial gametes and her role in society. Is her work controversial? "You can be helpful while I am struggling with this technical stuff every day," she concludes.

In what capacity can I be helpful? As an ethnographer trained as a social anthropologist and a former member of the Reproductive Sociology Research Group? This is the frame of my skill set, which centers around specific ethnographic tools such as relationality, talking, interviewing, hanging around, listening, observing, taking photos, reading, writing, and presenting. I have described the gap between future projections of the applicability of in vitro gametogenesis to artificial gametes and the actual routine work and views of some of the biologists working on this technology.

My work with the Reproductive Sociology Research Group took a somewhat audacious turn because, with the mentorship of Sarah Franklin and my co-worker Karen Jent (2018), I began to think about *sociology as a technology*—a term that came to me after a meeting with two stem cell biologists with whom Sarah Franklin and I were collaborating. Sarah and I were discussing how seminar sessions offered spaces in which sociologists could intervene in a way that rewired biologists' knowledge of their sociality, in turn perhaps empowering women to participate more fully in typically male-dominated Q&A sessions. "Yes," I added, "as you described how biology is a technology, what we are doing is sociology as technology." We smiled at each other—the birth of a new social science concept is always a special moment—and I stared at Sarah in shock until she said "You'd better write this down!"

The practice of sociology as a technology uses an interdisciplinary approach that entails not only being in the laboratory in order to develop an alternative narrative, but also integrating sociological tools into the lab's daily functioning. I reminded everyone that I am a social scientist and that my work in their lab entails intervening in their routines in a potentially disruptive but entirely empathetic and attentive way. My job was to enact a different way of being part of a basic science laboratory by using different tools to explore gaps between basic science and applications or media translations of the work. By questioning how the reproductive futures of artificial gametes and benchwork could be seen as separated by these gaps, I was able to make the gaps work for my ethnographic practice.

It is possible that the gaps that I identified do not work as well for biological scientists, many of whom tend to perceive such distinctions as irrelevant. Artificial gametes and scenarios generated by the media have very little to do with their daily struggles. From a feminist perspective, this is an unsurprising dimension of translational practices, especially if we think of Marisol de la Cadena's book *Earth Beings* (2015) in which she translates her conversations with Mariano and Nazario Turpo into English—*Runakuna* or Quechua people (see Chapter 11). She thinks of anthropological work as a practice of translation. She writes: "I translated what they said into what I could understand, and this understanding was full of the gaps of what I did not get" (Cadena 2015:3).

Other voices have joined Cadena's profound, humble, participatory, interdisciplinary and democratic move towards a more inclusive form of diversity. Sociological tools have proven helpful by reproducing historical perspectives for a democratic future. The journal *Nature*, for example, featured Sarah Franklin's (2019: 630) commentary about ethics and eugenics to mark the 150th anniversary of the publication of Darwin's 1859 *On the Origin of Species*. The conclusion of her remarks were a democratic call for inclusive, socially-committed science-making:

It turns out that what we have in common is less a single biological essence—or the ability to alter it—than a shared responsibility for human and non-human futures. The implication of this new model is that the most ethical science is the most sociable one, and thus that scientific excellence depends on greater inclusivity. We are better together—we must all be ethicists now.

My answer to Naoko's invitation to "help" is nurtured by my learning experience as a team member at Cambridge. I could not help Naoko on my own, but I can ask her questions and interrogate the texts that I have cited.

This chapter has explored a number of questions ranging from the ethics of testing the functionality of synthetic gametes and embryo selection to the problem of access to IVG. The chapter has also highlighted tensions between regenerative approaches to IVG, which potentially could remove mutated genes from germlines, and its prospective reproductive applications in terms of disability rights.

The chapter has left numerous other questions unasked, however. Colleagues working on related topics are exploring issues like the role of power in the merging of knowledge production, venture capitalism, and entrepreneurial science, while also raising fundamental questions about social and reproductive justice (Wiel 2020; Kirskey, in press; see also Chapter 4). As Marit Melhuus (2007) aptly points out regarding the legal and ethical debates surrounding IVF in Norway, "procreative imaginations" provide sites from which to consider the high-stakes interplay between wonder, values, and power dynamics in the face of technologies that are accompanied by controversies and inequalities. Because I mostly envision this chapter as a means of inspiring debate—a tool for enabling discussions, which is both the product and the medium of sociological technology—I propose that the debate be kept open by the addition of a few more questions: Who would use IVG if it were actually available, and for what purposes? Would they use it simply to increase biological knowledge and the understanding of hereditary diseases, or to actually cure these diseases and create artificial gametes for those who can afford them? (This imagined possibility is discussed in Chapter 5). And what does an inclusive, intersectional democratic technology-making process look like? How do "we" get there? That is my take on a *sapiens* who is also *techno*. If we frame our questions with care and investigate them using interdisciplinary tools, there is hope that we will uncover some answers, naturally.

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