CALL FOR PROPOSALS
EQUIPEX

2010

IPGG

SCIENTIFIC SUBMISSION FORM B

Acronym of the project	**IPGG**	
Titre du projet en français	Institut Pierre Gilles de Gennes pour la Microfluidique	
Project title in English	Pierre Gilles de Gennes Institute for Microfluidics	
Coordinator of the project*	Name: **Patrick TABELING*** Institution: **Fondation Pierre Gilles de Gennes/ Pierre Gilles de Gennes Foundation (FPGG)*** Laboratory: Gulliver Laboratory, ESPCI-PARISTECH* Unit number: UMR7083	
Requested funding	Phase 1 **€ 6.733 M**	Phase 2 **€ 1.482 M**
Disciplinary field	☑ Health, well-being, nutrition and biotechnologies ☐ Environmental urgency, ecotechnologies ☑ Information, communication and nanotechnologies ☐ Social sciences ☐ Other disciplinary scope	
Scientific area	Microfluidics, chemistry, biology, biophysics, translational medicine	

*NB: In line with its federative, multi-institutions nature, the project will be coordinated on an administrative level by the Pierre Gilles de Gennes Foundation, a RTRA already federating the different institutions involved. This will give the project a strong consistency and governance, and simple financial management (see section 4.2 below), but this structure is not easy to reflect in the above form: this explains, for instance why the Scientific Coordinator and his laboratory are not directly affiliated to the coordinating institution.

Organization of the coordinating partner

Laboratory/Institution(s)	Unit number	Research organization reference
Fondation Pierre Gilles de Gennes	N/A	ESPCI-PARISTECH/CNRS/Institut Curie/ENS/ENSCP/INSERM

Organization of the partner(s)

Laboratory/Institution(s)	Unit number	Research organization reference
Ecole Supérieure de Physique et de Chimie Industrielles de la ville de Paris - ESPCI-PARISTECH	N/A	City of PARIS

Laboratory/Institution(s)	Unit number	Research organization reference
Institut CURIE Section de Recherche	N/A	Institut Curie/CNRS/UPMC

Laboratory/Institution(s)	Unit number	Research organization reference
Ecole Normale Supérieure - ENS	N/A	Ministry of Research

Laboratory/Institution(s)	Unit number	Research organization reference
Ecole Nationale Supérieure de Chimie Paris - ENSCP	N/A	City of PARIS/CNRS/Univ. Paris 6

SUMMARY

The scientific context of the proposal is **the creation of a new Institute, IPGG (Institut Pierre Gilles de Gennes), dedicated to microfluidics and its applications.** The Institute will be located in the centre of Paris 5 (Calvin street in the Fifth district) on a surface of 3000 sq m provided by the City of Paris. The aim of the project is t**o build and equip,** in the Institute**, the first federative technology platform in France specifically dedicated to microfluidics.** In combination with its outstanding interdisciplinary scientific environment, this will yield a unique world-level excellence centre to develop this field and its applications. In addition, thanks to the synergistic **coupling with an incubator of 1000 sq m** that will be hosted in the same building, the project will generate **new entrepreneurial activities** that will provide **a major return on investment for the country.**

The number of potential applications of microfluidic technology is considerable, and we are at the very beginning of an exponential growth. It has a huge potential for medicine, environment control, energy, "green" and safer chemistry, cosmetics, food industry... As a key enabling technology for "lab on chips", it will allow faster, cheaper and more accurate multiparameter analyses; benefiting applications ranging e.g. from ultra-high throughput screening for pharmaceutical research to "point-of-care" for the general practice and personalized medicine. Microfluidics represents, for biology and chemistry, the equivalent of the revolution brought out in electronics and computers, by the advent of microprocessors, and it has to potential to bring major impacts regarding a large number of the SNRI priorities in health, environment, energy and support to industry.

The project aims at raising three main bottlenecks that hinder the take off of microfluidics and its applications in France:
(i) Technology: The techniques and materials used in microfluidics have considerably diversified over the last few years. More than ever, the field needs to combine different technological approaches to face new fabrication challenges. The existing microfabrication platforms, built under a vision dominated by microelectronics, do not meet these requirements.
(ii) Cross-disciplinarity: Integrative by nature, microfluidics is an extremely interdisciplinary field that produces important discoveries by developing cross fertilization between different fields. Wide-scope multidisciplinary integration is particularly critical in this field.
(iii) Leverage between academics and industry: microfluidics is an application-driven field that tremendously benefits from a synergy between industry and academics. In France, there is an urgent need to develop this synergy and exploit the leverage between academics and industry to build up a strong entrepreneurial activity along with amplifying the impact of fundamental discoveries.

One goal of the Equipex project is thus to raise the three above bottlenecks, by:
(i) Building a world class microfabrication infrastructure, in which a unique combination of technologies pertinent for modern microfluidics research and development will be available: conventional microlithography (spin coating, aligners,...) along with a large palette of non conventional tools (high speed micromachining, stop-flow lithography, hot embossing, roll embossing, 3D photolithography, planarization…), along with a few conventional materials (PDMS, glass) along with a large palette of non conventional materials (thermoplastic or photocurable, elastomer or plastic, olefin, acrylic, silicon or fluorinated). This will be complementary with the existing network of microfab centers.
(ii) Gathering in a single building and around it a community of researchers at the highest worldwide level, sharing a unique platform; The partners already represent a unique environment in France with a long-standing tradition of interdisciplinarity and competences in physics, chemistry, biology and medicine; The project will build further on this already strong basis, strengthening cross-fertilization by exchanges on a daily basis between researchers and students having different cultures and backgrounds, and the development of specific training programs. This will be in an unprecedented situation to build up a world leadership in the field.
(iii) Producing continuity between fundamental research and start-up creation. The continuity is guaranteed by the presence of a 1000 sq m incubator linked to the Institute. The combination of the Institute and the incubator in the outstanding scientific environment of Paris Centre will represent a unique situation.

In the work program, efforts will be organized along three synergistic directions:
(i) Fundamental research in microfluidic concepts and components, in order to permanently feed the field with innovation (e.g. flow in carbon nanotubes, single molecule manipulations, biphasic hydrodynamics at small scales);

(ii) Forefront technological developments, in order to expand the "toolbox" available to both fundamental and applied projects (e.g. "paper microfluidics" technologies for low-cost applications, fluorinated-polymer based technologies for applications in microchemistry and digital microfluidics, controlled architectures for performing quantitative studies of single cells, fast prototyping strategies);
(iii) Development of radical solutions to important societal problems: this involves, a point-of-care device for the pre-symptomatic detection of neurodegenerative processes towards preventive medicine for Alzheimer, the development of digital microfluidics for high throughput quantitative biology on single cells, instruments for the routine sorting of circulating tumour cells for cancer treatment, or the use of carbon nanotubes as next generation sources of pure water and/or energy thanks to their unique osmosis properties.

In all cases, there is a high potential to produce breakthroughs in a variety of domains:
Carbon nanotubes may be assembled to produce membranes converting energy with unprecedented yield, desalt sea water orders of magnitude faster. Microfluidic capillary technology may induce breakthroughs in the diagnostic domains. Similar comments can be made for the detection of neurodegenerative diseases, the cancer treatment, quantitative biology.... The list of potential applications is indeed too long to fit in here, and only some of them will be developed in the body of the text. As detailed in section 2.2, a number of them will have a major impact on several SNRI priorities.

About 30% of the French microfluidic community will be for the first time working together in the same Institute; this will have a considerable impact on its organization:
The creation of the Institute will lead more than 100 researchers to work together in a technological ensemble unique in the world. This move will have obvious consequences in term of the research organization in Paris Centre. Besides the projects directly developed in the Institute, researchers will keep their current affiliation, avoiding destructuration and facilitating the dissemination of the technology. This platform, unique in France and Europe will have a strong national structuring effect. It will be made available through a nation-wide network and will have an impact at European level by facilitating, for instance, the launching of new European projects.

The project has the potential to double or triple the number of microfluidic start-ups in France:
The partners have a strong involvement in start-up creation, transfer to the Industry, and already have extensive partnerships with large groups (Rhodia, Unilever, L'Oréal, Schlumberger, etc...). The 1000 sq m incubator will be made available to industrial teams, for R&D projects. This concerns any industry, from start-ups in incubation up to major groups. We have the potential to multiple by 2 or 3 the number of start-ups existing in France in microfluidics.

The governance of the IPGG will make use of the management tools developed and validated over the three last years by the Fondation Pierre-Gilles de Gennes as well as the web platform set in place to sustain Private-Public Partnering for innovation**.**

Last but not least, the City of Paris already committed to provide the building and support its adaptation to science, for an estimated total cost of 38M€.

1. SCIENTIFIC ENVIRONMENT AND POSITIONING OF THE EQUIPEMENT PROJECT

The scientific context of the proposal is the creation of a new Institute, IPGG (Institut Pierre Gilles de Gennes), located in Paris Centre, dedicated to microfluidics and its applications.

The name of the Institute will be "Pierre Gilles de Gennes Institute", in honour of Pierre Gilles de Gennes whose scientific achievements have inspired generations of researchers worldwide, who had identified the innovative potential of microfluidics very early, and who will stay a strong reference for the participants to this project, regarding in particular his vision that scientific activity and societal needs/industry form a virtuous circle, and his success at proving it. The creation of the Institute being a project as a whole, a LABEX proposal will be submitted as a complement of this Equipex one. As we shall see, however, this Institute's "heart" will be a unique, dedicated technology platform, and the present project is focused on this aspect of the project.

The number of potential applications of microfluidic technology is considerable, and we are only at the very beginning of an exponential growth.

Microfluidic technologies are already impacting substantially a number of industrial areas, pertaining to printing industry (currently its largest market), chemistry, biomedical field, cosmetics, food industry, digital display, oil industry: billions of microfluidic-based printer heads sold worldwide per year, one million of chips sold by Caliper Agilent for the analysis of DNA samples [1], an outcome of fundamental research carried out in the early days of microfluidics [2]; Millions of chips sold by Abbott [3], dedicated to Point of Care applications, etc. The latter analytical chips have rather simple structures - microchannels engraved in plastic cards equipped with electrodes -. Their success comes from their low unit cost, their simplicity and reliability. They are routinely used in various clinical instances (surgery, emergency). Now, complex chemical and biochemical analyses can be tackled on commercial lab-on-chips. An example is the HIV chip, which performs a sophisticated analysis, providing a reliable response to the patient [4]. Large quantities of such chips have been provided to underdeveloped countries with the support of Bill Gates Foundation. Notably, too, "Next Generation Sequencing" technologies, a major breakthrough in biology with strong potential for medicine [5], is implemented in machines based on different principles at the molecular level, but having in common an extensive use of microfluidic technologies. More generally, microfluidics provides tools able to perform operations that previously necessitated high-skill labour and long time. Point of Care chips can be viewed as one substantiation of this concept.

Globally, we expect that within 20 years, most biological and clinical assay equipments, a market weighting billions of dollars, will be microfluidics-based The indirect cost reduction for the health system, thanks to the development of low cost preventive medicine and better prescription of drugs and hospitalization (notably in the personalized medicine approach of cancer) is expected to be at least 10 times the direct market of the tests.
Microfluidics will also be a key asset in the fierce international competition between pharmaceutical companies, as the only technology able to cope at a reasonable cost, with the explosive development of assays generated by the advent of pharmacogenomics and personalized medicine approaches.
Beyond the biomedical field, microfluidics also has a strong potential for Chemistry (chemical engineering [5], chemical synthesis [6], and analytical chemistry [7]). Substances difficult to synthesize often benefit from miniaturization [8]. Microfluidics-based chemical reactors dedicated to the production of unconventional products already exist [9], and it has already been demonstrated for instance that quantum dots acquire exceptional properties when synthesized in microfluidic reactors [10]. The capability to speed up the screening of complex fluids by orders of magnitude has interesting consequences in chemical engineering. In France, Rhodia systematically uses microfluidic screening prior to design production lines [11]. Last but not least, microfluidic technology has the capability to produce extremely well controlled droplets of micrometric sizes [12], generating applications in a substantial number of domains: food industry [13], cosmetics [14], vectorization [15], electronic display [16]... Some founders of IPGG are indeed at the forefront of this activity.

Finally, applications of microfluidics in energy (e.g. energy conversion based on reverse electroosmosis in nanodevices [17,18]), environment (e.g. distributed monitoring devices for water and air control, pollution control and biohazards prevention [19]), consumer products (e.g. droplet based displays, paper technologies) are still in

early infancy, but new and impressive perspectives open constantly (more examples will be given in section 2.2.1).
The creation of an Institute dedicated to this field and its applications will foster the build up of a French leadership in the domain and provide a return to investment for the country by generating ambitious entrepreneurial activities, improved competitiveness of existing industries, improvements of health, safety and quality of life, and considerable savings to the health system.

Microfluidics is also an active and innovative field of fundamental research, both as a provider of new tools for studying unsolved problems, and as a provider of new questions.

A first example is the study of single polymers subjected to elongational stresses, carried out in the early nineties by S. Chu's group [20]. Here microfluidics allowed the generation of elongational flows under exquisite control. This experiment had a substantial impact in single molecule studies. More recently, microfluidic technology has exploited complex fluids for producing actuators [21], has invented new microrheometers with interesting performances [22], and discovered new instabilities [23]. In the domain of rarefied gas dynamics, microfluidic technology has produced impressive sets of experimental information allowing for the first time to confront theories to experiment [24]. Many other fundamental fields of research are concerned by microfluidics, whenever fluids have to be or gain to be manipulated at the micrometric scale: functional biology [25], proteomics [26], genomics [27], crystal growth [28], material sciences [9, mesoscale physics [5], colloidal sciences [15]. A particular mention should be made for cell biology: Microfluidics provides the right tools to address physical, biological and chemical stimuli at the single cell level, and it is really revolutionizing this field at this very moment.

The scientific activity in microfluidics in France is well recognized (typically at the 4th to 6th rank worldwide), but this is insufficiently reflected in the French industry.

Measured on publications and participations to conferences, France has a good position in microfluidics on the academic level (at relatively even level with Switzerland, the birth country of microfluidics, or Sweden, behind the USA, Japan and Korea). On the industrial side, though, the USA have an insolent domination, followed by Japan and now Korea. The same countries that succeeded in microelectronics twenty years ago now lead the way in microfluidics. As an emerging technology with a rapid rate of innovation and technology obsolescence (which microelectronics was 20 years ago), microfluidics is well served by the "start-up" innovation paradigm: academic innovation stimulates start-ups which either die, or succeed in maturing technologies until they transfer it majors, or become major themselves. This industrial development, in turn, stimulates collaborations and reinforces academic research and innovation. Despite this strong potentiality of microfluidics in terms of start-up creation, there exists only a few microfluidic-based company in France (against 40 in the world). Even countries comparable to France or weaker on a strict academic level (Sweden, Switzerland, England and Germany) tend to do better industry-wise.

With too few exceptions, "lab on a chip" in France remains "chips in the lab".

This is probably one of the weakest points in our country at the moment. A full analysis of the reasons for this is beyond the scope of this presentation, but some elements directly relevant to our project must be noticed:
Entrepreneurship was traditionally weaker in France than in the USA, but this situation has been evolving fast in the last, say 10 years, and both strong institutional tools (OSEO, incubators) and a strong motivation among researchers now exist. Private financing, however, remains much weaker than in the US, notably for the early, most risky parts:
A difficulty, more specific to our field, is the lack of big majors of the Instrumentation industry in France, as compared to the countries leading the game (Beckton Dickinson, General Electric, Applera, Beckman-Coulter, J&J in the USA, Hitachi in Japan, Roche in Switzerland, Bruker in Germany, etc...). It is thus of paramount importance, to develop in France new companies able to enter the field, and to facilitate the access to the technology for existing medium scale companies already in the field (e.g. Biomerieux) or larger companies interested (see section 3 below).
Directly relevant to the project, finally, infrastructures able to develop microfluidic technologies along process lines easily transferable to mass production (i.e. the equivalent of the technology centres for microelectronics) do not exist in microfluidics in France as they exist at least to a better extent in other countries.

There is currently no platform in France, or even in Europe, proposing a panel of technologies well adapted for efficient problem-solving, application-oriented microfluidic research and development.

France has developed a strong network of micro and nanofabrication technology centres, which have stimulated the dynamism of its microelectronic industry (e.g. ST micro). Mostly, this field is based on a limited number of materials strongly dominated by silicon technology, and a race towards resolution (essentially linked to the cost of equipments!). Microfluidics shares with this field a strong dependence on technology, but in contrast with microelectronics, it has to manipulate a high variety of objects (chemical and biological molecules and components are hugely more diverse and complex than electrons and photons!), and must use for that use a wide variety of materials: glass, silicon, PDMS (PolyDimethylSiloxane), variousplastics, photocurable polymers, paper,... To take two examples, PDMS is excellent for rapid prototyping and valving but is unable to sustain pressure and has poor compatibility with many organic solvents. A thermoplastic, as e.g. COC, is a low cost raw material well suited to mass production, but it does not allow easy on chip valving, and only three labs in France are more or less equipped to process it for microfluidic applications. Finally, many of these technologies, such as silicones, micromachining, are a danger for conventional clean rooms, and thus forbidden in general-use clean rooms. Most often, microfluidic laboratories get specialized in one or two microfabrication techniques only, because technological developments are time-consuming and equipment-costly. Thereby, laboratories hardly investigate microfluidic applications that would require materials they are not accustomed to, or do their best with the technology they have, even if it is neither the most appropriate material nor the right technology. This has not deterred French labs to develop nice fundamental research and concepts, but this is a strong hindrance to downstream progress towards integrated, real-life and industrializable systems.
Because of the speed of evolution of the domain, and of the lag already existing, a FAST and STRONG action, levered on a strong existing community on the fundamental side, is an emergency.

Too many French biologists and chemists are disconnected from microfluidics technology and may loose competitiveness. Dissemination of microfluidic technology in the direction of end-user researchers and students must be reinforced.

The biological and chemical communities must be prepared to the advent of a paradigm shift, triggered by the microfluidics revolution, and at the moment, they are far from being sufficiently connected to the field. In addition, those interested in using the technology face difficulties, because the "specialist" teams have the good will to collaborate, but often do not have at home the technology suitable for each application, or simply the capability to produce the number of chips required by ambitious biology projects.
Moreover, the exposure of students to microfluidics is not sufficient at the moment in the French University. Most French students are well educated in a number of traditional subjects, but are unaware of the existence of this field. This contrasts with the US, where essentially all of the leading Universities teach microfluidic courses.
The situation would improve with the action of an Institute, organized to disseminate technological ideas towards researchers and students, and providing them with direct hands-on experience on the most relevant equipment. It is known that early exposure of students to a field is the best way to see them apply it later on in their own research, and to create cross-disciplinary synergies.

The Pierre-Gilles de Gennes Institute for microfluidics will create synergy between scientific expertise of excellence and an equipment platform able to manage an unprecedented variety of materials and techniques. This Equipex proposal concerns that equipment platform.

The partnership of this project (co-founders of the IPGG) will gather the scientific expertise of 5 resident teams led by P. Tabeling (ESPCI-PARISTECH), J.L. Viovy (Institut Curie), M. Piel (Institut Curie), J. Fattacioli (ENS) and M. Tatoulian (ENSCP). Non resident laboratories from Paris Centre will also have easy access; overall, the equipment platform will gather 13 laboratories representing 30% of the microfluidics community in France. Then, due its uniqueness in France, the project has a vocation and commitment to have a structuring role at the National and European level (see section 2.1 below). The management of the project will be ensured by the Fondation Pierre Gilles de Gennes, capitalizing on a proven model for research and development project coordination.
The foreseen equipment facilities will focus on rapid, low-costs processes for design and implementation. This unique combination of technologies associated to standard clean room equipments will favour the emergence of a world class centre of microfluidics, fostering the build up of a French leadership in the field.

2. TECHNICAL AND SCIENTIFIC DESCRIPTION OF THE ACTIVITIES

2.1. ORIGINALITY AND INNOVATIVE FEATURE OF THE EQUIPMENT PROJECT

By combining almost all the technologies suitable for rapid microfabrication existing at the moment, the equipment of the proposal will place the partners of the project in a situation unique in the world.

As said above, microfluidic technology makes use of a wide variety of materials: glass, silicon, PDMS, thermoplastics, photocurable polymers, paper... Most of the labs including partners of the project currently specialize in one, two or three microfabrication techniques at most, because technological developments are time-consuming and costly. This constraint is a real limit to unlock scientific bottlenecks. The project aims at circumventing this difficulty by setting up a platform incorporating an unprecedented diversity of materials, methods and expertises: this involves the coordinated conception and equipment of a clean room, a "grey room", culture rooms and microscopy rooms. The technologies to be acquired are focused on rapid, low-cost processes for design and implementation including soft lithography, plastic moulding, nanoimprint, photocurable resins and micromachining. The combination of these technologies, associated with standard clean room equipments, and specific characterization tools, will indeed be unique in the world, and consequently will favour the emergence of a world class centre of microfluidics, fostering the build up of a French leadership in the field.
This will provide, for the first time, a large microfluidics community, and a wider community of potential end-users (see organisation just below), means to use the optimal technology for each application, with minimal time and effort, and to keep up with the explosive evolution of the field with a reactivity out of reach of individual labs.

Local and National structuring effect: The project will structure the microfluidic community of Paris Centre, reinforce its international visibility, and nourish the whole national public and private community in the field with a strong research-based innovation flux. Association with a 1000 m² projects incubator to be hosted in the same building will be a winning strategy to foster public-private partnerships.

Gathering roughly 30% of French research in microfluidics, a strong scientific community is currently located in the Centre of Paris in the Montagne Ste Geneviève. Different groups already have collaborations but they are physically scattered in different places and developed locally several small scale microfabrication setups, altogether redundant and too limited in scope, performance and availability to others.
Hosting about 100 researchers in a unique building located in Calvin Street will reinforce everyday collaboration, allowing the unlocking of many scientific bottlenecks. Interactions between e.g. young researchers or students and more experimented ones, researchers mastering various microfabrication techniques, researchers providing a unique variety of expertises on different materials and surface properties, will produce a strong synergy in Paris Centre. This structuring effect will be reinforced with the opening of the Institute to other non-resident national and international teams. This will be organized in different “circles”:
- As a "first circle" (Equipex partners), five teams (mentioned in section 1) will move into the building located on Calvin street. Additional space will be set aside for hosting for typically 5 years additional outstanding junior teams, in order to bring in new subjects and expertises and favour dissemination and seeding.
- Physically not located at Calvin Street, seven research groups will belong to the Institute, forming what we called a "second circle". These groups are led by J. Bibette, (ESPCI-PARISTECH) MC Hennion (ESPCI-PARISTECH), J. Vinh (ESPCI-PARISTECH), U. Bockelmann (ESPCI-PARISTECH), Pierre Gareil/Christian Girard (ENSCP), V. Croquette/D.Bensimon (ENS), Y.Chen (ENS), M. Dahan (ENS), P. Silberzan and A. Buguin (Curie). Benefiting from an attractive effect, we are convinced that a number other groups and projects on the Campus could benefit from microfluidics, and will be motivated to join this second circle when its potential will be made stronger, more easily accessible and more visible by the project.
Finally, this local structuring effect will also favour transfer towards industry and end-user market, thanks to the strong existing entrepreneurial culture and personal network of some partners, and to the associated projects incubator (detailed in section 3.2)

The action of the Institute will help structuring research in France and in Europe.

Such a unique combination of equipment in France will benefit the whole French microfluidics community (through a "Third Circle" network) by providing a set of tools it currently lacks. The project **will complement the national network of micro-nano-technologies** "centrales", **not duplicating** expensive equipment available there, such as e-beam, high resolution electron microscopes, large wafer technologies, **but focusing on alternative and non-conventional technologies**.
With the number of researchers involved, the Institute will strongly increase the international visibility of the French Community, and have the capacity to heavily contribute to the initiation of networks in France or in Europe. Nationally, it will e.g. be an active member of GDR microfluidics. It will help existing networks (such as Optics Valley) to get involved in microfluidics, and will also be in synergy with the Saclay campus and Nano-Innov initiatives. Finally, several partners are already strongly involved in European projects (see section 2.2), and the Institute will increase their leverage.
At the education level, the Institute will create a new Master2 centred on fluids and microsystems. This new Master will expose students to fields likely to play a role in the development of their professional careers. Owing to the crucial roles the student play in the laboratories, this action will also be a factor of structuration of the scientific community in France.

Multidisciplinarity and complementarity of the partners will be key assets for the Institute.

Furthermore, microfluidics is intrinsically a multidisciplinary and multi-applicative science and experience has shown that benefiting from cross disciplinary interactions is a key for success. The Institute will host chemists, physicists, physico-chemists, biologists and biophysicists. They will cover a uniquely wide range of skills necessary to complete microfluidics innovative research and to successfully optimise and use all technologies involved in the equipment. Furthermore, combining various skills allows the venture of riskier projects with high potential impacts and added value.

The foreseen combination of equipment in the building on Calvin Street will generate an attraction for all researchers involved in microfluidics activities. The dissemination and exploitation actions will be based on this "attracting effect" to radiate towards the public, scientific, student communities and industries. In addition, exploitation activities will be performed in the framework of the outstanding entrepreneurship culture of the Equipex partners (ex: ESPCI-PARISTECH) and a synergy with the 1000 m^2 incubator to be hosted in the same building.

2.2. DESCRIPTION OF THE PROJECT

2.2.1 SCIENTIFIC PROGRAMME

International positioning and originality: the project of creation of the Institute, the way how we envision it, and the equipment we are applying for, are unique in the world.

Various Institutes dedicated to microfluidics exist; however, they differ in many aspects from the one we propose to build. Starting with Europe, we may mention the following Institutes:

- MESA+, located in the Netherlands, is one of the largest nanotechnology research institutes in the world. MESA+ employs 500 people, with 275 PhD's students or postdocs. It holds a 1250 sq m clean room and has been the breeding place for more than 40 start-ups. The scope of MESA+ extends well beyond microfluidics. The clean room of MESA+ is focused on Silicon technologies and it has not developed substantial activities based on rapid technologies. There will be an obvious complementarity between this Institute and the one we propose to create, but our aim and content will be very different, since MESA+ main focus and equipment remain on "hard" MEMS and micro-nanoelectronics (in this respect it is closer to the spirit of e.g. MINATEC), whereas we focus on microfludics and technologies NOT AVAILABLE in "hard microfabrication" clean rooms.
- MIC, located in Denmark, was funded in 1991 to promote the creation of new high tech micro and nanotechnology based industrial activities in Denmark. It employs 110 people, and has a 700 sq m clean room, whose conception is essentially inspired by microelectronics. Similar to MESA+, there will be a complementarity between MIC and the Institute we propose to create (Notably, partners of the project are involved in strong European collaborations with MIC).
- The Institute for Microtechnique in Mainz (IMM) (specialized in applications to chemical engineering) and the Institute of Micro and Nano Fluidics of Darmstadt includes 12 people, are not comparable to our project.

Outside Europe, microfluidic research is mostly organized in groups led by individual professors. Their size varies between 10 and 60 researchers (D.Weitz and G. Whitesides, Harvard and S.Kitamori, in Tokyo are the largest groups). The structure of these entities is different from the one we plan, which brings together several teams. Nonetheless, a few structures offer interesting models with partial overlap with the project of Institute we propose.

- Micro/Nano Fluidics Fundamentals Focus (MF3) is a structure that incorporates ten professors in San Diego University and ten external professors. The centre, supported by DARPA, is dedicated to bring closer fundamental research and industrial activity. This is what we plan to do in the Institute.
- The “Stanford Microfluidics Foundry” was founded in 2005 by Prof. Stephen Quake. The platform proposes its services to the industry and academics as a subcontractor, providing consulting, process development and fabrication of custom design microfluidic devices (microfluidic valve technology and chips) upon given specifications. The Stanford Microfluidics Foundry is focused on a mono-technology of soft-lithography using polymer materials (polydimethylsilane: PDMS), so in this respect its scope is narrower than ours (and, with all respect due to S. Quake and the success of Fluidigm, less potential for industrialization, because PDMS technology has a much narrower range of applications there than e.g. thermoplastics). However, this foundry will be a source of inspiration for us concerning the dissemination of technologies among different communities.
- Prof Kitamori (University of Tokyo and KAST, Kanagawa Academy of Science and Technology, in Japan) has also developed an interesting model, in which fundamental research around the concept of "integrated laboratory" is performed around a 1000 sq m clean room, but space is also reserved on site for industrial teams within time-limited projects using the infrastructure in collaboration and the help of researchers. Although this platform is essentially focused on glass, and thus less wide scope than ours, and "mono-partner" on an academic sense, we got inspiration from it as a powerful way to foster academy-industry partnerships and technology transfer.

Notably, the above model for technology transfer is also the one chosen in France, at Institut de la Vision, led by Prof J. Sahel, who is providing us advice about the specific institutional aspects of this model in France. As a difference, this Institute is focused on a family of applications, and ours is based on a family of technologies, and open to applications in various fields.

This brief review shows that the project of creation of the Institute, the way how we envision it, and the combination of equipments we are planning, have taken inspiration from success stories all around the world, but are indeed a unique combination worldwide in terms of domain, scope and structure.

The groups involved were selected for their strong international recognition and achievements in the field (the partnership is described in sect. 4.2.1, for the sake of terseness we do not repeat it here), but the project of creation of a federative Institute in this topic and the platform to be built, are completely new. It stems from exchanges between ESPCI-PARISTECH, Curie, ENS and ENSCP who reached the conclusion that microfluidic research should substantially expand, and that the Paris centre campus is the ideal scientific environment to do it. The availability of the 4000 sq m rue Calvin, placed in a close proximity to all the partners, in a location where space is extremely rare, is a unique opportunity to achieve this synergy. Notably, too, it allows this build-up while keeping all researchers affiliated to their current laboratory, i.e. without any destructuration of the existing research, and maximizing the potential of irrigation towards a vast scientific and industrial community.
The project will substantiate and amplify the action of the Pierre Gilles de Gennes Foundation consistently with other initiatives (Institute of the cold atoms, IBENS[1], Development Biology Department of Intitut Curie and Institut Langevin), IPGG will demonstrate all the benefit the community may gain from fostering synergies between researchers in Paris Centre, and somehow encourage them to work in similar directions.

Microfluidics, in particular the development of highly integrated, operation systems, is intrinsically highly interdisciplinary, and the partners have demonstrated their ability to lead interdisciplinary projects. To avoid repetitions, we shall not insist on the added value of the consortium in this respect, since it will be described further in section 4.2. We focus here on practical implementation, taking as examples a few specific projects that will extensively use the equipment, and respond to major SNRI challenges.

Operationally, three types of research tracks will benefit from the platform, and from mutual interactions:

- **Fundamental microfluidics**: Past experience shows that the "de Gennes paradigm" of cross-fertilization between fundamental and applied research works extremely well in microfluidics. As a single example among many possible, the MMBM group discovered a new electrohydrodynamic instability in microspace, while searching for improved DNA analysis methods [29], which in turn led to a series of theoretical and experimental studies [30,31] and new applications [32]. The consortium's fundamental research will benefit from the new tools offered by the platform, by interactions with end users, and will in turn benefit to more finalized project by providing model experiments and powerful interpretation frames.
- **Technology:** Most partners in the project have already strongly contributed to the development of new technological concepts or "bricks", in microfluidics and non-conventional microfab (see e.g. [33-36]). This will be intensified thanks to the equipment, yielding innovation and providing the Institute and the French microfluidic community (both academic and industrial) with unique tools and competitive advantages. Surface properties, microreactors, spectral characterization, functionalization are ubiquitous components of microfluidic devices. Chemists will also have a strong technological contribution, helping to understand the chemical processes at hand and proposing solutions.
- **End-user driven research:** Obviously, biologists, clinicians, chemists, instrument developers, will benefit, thanks to the project, of the best technologies and expertises to develop instruments and experimental platforms not available in combination in a single place anywhere else in the world. This will benefit fundamental research, clinics, and industry;. Conversely, physicists and chemists involved in biotechnological projects will need the experience of the biologists. Microfluidic integration of lab on chips often requires abandoning current protocols and inventing new ones. This can be done only by combining the knowledge of biologists on the behaviour of their objects of study, and the knowledge of physicists and technologists, about what is possible in microfluidics.

The scientific objectives of the project will combine build-up on the themes already pursued by the different teams, strengthened by the new equipments of the Institute, and radically new projects feasible only with the new

[1] Institut de Biologie de l'Ecole Normale Supérieure

equipment. Considering the size of the community concerned, we can provide below only an exemplary selection of projects[2]:

Cells in confinement (fundamental): Cells in tissues lack space: they are confined by extra-cellular matrices and by other cells. This simple fact has been underestimated in setting cell culture devices, and recent discoveries on immune cells showed that it is a key element to consider when studying cell behaviour. Only micro-fabrication can provide a way to build devices with relevant geometry and physical properties. **Relevance:** Materials to be used in such devices must have special properties, confining cells at micron scale but allowing molecules to diffuse to allow cell survival and growth. Such materials could be hydrogels. **Bottlenecks*:*** Combining microfluidics and hydrogels at micron-scales, and performing high resolution microscopy has been achieved only in a few very simple cases. **Expected outcomes:** New devices allowing cells to be cultured and studied in complex 3D environments with control of mechanical properties as well as nutrients and other chemicals. Such devices will allow new fundamental discoveries and could also be a starting point to design artificial organs. (SNRI priority "improve our understanding of the mecanisms of life")

Energy (End-user and fundamental): Microfluidics contributes to the energy issues of the planet in various ways: miniaturization of conversion devices, improvement of oil extraction technologies, enhancement of energy storage capacities. Nanofluidics will contribute as well: slippage phenomena in carbon nanotubes may lead, if confirmed, to invent entirely new conversion energy systems (based on reverse electroosmosis), with an impressive yield - almost 100%-. **Relevance*:*** With the existing groups involved in these subjects, and the hosting of a non permanent researcher in the Institute, there is an opportunity to amplify the action of French research in the domain of the energy, thus contributing to face challenges exceedingly important for the planet. **Bottlenecks*:*** this is still a very early field, and first bottlenecks lie in the accurate characterization and confirmation of the phenomena: providing estimates for slippage along graphene/graphite surfaces, or within nanotubes that would allow the assessment of the extent to which nanotubes membranes may be usable for energy conversion. **Expected outcome*:*** In the long term, a new energy generation system based on osmosis (which could also in a different setup, be use for water purification, another major environmental issue), thus responding to SNRI priority "ensure a carbon-less energetic future".

Micro-biology in microfluidics (end user driven, fundamental): Single celled micro-organisms constitute the largest biomass on earth. Many of these organisms have become model systems to study fundamental biological processes, as they are often easier to genetically manipulate. The knowledge accumulated now allows using these organisms in industrial contexts, ranging from food to organic chemical synthesis (the French company Metabolic-Explorer is a world leader in this area) and even building industry with bacteria selected to produce 'bio-concrete'. These organisms which most of the time live in liquid environments, allowing not only fundamental studies, but also in vitro Evolution, selecting best fit cells for a given purpose. **Relevance*:*** Miniaturization allowed by microfluidics makes it possible to perform high throughput experiments on small scale devices with unprecedented control.. **Bottlenecks*:*** The challenge will be the integration of the analysis device (for example microscopy, fluorescence etc…), the cell sorter and the microfluidic device handling cells (allowing growth in controlled conditions, and recovery of selected cells). The Institute will gather leaders in microfluidic sorting (JLViovy, P Tabeling), integrated analysis tools (JL Viovy, Y Chen), cell handling (SR Quake), making it the ideal place for a micro-biologist to develop such approaches. **Expected outcomes*:*** Outcomes would range from fundamental research on micro-organisms (performing efficient high-throughput phenotypic screens on mutant collections, to Experimental Evolution (a component of SNRI priority "development of synthetic biology"); These technologies can e.g. be applied to selection of mutants best fit for given purposes (notably biotechnologies for health or bioremediation)

Paper microfluidics and wettability patterning (technology): Paper technology was initiated in Whitesides's group (Harvard). It completely renews microfluidics: no more top and bottom walls, no pump, all fluid movements are based on capillarity and wetting. This cheap technology, based on materials available across the world (as long as there is wood), has interesting applications in the low cost diagnosis domain, and is contributing to health care issues in underdeveloped countries. **Relevance:** With the combination of expertises existing in the Institute,

[2] To facilitate follow up by readers of the projects, which are very diverse;, we shall comment for each of them sequentially on the project's content, the relevance of the equipment, the bottlenecks, and the expected outcomes and evaluation criteria

in the domain of fluidics, diagnostics, technology (P.Tabeling, JL Viovy, M. Tatouilian), the subject can be easily taken up. The method will rely on complexifying paper devices, and work on sheets made in different materials. **Bottlenecks:** The bottleneck will be to find techniques that would allow paper (or other material) technology up to perform tasks similar to standard microfluidic devices so as to broaden the scope of this elegant approach. **Expected outcomes**: Much remains to be done to improve the technology. Can we drive droplet through sheets? Can we monitor all sorts of chemical products? Use electric fields? On the applied side: Development of the capabilities of this approach in the diagnostic domain, in biology (where direct access to the microchannels with micropipettes may offer substantial advantages), contributions to health care issues in underdeveloped countries (SNRI priority "respond to major challenges in public health").

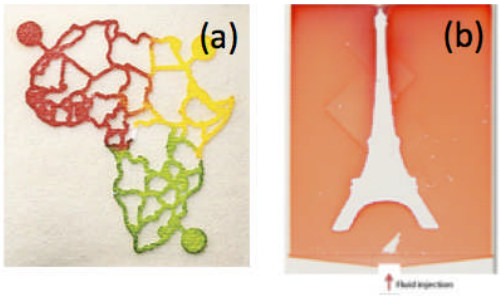

Figure 1: Patterned wettability can be used to drive fluids: (a) is an example provided by Whitesides's group, where colored water is driven through the pores of a patterned sheet of paper by capillarity, (b) example provided by M.Schneider (MMN), in which oil (red) is driven selectively through a PDMS network of 200000 microchannels where surface properties have been patterned. Surface property patterning can be used with many materials, opening new avenues in microfluidics.

Development of "Fluorocarbon" microfluidics (Technology): Finding compromises between cost, processability, biocompatibility or chemocompatibility and physical (for instance optical) properties is often a "squaring the circle" challenge in microfluidics. Fluorocarbon based chips would be interesting regarding chemical inertness, but so far only an extremely expensive material [37] was available for microfluidics. **Expected outcome:** We plan to develop a new fabrication line for fluorocarbon chips combining good optical properties, biocompatibility and low cost. This technology will, among others, be useful in the project "single cell studies"; and for the development of "green chemistry" (SNRI priority "support new industrial tracks in environment") **Relevance:** This kind of technology is not available elsewhere in the world, it is thus typically a win-win development, which will benefit from the unique equipment of the platform (roll embossing) and will in turn give a unique advantage to many other projects. **Bottlenecks:** Processing and bonding of fluoropolymers is problematic and requires innovation. **Success criterion*:*** A robust, reliable and industrializable protocol, and validation in routine bio applications.

Biomaterials and nanostructures for regenerative medicine and tissue engineering (Technology): With the rapid increase of the life expectancy, all countries are facing the aging problems in various aspects. One solution is to develop regenerative medicine and tissue engineering technologies for repairing or replacing damaged organs or tissues. Different strategies have been proposed but all of them rely on both fundamental understanding of cell culture and different behaviours, cell-material interaction, as well as advanced technologies for material processing and device fabrication. **Relevance**: The most fundamental issue in this field concerns microenvironmental regulation (and monitoring) of cells at both single cell and tissue levels. Therefore, the development of new biomaterials, nanostructured microfluidic network has the great relevance for the remodelling of both extracellular matrix and soluble cell factor flows. **Bottlenecks**: The bottleneck is the three dimensional integration of cell-material systems and the mass fabrication of the proposed architectures. Combinations of both conventional and non conventional fabrication technologies will be used to reach the objective. **Expected outcome**: The development of several state-of-the art technologies that can be relied on for different tissue models and regenerative medicine investigations (SNRI major challenges "strong expectations regarding quality of life" and "age related diseases").

Liquid/liquid extraction: short times phenomena (End-user driven)
Microreactors (continuous flow or droplets ones) accelerate separation and allow strategies to take in charge selectivity for the extraction of inorganic cations. They can be used as convenient tools to investigate separation phenomena, explore selectivity of extractants and screen their efficiency, of courses as soon as spectroscopic techniques, allowing a local characterisation of the species in the channel, are available. **Relevance*:*** The understanding of the extractants selectivity is a key issue for nuclear engineering and optimization of fuel cycle.

Collaborations with CEA/DEN and CEA/DSM will be established on this program. **Bottlenecks*:*** Local concentration measurements techniques have to be imagined; local phenomena at the nanometric scale will be difficult or impossible to image. **Expected outcome*:*** Understanding the origin of the selectivity of extractants and optimisation of extraction processes.

Point-of-Care Device base on the On-Chip Fabrication of Nanosized Drug Delivery Particles (End-user and Technological): Blood injectable drug carriers are complex muticomponent colloidal particles since the active molecules should be embedded in a carrier material rendered stable in the physiological medium but also specifically adherent to target cells within the organism. Moreover, the size of the particles should be small enough, less than 100 nm, to circulate freely in the blood tract in an harmless way and with the most efficient biodistribution [38]. **Expected Outcomes**: Fabricate a microfluidics « point-of-care device » able (1) to monitor a biochemical signal (2) to fabricate on-chip nanosize (<100 nm) particles with a varying composition of the active molecules that depends on the input biochemical signal, (3) inject the particles in the blood tract of the patient; **Relevance**: This project asks for a background in (1) device and micropumps fabrication, (2) design of particles and their physical chemistry, and (3) biochemical characterization of diseases, which makes the institute as the most suitable place to perform it; **Bottlenecks**: The bottlenecks are (1) the fabrication of nanosize particles in a microfluidic device. The solution we propose is to integrate anodic alumina membranes in a chip so we can use their internal structure made of regularly ordered nanosize pores as an emulsification mean [39]. The particles will be then used in a liquid state or after solidification/polymerization (2) the fluid handling in the chip without microsyringes or big pumps. The chip should be able to work easily with micropumps (e.g. Electro-osmotic pumps) to minimize the size of the final device; **Success Criterion**: The project should lead to the fabrication of a demonstration device able to work *in-vivo* on small animals such as mice.

Cell-based Molecular Diagnosis of Cancer (end-user driven): 90% of cancer casualties are due to metastatic relapses, due circulating tumour cells (CTC) that escape from the primary tumour, circulate in the blood, stop in some distant organ and develop again. They often acquire in the process new features that make them resistant to treatments. Detecting and typing these CTC for therapy optimization is a major challenge in cancer today. We shall use for that a self-assembly technology Ephesia, invented by partners of the Project [33]. **Expected outcome**: We plan to develop microfluidic integrated systems able to detect and type CTC with high sensitivity; Applications involve molecular typing for treatment optimization and fundamental research on the metastatic process (SNRI priorities "respond to major challenges in public health", "age-related diseases" and National Priority "Fighting Cancer"); **Relevance:** This project (associated with a EU project CAMINEMS coordinated by Curie Institute) is a complex microfluidic development, that aims at chips that can be mass produced at low cost, i.e. require the Platform equipment; **Bottlenecks:** A clinical validation of Ephesia was made on microsamples [40], but the extreme rarity of CTC will require the processing of several ml of blood and a huge specificity with regards to normal white blood cells; the complexity of cell surface-interactions. **Success criterion:** blind comparison with competing technologies on clinical samples at Curie hospital.

Early diagnosis of Alzheimer for preventive treatments (End-user driven): Alzheimer's disease is a dramatic health problem. It is associated with a progressive neurodegenerescence that starts 10 or 20 years before the first symptoms. No cure exists, but protective treatments able to retard neurodegeneration are under development. **Expected outcome:** to develop a microfluidic "point of care" system able to detect, in blood, biomarkers of neurodegenerescence as early as possible before the symptoms, in order to apply preventive treatments. Curie is involved in a large EU project (NADINE, 11.6 M€) towards this high-risk/high impact challenge, corresponding to SNRI challenge "development of age-related diseases". The same technology toolbox will also be applied to a point of care device for rapid and low-cost diagnosis of nosocomial infections (SNRI challenge "emergence of infectious diseases". **Relevance:** The Platform will strongly increase the chances of the success, notably because the final aim is a routine, low cost device for preventive medicine that will require plastic-based, mass produced chips. **Bottlenecks:** The main bottlenecks are first, the complexity and variability of biomarkers in blood (a challenge for biologists and clinicians), and second the extremely low concentration of some of these biomarkers, making innovative microfluidic and detection technologies necessary. **Evaluation criteria:** clinical screening and ability to detect Alzheimer disease and differentiate it from other neurodegenerative conditions

Single cell studies (end user driven): Single cell studies based on droplet technology request materials that are rapid to microfabricate (in order to change geometries easily), impose producing droplets under control (imposing specific surface properties) and in many cases, impose performing RT or PCR studies (imposing small thermal expansion and no gas permeability). **Relevance:** PDMS is not suitable for this task. Using different materials (fluorinated materials, NOA, plastics) will be feasible in the technological platform of the institute. **Bottlenecks:** Technology is not the only bottleneck. The pertinence of the biological analysis to be made with single cells, the constraints conveyed by the molecular biology techniques, the compatibility with droplet dynamics, will require exchanges between biological and hydrodynamical expertises. Collaborations between various partners (for instance JL Viovy and P. Tabeling's teams) within the Institute will have the potential to generate a leadership in this area; **Expected outcomes:** Realization of prototypes operational for biological and biomedical studies, generation of new insights into the behaviour of cell populations, high throughput platform for systems and synthetic biology (an SNRI priority), and performing analysis pertinent for biomedical applications.

Reconstruction of complex, biomimetic neuron architectures (End-user driven): The connectivity architecture of the nervous system is at the heart of its function (transmission, processing and storage of information) and dysfunction (i.e. the propagation along neuron network of neurodegenerative processes). Current experimental models for neurosciences involve either biological tissues, which have the right connectivity but can hardly be studied at the single cell level, or in vitro culture, allowing single cell observation but lacking physiological organization. In collaboration with neuroscientists (willing to join the platform) we invented a new concept, the "neuron diode", allowing for the first time the in vitro reconstruction of complex, deterministically directed and physiologically relevant neuron networks [41]. **Expected outcome**: We plan to develop a full microfluidic platform of technologies based on the neuron diode, as a new experimental model for neurosciences. Applications will be, for instance, understanding the cell signaling processes at play in Alzheimer, the testing of neuroprotective drugs (SNRI challenge "development of age-related diseases"), or cognitive sciences studies; **Relevance**: Again, this will require major microfluidic developments, intense chip production, and technological innovation. **Bottlenecks**: The fragility of neurons, the complexity of their mutual interactions, and the need for exquisite fluidic control to keep neurons alive and well controlled for weeks. **Verification means**: Achievement of spectacular neuroscience studies.

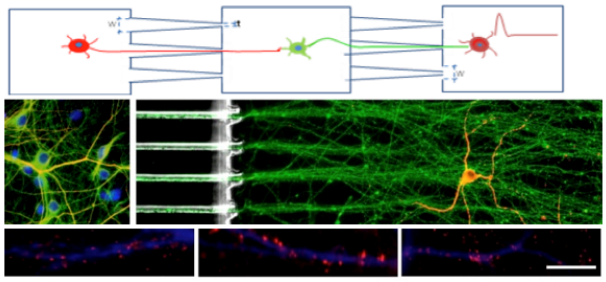

*Fig 2: **top**: example of a simple use of "neuron diodes", to cultivate three different populations of neurons in an asymmetric connectivity sequence identical to that appearing in live organisms. **Middle:** Cortico-Striatal coculture: Striatum neurons (yellow) were cultivated in the right chamber, and then cortical ones in the left chamber (nuclei stained in blue), projecting axons (labelled in green) towards striatal ones across neuron diodes. Bottom: higher magnification (scale bar 10 µm) of synaptic markers (red) onto striatal dendrites (blue), demonstrating functional synapses with the cortical axons.*

From cells to tissues (end user driven): On the way to the holy grail of tissue engineering, micro-fabrication and in particular microfluidics has a lot to bring. Growing tissues might involve manipulating several cell types, grown together in a well defined 3D configuration defined at the micron scale, it also requires bringing nutriments to the heart of large cell assemblies, which could be performed by artificial 'blood vessels' using microfluidics. **Relevance:** Assembling complex tissues will require a good knowledge of cell biology but also innovative microfluidics. No place in France combines both expertises in a single structure. **Bottlenecks:** Providing nutrients to cells in a large architecture is one of the challenges of such approach. **Expected outcomes:** Fundamental discoveries about complex multi-cellular assemblies; new methods for tissue engineering; application to the study of tumour growth ex vivo ((SNRI priority "improve our understanding of the mecanisms of life" and national priority "Fighting Cancer").

Regarding the economic advantages, the foreseen equipment dedicated to the above described projects will provide solutions to numerous bottlenecks in a wide range of research themes, which would not have been possible without this combination of equipment owing to cost and time-consumption in mastering all these techniques.

2.2.2 STRUCTURE AND BUILDING OF THE EQUIPMENT

The building blocks composing the equipment will be set-up in the building located "rue Jean Calvin, 75005 Paris" within the Institute premises. All building blocks are brand new pieces of equipment unless identified otherwise. The equipment was broken down according to the following building blocks:

Elements #1,2&3: The clean room will be the central part of the Institute. It will replace and extends the one currently present in ESPCI-PARISTECH (40 sq m). Designed to host 15 users max everyday, this clean room will be dedicated to critical operations necessitating purified air, hygrometry control, temperature control, desionized water. Some microscopes will also be set-up inside. The class will be 10 000 (ISO7). Associated to the clean room, the maintenance rooms will host all the necessary facilities for the clean room operation such as: air filtration devices, water purification systems, insulation, pumps, thermal regulation systems, sonic attenuation system... All details concerning the clean room and the maintenance room can be found in the cost estimate established by VEPRES company, joined to the proposal.

Element #4: A grey room will be installed for operations requiring lower levels of cleanliness (Class 1 000 000, ISO9), and temperature and hygrometry control. This room will enable to speed-up a part of the microfabrication processes. It will expand and replace the grey room already existing at Curie, and the equipment already purchased will be transferred to the new Institute (for a total estimated value around 150 k€). This includes small scale hot embossing and roll embossing equipment, hood, optical profilometer, an original convective self-assembly setup, clean hoods. The details concerning the grey room and the associated maintenance room can be found in the cost estimate established by VEPRES company, joined to the proposal
The additional equipment claimed within Equipex is listed below

Element #5: An observation room will also be implemented and will be equipped with a scanning electron microscope equipped for material analysis and a large variety of microscopes allowing observation of biological samples as well as materials and video follow-up.

Element #6: A cell culture room will be designed dedicated to biology experiences on living cells.

Element #7: Specific equipment in teams' laboratories will be needed to conduct research projects.

The detailed composition of the new equipment is detailed below:

Element 1: Clean room (class 10 000)

Technical space	space dedicated to host filtering, extracting systems, desionzed water sources, thermal regulation systems, hygrometry control systems assiociated to the clean and grey rooms
Room layout	Facilities, ground, standard laboratory equipment, electricity, fire detection, hoods…

Element 2: Equipment for the cleanroom

8 Hot plates	Dedicated to soft-bake photoresists in the photolithgraphic process
Spincoater	Spreads photoresists onto a wafer under precise control
Reactive Ion Etching	plasma etching technique used to pattern thin layers on various substrates
Deep Reactive Ion Etching	Useful for accurately etching deep microchannels in different materials
PECVD system	Plasma Enhanced Chemical Vapor Deposition system : PECVD is a process used to deposit, on a surface, thin film of materials starting from gases.
Aligners	Crucial equipment for the photolithgraphic process; it allows to align masks and wafers mechanically; under UV illumination, il allows to transfer patterns from the mask to photoresist layers
Microsonic multipurpose bonder	Used for bonding with accurate positioning (few µm)
Wire bonding	Used for interconnecting electrical devices, integrated cicruit or electrodes
Oven	Used for harden photoresists patterned by the photolithgraphic process
Oxygen plasma	Activates surface to favor bonding and hydrophylicity
Direct lithography	Apparatus dedicated to transfer directly patterns from a mask to a substrate
Profilometer	Allows to determine microchannels or moulds profile with a nanometric accuracy
Ellipsometer	Equipment for surface characterization

Element 3: Observation systems for the cleanroom

reflection straight microscope	Allow observation for non transparent substrate with different modes: bright field, dark field, interferential contrast
Scanning Electron Microscope	Used for high resolution (down to 10 nm) observation and surface analysis of patterned substrates

Element 4: Grey room (class 1 000 000)

UV Lamp	Used for polymer curing or for low resolution photoresist exposure
Aligner/Holder	Allows to align two pieces of sizes larger than standard wafers
Plasma system	this system will be used for surface activation and cleaning
Spin coater + Spin coater PDMS	Required to deposit uniform layers of various polymers and photoresists on surfaces
Hoods	Provide clean environment for substrate handling protected areas for solvent manipulation
2 inverted microscopes	Low magnification microscope and conventional inverted/straight microscopes for patterned surfaces characterization or microfluidic channel observation
Reflection straight microscope	
UV oven	For solidifying photocurable glus and achieve bonding ("sticker technology")
Micromilling	Used for low resolution (>10µm) polymer or metal surface structuration and microfluidic device fabrication. Adapted to rapid prototyping.
Hot embossing system	Used for low chip fabrication though polymers molding at high temperature and pressure
Roll embossing	High throughput polymer chip fabrication
Injection moulding	Semi industrial system used for the manufacturing of small series polymer microfluidic devices
Room layout	

Element 5: Observation room

Confocal classic microscrope	Microscrope to realise optical sections in thick samples
Spining disk confocal microscope	Microscope to realise high spatial resolution fast confocal microscopy on living cells
Video-microscope	Microscope to follow up automatically living cells with high spatial and time resolution
3 biostations	microscope to realize video-microscopy experiences with low or medium magnification
Room layout	Black ventilated room

Element 6: biospaces

3 hoods	Laminar flow worstation to allow steril work
3 incubators	Cell incubator with temperature, humidity and CO2 control and automatic sterilization
3 microscopes	Inverted microscopes for fluorescent cell observations with low magnification
Confocal macroscope	Crucial equipment for determining the spatial distribution of fluorophores in micrometric systems
Centrifuge	Bucket centrifuge to collect cells with temperature control
Liquid nitrogen storage	Liquid nitrogen canisters for long term cell storage
3 sterilizers	Sterilizer for yeast and bacteria incubation on petri dishs for various temperatures (23/30/37°C)
3 thermostatic shaking baths	For yeast and bacteria liquid growth
Cell culture	
Room layout	P2 standard, air conditioning, filtration, overpressure for sterilised environment

Element 7: laboratories

Team equipment	Standard equipment for each laboratory space
Start-up package for hosted teams	Standard initial equipment for new hosted teams

2.2.3 TECHNICAL ENVIRONNEMENT

As described above, the equipment will be installed in a building located in the centre of Paris, in the vicinity of the co-founder partners in the "Montagne Ste Geneviève": 6 rue Jean Calvin, 75005 Paris [Fig 3, left].

Figure 3: (left) picture of the front of the building hosting the Institute, Calvin street. Seven floors will be used by the new Institute; (right) localization of the Institute, showing its proximity with the partners of the project

The localization of this 4000 sq m building is a crucial asset of the project as the allocation of such area in Paris Centre is a remarkable incentive. This proximity with the co-founding partners [Fig 3, right] will provide a campus effect, combining equipment, research teams and a coupling with the incubator of 1000 sq m in the same building.

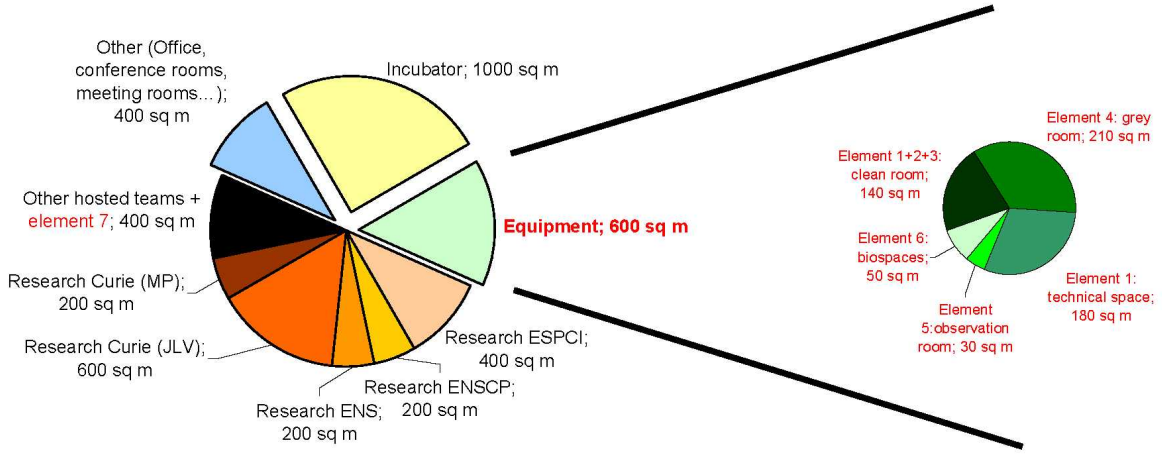

Figure 4: Surfaces allocated to labs, partners, clean room, grey room, and incubator in the IPGG building

The environment dedicated to the equipment (600 sq m) is shown in Figure 4. The equipment (light green sector) will be located in the same building as the research teams and the Incubator (yellow sector). The surfaces

allocated to the clean room, grey room, microscopy room, microbiology room and the technical annex are shown on the right of the figure.
The building is currently owned by the City of Paris which considerably contributes to the project by allocating the site to the Institute. In financial terms, this represents, for a typical floor space cost of 6500 € / sq m in the area, about 26 M€ worth in building allocated to the project. Commitment letters from the Rectorat and the City of Paris, concerning the allocation of the building are joined in Annex 6.3. From the viewpoint of the City of Paris, this operation will contribute to reinforce the scientific attractiveness of the city, increase its international identity and visibility as a "campus of excellence", and foster its industrial visibility as a strong nucleus of innovation and technology transfer. In addition, **the City of Paris will finance the transformation of the trays of the actual building into renovated scientific labs. The estimated cost is 12 M€.**

Concerning the agenda of the operation, already 1000 sq m are free and can be invested immediately. The remainder (3000 sq m), which hosts CNOUS (Centre National des Oeuvres Universitaires et Scolaires) will be made available in 2011. CNOUS will move out in buildings allocated by the City of Paris. A realistic schedule, including a time delay necessary for adapting the existing space to the activity of a scientific Institute, brings us to the mid of 2012 for an operational structure.
The restaurant located at the first floor will stay in the building. An analysis conducted by experts of the City of Paris confirms there is no incompatibility between the activities of the Institute and the presence of the restaurant.

As shown in Fig 4 (right), the surface of the clean room will be 130 sq m and a possibility of extension up to 145 sq m. This clean room will be divided in 5 subspaces:

- Two lithographic rooms (20 sq m each) that include the aligner, the masker, two chemical extraction hoods, spincoaters, ovens, hotplate;
- One room (15 sq m) hosting the MEB;
- The entry lock;
- The main room includes the following equipments: anodic bonding, DRIE, Oxygen plasma, PECVD, Metallic deposition equipment, profilometer, RIE along with 3 extractive fume hoods.

The characteristics of this clean room will be ISO5 (class 10 000). The hygrometry will be 50±10 %, the temperature 21±1°. An electronic system will identify the users and allow the production of statistical studies on the platform utilisation.

As shown in Fig 4 (right), the surface of the grey room will be 210 sq m and a possibility of extension up to 300 sq m. This grey room will be divided in 3 identical subspaces of 70 sq m. The class will be 1 000 000 (ISO 9) and there will be no entry lock. The hygrometry will be 50±10 %, the temperature 21±1°.
An equipment dedicated to fast microfabrication technologies will be distributed in this space. This equipment is described in detail in Section 5.1.

A technical space of 180 sq m will be located close to the clean and grey rooms. It will notably include: filtration units, DI water production unit, cold water production units, grids, pumps, acoustic attenuators and pipes.

3. DISSEMINATION AND EXPLOITATION OF RESULTS

3.1. DISSEMINATION OF THE RESULTS OBTAINED WITH THE EQUIPMENT

3.1.1 TOWARDS PUBLIC, SCIENTIFIC AUDIENCE, INDUSTRY

The partners have strong experienced and communication departments, and will be in a good position to disseminate results to the public, in terms of communication and direct use for patients.

The partners have outstanding track record in this respect. For instance, the achievements of Curie's teams in microfluidics were already publicized to the public through several TV broadcasts (Magazine de la santé, TV5, TV News, TF1), nationwide actions (Courir pour la Vie), press releases; those of ESPCI-PARISTECH's microfluidic teams have been publicized in France 3, Le Figaro, France Inter, Telerama, Radio France International, and other thematic TV. A number of actions toward public audience will be undertaken by the IPGG Institute, using help and experience from the partner institutions, notably the creation of a professional website.
Importantly, too, in medicine not all dissemination and exploitation requires the intervention of the Industry, and some results of finalized research can be of use to patients by direct means, thanks to clinicians directly involved in research projects and the establishment of clinical protocols. This type of direct transfer is particularly active at Curie Institute, in particular thanks to the Translational Laboratory. J.L. Viovy, participant of the project's first circle, is strongly involved in this form of dissemination-translation, as a member of the steering committee of the Translational Laboratory, and coordinator (together with Dr Pierga, oncologist) of a translation program on the application of new technologies to micrometastasis diagnosis.

The partners have a strong track record of dissemination to the scientific community, with regular publications in the most prestigious journals, and the Institute will help to increase further their visibility as a single centre of excellence.

Participants to the project have a strong international publication activity with regular publications in the most prestigious journals (see section 6.2). They also participate in the editorial board of important international journals in the field (PNAS, Biomicrofluidics, Lab-on-Chip, Phys. Rev. Letter, and members of National and International Scientific Societies (Chemical and Biological Microsystems Society, Intl. They have invited conferences in the major conferences of the field (MicroTAS, Biophysical Society, ACS, APS, or organize conferences (For Instance, J.L Viovy, L.Malaquin and P. Tabeling, S. Descroix, all members of the project, jointly organized in Paris MicroTAS 2007, the most important conference in the field of microfluidics (1000 persons). The building at Calvin Street will be equipped with a modern conference room so that it will frequently host conferences in the domain of microfluidics or in relative fields.

3.1.2 TOWARDS STUDENTS

A Master Research will be created, in association with the project.

Most partners of the project are already involved, at various levels, in teaching activities regarding microfluidics. Notably J. Bibette, J.L.Viovy (with A. Ajdari) launched in 2004 in Cargese the first International Advanced Summer Institute on Microfluidics, which is now established as a regular course under the auspices of the CNRS Microfluidic Network. The IPGG Institute, however, will allow a much more intense and regular activity. In particular, a dedicated Master will be launched. This master, called “Microfluidics” will be under the supervision of P. Tabeling and M.C. Jullien (MMN group). Topics such as nanofluidics, biotechnologies, microfluidics hydrodynamics, analytical chemistry and separation, physics and chemistry for microfluidics, micromanufacturing (including practical works), surface treatments or biology issues will be taught. There will be industrial contributions in the program of the Master coming from companies such as Unilever, IFP, CEA, Rhodia. Students will have a 6-month internship in a laboratory in France or abroad. The master will be associated to ParisTech, P6 and ENS. Obviously, the foreseen equipment will strongly contribute to reinforce practical courses, and expose students to a variety of forefront technologies out of reach of any other teaching structure in France.

3.2. EXPLOITATION OF THE RESULTS OBTAINED WITH THE EQUIPMENT

As explained in the section 1, the project largely stems from the recognition that microfluidics main vocation is to yield societal useful achievements through fundamental research, innovation and technology transfer, and that the third component of this chain is too weak in our country. After study of the different international models and experiences, we have devised an original structure to overcome this bottleneck, and the Equipex support will be a critical component of this solution.

The technologies to be implemented through the project are selected from the beginning to permit future industrialization.

We have shown in our "diagnosis" of the bottlenecks to technology transfer in microfluidics (see section 2.2.1), that either the conventional microfabrication processes of the microelectronics industry, or the "PDMS" technology used in most academic laboratories in microfluidics can only satisfy a very minute portion of the full potential applications of microfluidics. The main aim of the project is to equip the IPGG with non-conventional technologies that will increase the efficiency of research, AND pave the route to a more direct, faster and more secure transfer to the Industry. Notably, changing the chip material in a bioprocess generally requires a deep reconsideration of the process, thanks to the temperature fragility of biomolecules, and specificity of surface interactions, so it is critical to use as early as possible in the innovation and development process, with a material having a plausible industrial future regarding production processes, cost or regulations.

There exists a strong culture of start-up creation and industrial relations culture among the partners of the project.

Several partners of the project have already successful experiences in the domain of start-up creation: JL Viovy (co-founder of Fluigent, the first microfluidic company in France), M. Piel (co-founder of Cytoo), J. Bibette (cofounder of Raindance, an important microfluidic company in the US, and now Capsum, the first microfluidic company in the domain of cosmetic ingredients and formulation), V. Croquette (co-founder of Picotwist). There also exists many long term collaborations between partners of the project and industry for the domain of microfluidics (L'Oréal, Schlumberger, Total, Saint Gobain, Unilever, Rhodia...).
The outstanding entrepreneurial culture of some of the partner institutions of IPGG (in particular ESCPI and ENSCP), their extended network will represent a strong support for managing and stimulating contacts between the Institute and industry.

The environment of the Institute will further favour an increase of the entrepreneurial activity in France for the domain of microfluidics: today, several projects of start-up creation are in gestation.

Several projects of start-up creation, issued from the research performed by the partners, may be foreseen in the first years of existence of the Institute: Blue Arrow (dedicated to ultrasound microfluidic delivery, with M. Tanter, P.Tabeling, V Cerbois, G. Rubinstenn), and others, much less mature, related to single molecule and electronic paper.
As regards to the impressive number of research themes which will be conducted, impacts will thus be wide. Indeed, one can identify long term fallouts while considering fundamental research such as artificial organs with reference to studies of cells in confinement or production of energy with an impressive yield of almost 100%. Even if these projects have a potential high-impact, they still need maturation. Considering medium term impacts, expected results are to be generated in domains such as neurosciences, paper technology or tissue engineering. As regards to the maturity of these projects, creation of start-up companies would be considered. As a consequence, all themes described in section 2.2.1 of the project are able to provide a major impact on day-to-day life on a short to long term.
Should these ventures succeed, this would double or triple the number of microfluidic companies existing in France today. We believe that the IPGG will play a key role in releasing this potential and will therefore contribute to further increase the entrepreneurial activity in France in the microfluidic domain.

We send a strong signal by allocating 1000 sq m to industrial teams on the basis of projects involving the specific equipment of the Institute.

In an area where the scientific environment is outstanding, but space is particularly rare, we shall allocate 1000 sq m, i.e. 25% of the available surface of the Institute, to Industrial teams needing the expertise and equipment of its Institute for its R&D projects. This is a strong commitment to private-public partnering. It stems from the recognition that, in particular in microfluidics where technology is complex, diverse, rapidly changing, poorly known by end-users and critical for success, achieving a physical continuity and day to day collaboration between fundamental research and industry is mandatory from the viewpoint of the valorisation of the research results.
This interest is indeed reciprocal, since several companies have expressed their interest in the project (Rhodia, Fluigent have moreover written letters). The possibility of having industrial teams in the same building as fundamental research, with access to the same equipment, on a contractual basis respecting confidentiality, will be a strong originality and strength of the project to reinforce public/private partnerships.

The philosophy of this academy-industry partnership will be open-minded, and focused on the optimization of the use of the specific equipment and competences of the Institute.

As recalled in section 2.2.1, several different models exist in the world for foster technology transfer. We choose to allocate space to technology transfer projects, on the basis of optimization of the global benefits and adequation of the project with the Institute's infrastructure and competence, regardless of the size of the involved company; This stems from the fact that all kinds of companies, from start-ups in early incubation, to "majors", may benefit from hands on experience on the unique Institute's, equipment. Also, the Institute does not have the vocation to compete with established incubators or “pépinières”, towards which we wish to act as partners rather than competitors or alternatives. Thus partnerships are possible with the pre-incubator “Paris Biotech Santé” dedicated to biotechnology and human health and with the incubator “Paris Santé Cochin” which is the first French incubator located inside a hospital. As mentioned above, this model has already been experienced with success in Japan for microfludics (KAST) or in France in "Institut de la Vision".
Finally, the IPGG itself will only comprise academic partners or foundation, i.e. non-profit organizations. The partners will keep their institutional affiliations, the coordinator, FPGG, has no claim on IP, so the work done within IPGG will follow the already established rules and conventions between the partners; Of course, projects in partnership with industry, and access of industrial to the IPGG space, will require a different treatment. The Foundation Pierre-Gilles de Gennes (FPGG), the coordinator of the project, will be the ideal entity for that: it has demonstrated its efficiency in fostering and managing private-public partnering for science and innovation. It notably designed and marketed a disruptive contract R&D offer that generated €2.6M of sales 18 months after its launch in January 2009 (For more details on managerial aspects, see section 4 below).

4. PROJECT MANAGEMENT

4.1. MANAGEMENT

4.1.1 RELEVANT EXPERIENCE OF THE PROJECT COORDINATOR

Dr. Patrick Tabeling is the scientific coordinator of the project Institut Pierre-Gilles de Gennes. Since 2001, he is leader of the group MMN (Microfluidics MEMS and Nanostructures) composed by 20 researchers (permanents, PhDs and Postdoctoral students). Before that, he occupied various positions in different laboratories: Visiting researcher in Chicago University (1984-1985), Chargé/Directeur de Recherches CNRS in the Department of Physics in ENS (1985-2001), visiting professor at UCLA,; he was professor chargé de cours at the Ecole Polytechnique (1996-2008) He is the author of 191 scientific papers (among 114 in International refereed journals), 7 patents (citation index 3000, h factor 33), 65 invited talks in international conferences; he is divisional editor of Physical Review Letters. He published the book entitled "An introduction to microfluidics" (Oxford University Press - a French version being edited by Belin) in 2005.

Experience in research project coordination:
Between 2000 and 2003, he was the coordinator of the European Network "Intermittency", composed of 9 European laboratories in the domain of turbulence. He has already gathered scientific community while creating the French network "Microfluidique" in 2001 now called GDR led by AM. Gue (400 researchers). He was also the chairman of several International conference dedicated to microfluidics such as the Minisymposium "Microfluidics" in the International Conference on Theoretical and Applied Mechanics in Poland in 2004, the first Brasilian Microfluidic Conference (ICMMP Brasilia) in 2006 the Second French Chinese conference in 2009; he has been coorganizer of MicroTAS2007 (1000 participants).

Links with industry:
Being consultant for Schlumberger since 1988, he also has solid relationships with industrial partners such as EDF, Bertin, Total, IFP, L'Oréal, Unilever, Saint Gobain or Rhodia. Besides, he also holds a 500 k€ contract with the Advanced Energy Consortium including BP, Shell, Schlumberger, total, Alliburton, Baker and Petrobrals.

Coordinating organisation:
« Fondation Pierre Gilles de Gennes pour la recherche » (FPGG) will be the coordinating partner. This entity is a scientific cooperation foundation built in the "Réseau Thématique de Recherche Avancée" (RTRA) French scheme in 2007. The Foundation already gathers the partners of the project IPGG: ESPCI-PARISTECH, ENS, ENSCP and Institut Curie but also CNRS and INSERM. The FPGG combines unique high-level research teams in a wide range of fundamental fields providing unique knowledge concerning middle-scale research (from 100 nm to 50 µm). Moreover, the FPGG supports public-private projects by assuming the role of unique contact point for setting up scientific partnerships to encourage projects and rapidly develop innovations up to the market.
With an initial of share capital of 20 M€, the FPGG gives its agreement to various projects mainly in the field of health. It has already initiated 9 projects dedicated to microfluidics involving some teams from the founders institute for over 1 M€ during the period 2008-2010.
Benefiting from its central position, from knowing each partners of the project and considering its involvement in developing public-private projects, the FPGG represents the best coordinating partner. With his experience in structuring scientific networks and his scientific excellence related to the field of microfluidics, P. Tabeling has the legitimacy to take on the role of coordinator of the project IPGG.

4.1.2 COORDINATION MODALITIES

The management structure [fig 5, left] is based on the FPGG management model, proven to be efficient for the coordination of research projects already involving the co-founder organisations. The structure dedicated to the Equipex project will therefore rely on proven processes, adapted to the management of similar research projects.

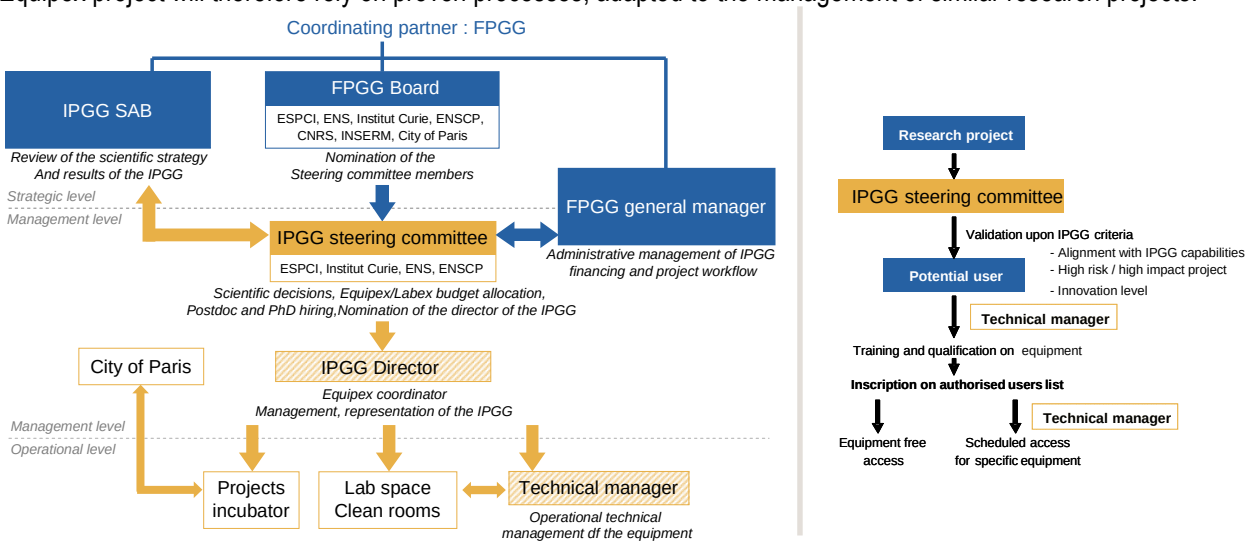

Figure 5: (left) IPGG Coordination organisation for Equipex (right) Process for equipment access

There will be no creation of CNRS laboratory. All teams will keep depending on their own Institution. IPGG will therefore involve no institutional restructuration.

The Equipex coordinating partner (FPGG) will be responsible for the management, the financial follow-up and control of the project and the reporting to the ANR during the project period. The IPGG will rely on existing bodies of the FPGG. Thus, the existing FPGG's governing board is responsible for all strategic and administrative decisions affecting the project and will meet every 3 months. The FPGG's international scientific advisory board (SAB), composed by international outstanding scientists along with industry and institution representatives, will evaluate the activity of the Institute and provide advices on its evolution and on any questions submitted to it by the steering committee and the director.

In addition, a steering committee will be formed as a management body for the Equipex project, this body will be under the responsibility of FPGG. The members of the Steering Committee will be nominated by the FPGG board.

The Director of the Institute will be nominated by the steering committee. He will be in charge of the practical life of the Institute; he will handle the relations with the supporting Institutions, promotes interactions and develops the communication at the national and international levels.

At an operational level, the Technical Manager, nominated by the Director and working under his responsability, will be in charge of the establishment and day to day follow-up of the planning of equipment. He will especially implement and ensure the timely availability of the equipment for the selected projects. Moreover, he will be in charge of the "authorised user list" [fig 5, right], which is the key for an access to the equipment. A new user of the equipment will have to undertake training and qualification on the equipment to be recorded as authorised user. These rules are similar to those that have prevailed in the existing technological platforms of Paris Centre for one decade. The main stakes are to ensure flexibility and reactivity towards internal and external requests.

For the teams of IPGG (1st and 2nd circle), the fees charged for the access to the equipment will be settled on the basis of 50 €/day/user whereas for external users (3rd circle), fees will be settled on the basis of 300 €/day/user (see section 5. for more details). These contributions will be used to upgrade the standard equipments of the platform (microscopes, computers…), buy new equipments and add new capabilities. These fees will be invoiced by the FPGG to the users of the equipment. In the long term, the maintenance of the platform and the renewal of the equipments will be supported by the resources of the teams, contributions from the institutional partners and specific funding obtained at the regional, national and international levels.

The incubator will be placed under the responsability of the City of Paris. The incubator will be managed synergistically with the research activities of the Institute.

4.2. COLLABORATION ORGANIZATION

4.2.1 PARTNERS DESCRIPTION, RELEVANCE AND COMPLEMENTARITY

- *Description of the Equipex partners*

Fondation Pierre Gilles de Gennes (Coordinating partner: partner #1)

The Pierre-Gilles de Gennes Foundation for Research aims for scientific cooperation. This foundation is governed by private law and is considered of public interest. Founded by three centres of excellence (ENS, ESPCI-PARISTECH, Institut Curie) in collaboration with the CNRS and INSERM, the Foundation relies on a network of 145 laboratories and more than 1500 researchers to launch discovery and application programs. Recently, ENSCP has joined FPGG as Founding Member. FPGG thus acts as a common network for all the partners of IPGG.
Beyond its innovative and efficient model, the Foundation especially intends to promote projects in the field of health:

- Projects between different establishments to optimize latent synergies in research laboratories.
- Transdisciplinary projects to abridge the discovery & innovation cycle by interfacing physics with biology and chemistry.

With an initial share capital of €20 million, the Foundation has built up a fund to help launch high risk-high impact projects by investing over €2.5 million in projects submitted by research teams.
The foundation also organizes events aiming to reinforce the scientific influence of its network: scientific conferences, summer schools, and university chairs.
FPGG places its sustainability in its successful role as the contact point in setting up public-private partnerships. The Foundation is particularly suited for growing French and European companies whose still-modest size often prevents them from accessing big-time upstream research. The Foundation can provide help to such companies by simplifying contractual issues, organizing and running projects, ensuring that “proof-of-concepts” are obtained to exploit industrial innovations and recommending attractive tax options.

Ecole Supérieure de Physique Chimie Industrielle de la ville de Paris (partner #2)

ESPCI-PARISTECH ParisTech is home to 18 high-profile laboratories advancing scientific knowledge and pioneering technical know-how in a variety of research areas, ranging from polymers to telecommunications, from nanobiophysics to organic synthesis, from environmental science to biomedical imaging, from neurobiology to microfluidics, from soft matter to quantum physics, from colloids to prototyping for industry.

Research at ESPCI-PARISTECH ParisTech lies ahead of the industry R&D curve. It focuses on anticipating needs that will arise in the short to distant future, and on inventing the adequate solutions. Using these real-world opportunities to explore and understand fundamental aspects of nature or matter, scientists at ESPCI-PARISTECH ParisTech publish one peer-reviewed article per day.

The teams involved in the project are the Microfluidic Lab of ESPCI-PARISTECH (MMN), led by **P. Tabeling**. This team, dedicated to microfluidics and its applications in various fields (physics, chemistry, biotechnology) currently includes 20 researchers; it is one of the largest groups for Microfluidics in France. The team has founded the Reseau Microfluidique (now GDR Microfluidique led by AM Gue, 400 researchers). It has published 80 papers over the last ten years, organized or coorganized four international conferences on microfluidics. The team has currently numerous industrial collaborations (Total, Schlumberger, IFP, L’Oréal, AEC); in the past, the collaborations also included Unilever, Rhodia, Bertin, Saint Gobain.

The other teams involved in the project belong to the "second circle" of the Institute: they are led by **J.Bibette, U. Bockelmann, M.C. Hennion, /V.Pichon, and J.Vinh.** J. Bibette is an international leader in the domain of emulsions; Prof Bibette has an outstanding records in term of entrepreneurial activity: he founded Adamtech, Raindance (a major player in the microfluidic industrial area), and now Capsum, a creative young company that is introducing microfluidic technology in the cosmetic domain. His group includes 15 researchers. U Bockelmann is a worldwide known researcher in the domain of solid state physics and single molecule biophysics. MC Hennion/V.Pichon are worldwide leaders in the domain of Analytical Chemistry. The lab they lead has made outstanding contributions by coupling microfluidic technology to analytical chemistry. Joelle Vinh is a young researcher, well known in the domain of proteomics. She is in charge of an outstanding Mass Spectrometry platform located in ESPCI-PARISTECH. She has creative projects aiming at coupling droplet technology with Mass Spectrometry.

Institut Curie (partner #3)

The Curie Institute is a non-profit foundation dedicated to cancer research and treatment. It was founded by Marie Curie and her family, with the aim of applying the progress of science to human health. This interdisciplinary spirit is still at the heart of the Institute's strategy, and Curie is recognized as one of Europe's best renowned models for interdisciplinary research and translational medicine.

The group MMBM at Curie Institute is one of the largest and leading groups in France for Microfluidics. MMBM transposes to this field innovations and concepts from soft matter physics and chemistry. For some aspects, such as the use of self-assembly strategies or the convergence between microfluidics and single molecule studies it had a pioneering role in the world. Overall**, J.L. Viovy** totalizes more than 160 papers, 4500 citations ("hfactor" 37) and 16 patent families, 5 of which are commercially exploited. The group fostered the creation of the first French microfluidics-dedicated start-up Fluigent (currently 20 persons). Finally, the team has a strong European commitment and impact (about 10 projects so far, 3 ongoing): CAMINEMS on tumour cells screening, as coordinator, NADINE, large project on Alzheimer early diagnosis, DiaTools, on cancer diagnosis.

The group "Systems biology of cell polarity and cell division" is a junior team led by **M.Piel**. This group is one of the few biology teams in France exploiting nano and micro-fabricated tools to tackle fundamental questions on cell polarity. The group demonstrated that micro-patterns of extra-cellular matrix molecules determine the polarity and division axis of cultured cells (Théry NCB 2005, PNAS 2006, Jiang PNAS 2006). This finding induced the creation of a start-up company (CYTOO) and inspired many biologists to engage in this new way of studying cells. M. Piel is author of 29 publications (between 2000 and 2010) in peer reviewed journals, with a total of more than 1200 citations (H factor 15). He holds two patents and is a co-founder of the CYTOO Company.

P. Silberzan and A.Buguin lead the « biology inspired physics at mesoscales » group at the Institut Curie (Physicochimie Curie laboratory). They have been among the first in France to be involved in microfabrication and microfluidics for soft condensed matter and biology, by dedicating a small clean room facility to these activities as early as 1995. They presently use these technologies (microstructured surfaces, micro-stencils, micro-channels or micro-chambers to name a few) for microbiology and cell biology applications. They have been the first to describe permeation-induced flows in silicone microchannels.

Ecole Normale Supérieure (partner #4)

The Ecole Normale Supérieure is an institution of both education and research, with excellence as a sole objective. It is characterized by a relatively small size, a strong spirit of multidisciplinarity, an education through research, highly selected students and world-recognized research departments. The Department of Chemistry of ENS is composed of world-recognized teams developing concepts and methodologies at the frontiers of chemistry, with a particular interest for biological systems.

J. Fattaccioli is a young teaching assistant with major interests in Soft Matter, Chemistry and Biophysics. He belongs to **Y. Chen's** group (Microfluidics, Chemical Organization and Nanotechnology) which has been created in 2003, with the main objective of developing new tools and models for life sciences. Since its creation, the group has implemented a flexible base for advanced research purposes, including a complete set of facilities for micro and nanostructure engineering, microfluidic device design and fabrication as well as advanced biophysical and biochemical analyses. During the last few years, the group has been involved in a large variety of interdisciplinary studies and collaborations for integrated cell-material sciences including biomaterial design and device processing, stem cell culture and differentiation and single cell patterning and manipulation. Y. Chen has authored or co-authored more than 280 ISI papers (4800 citations). He has also contributed to more than 10 contracted European projects and a number of national and international projects in the field of nanosciences and nanotechnologies.

V. Croquette, D. Bensimon and M. Dahan are international leaders in the fields of single molecule and neuron research. Vincent Croquette has launched a company specialized in single molecule handling; he has a project of launching a new company exploiting microfluidic technology for DNA sequencing. Maxime Dahan has made use of microfluidic technology to control the stimulation brought to neurons placed in a microenvironment.
All researchers are extremely interested in the creation of the Institute and take part to it. They will take advantage and amplify the synergy that will be generated by the IPGG Institute. They will expand and harness their projects based on microfluidic technology.

Ecole Nationale Supérieure de Chimie de Paris (partner #5)

ENSCP (Chimie-ParisTech) is a graduate school which trains chemical engineers and chemists in order to make them assume high level positions in the chemical and related industries. Besides this teaching assignment, Chimie ParisTech is a multidisciplinary research center, made of 7 research laboratories, 110 permanent researchers and professors, 100 technical and administrative staff, 90 PhD and post doctoral fellows. It is organized around two fundamental themes :

- energy, materials and process engineering (Moissan department),
- molecular chemistry and life chemistry (Friedel department).

ENSCP has a strong expertise in the field of Plasma processes for microsystem applications. Since 2005, in collaboration with P. Tabeling**, M. Tatoulian** succeeded to elaborate an efficient and innovative protocol to fabricate stable hydrophilic and patterned hydrophobic/hydrophilic surfaces microchannels. Their method is based on plasma polymerization for the modification and control of the surface properties of the materials used for the microsystems (glass, PDMS…). His group is at the present time involved in a collaboration with ENS, in order to develop a novel measurement technology for the on-line, on-chip detection of reaction kinetics and flow dynamics within microreactors, based on the use of Multiplex Coherent Anti-Stokes Raman Scattering (CARS) spectroscopy. M. Tatoulian will play a key role in enhancing interactions between microfluidic researchers and his team (10 persons), specialized in surface modification and surface characterization. In another domain, **N. Badioui** has well recognized expertise in Electrochemistry and has made contributions in the domain of microactuators.

ENSCP will thus declare as a priority the development in its research center of chemical engineering in microdevices, coupled to the development of teaching programs for its engineers. The setting-up of such a new activity at a high level commands to be able to attract outstanding senior and junior researchers (for example colleagues from Jensen's lab or Kitamori's lab). IPGG will be a very exciting and visible place for these foreign colleagues, and will fasten the development of this activity in ENSCP.

- *Partnership synergies and multidisciplinarity*

Developing operational microfluidic systems require knowledge and creativity in various fields, including (non-exhaustively!):

- **Physics** (because of the specific behaviour of fluids at ultra-small scale, and because even the well-known laws, e.g. of hydrodynamics, are put to play in a domain of parameters which are new)
- **Surface chemistry** (because, e.g. of the paramount role of surface interactions, high surface/volume ratios and numerous surface-driven effects such as electroosmosis or capillarity)
- **Analytical chemistry**, since numerous applications of lab on chips are indeed analytical
- Biochemistry (because of the paramount role of biochemical interactions for the development of bioassays or, for instance, for controlling cell-surface interactions
- **Micro and Nanosystems**, because most microfabrication strategies in microfluidics, although different in many respect from "hard" microfabrication, also share with that field a lot of expertise and tools
- And last but not least, direct and strong involvement of end-users with their specific expertise in **biology, diagnosis, medicine, environment, chemical engineering**, because in general the good route to innovation in microfluidics is not to downscale existing protocols, but to co-invent new biological or chemical schemes, that would be too complicated or infeasible a the macro scale, but become the best one on the microscale;

From this perspective, the project stands in an excellent position: individually, the partners have very different backgrounds and experiences. They are chemists (L. Jullien, MC Hennion, V. Pichon), surface chemists (M. Tatoulian), physicists (P. Tabeling, P. Silberzan, U. Bockelmann), physico chemists (J. Bibette, JL Viovy) biologists (J. Vinh, M. Piel), biophysicists (JL Viovy, V. Croquette). We will host researchers, keeping their current affiliation and interested in developing their own applications in closest collaboration with microfluidic researchers. Examples are M. Dutreix (inventor of "DNAbaits", a new generation of anticancer drugs, and founder of the OSEO award winner start-up DNA Therapeutics), or JM Peyrin (Neuroscientist, UMR 7102 Neurobiology of adaptative processes, UPMC).
Partners have strong experiences of interdisciplinary and cross disciplinary research, and indeed already have numerous collaborations (this is illustrated by joint publications, appearing in the partner's list of publications

below). Bringing them together will obviously create the conditions for developing even more ambitious projects in a field where everyone understands that cross-disciplinary collaborations play a strategic role. Institutionally, partners in the project (Institut Curie, ENS, ESPCI-PARISTECH, are indeed interdisciplinary in essence, and considered as models worldwide for successful interdisciplinary actions). Finally, the scientific environment of the project is the best one achievable, regarding the possible access and involvement of end-users in many fields of interest of microfluidics.

All partners have strong international recognition and networks (section 2.1 and references in 6.2), that will both be reinforced by the Project, and increase its strength and international impact. Notably, space will be available to welcome international leaders for sabbatical stays - examples will be S. Quake (Stanford University) (who will have a small lab), D. Weitz (Harvard) D. Pine, P. Doyle (MIT), and others.

4.2.2 QUALIFICATION, ROLE AND INVOLVEMENT OF INDIVIDUAL PARTNERS

The Table below includes the team leaders involved in the EQUIPEX Project (1st and 2nd circle of IPGG). All the leaders join IPGG and the project with their own groups. These groups include permanent researchers/engineers, and many post doctoral and PhD students. All together, they gather more than 100 persons and there is no space in the Table to display all of them. To be more specific, the names of the permanent researchers/Assistant Professors/ engineers involved in the Institute and the EQUIPEX project, additionally to the team leaders, are: H. Willaime, M. Reyssat, MC Jullien, F. Monti, S. Descroix, J. Baudry, N. Bremond, J. Hercovichi, S. Griveau, C. Girard, C. Beauvineau, A. Varenne, C. Guyon, N. Delaunay, Y. Verdier, E. Demey, Y. Haddad, B. Ducos, J.F.Allemand, N. Desprat, D. Beigl, G. Cappello, N.Henry, L. Malaquin. The rest of the persons involved in the project are PhD and PostDoc students, along with administrative staff members.

The stripped background outlines the partner coordinator and the grey background indicates that the researcher belongs to the first circle. The absence of background indicates that the researcher belongs to the second circle.

We thus emphasize here that the project includes, as a whole, more than 100 researchers who will benefit from the equipment supported by EQUIPEX along with the strong structuring effect induced by the project.

Partner	Surname	First name	Position	Domain	Organization	Contribution to the project
FPGG	**RUBINSTENN**	Gilles	General Manager, PhD, MBA	PhD in physics Business Administration	FPGG	Partner coordinator
ESPCI-PARISTECH	**TABELING**	Patrick	Director of Research	Microfluidics	FPGG/CNRS/ESPCI-PARISTECH	Coordinator. Team leader of a group of 20 researchers
ESPCI-PARISTECH	**BIBETTE**	Jerome	Professor	Emulsions	ESPCI-PARISTECH	Team leader of a group of 15 researchers
ESPCI-PARISTECH	**HENNION**	Marie-Claire	Professor	Analytical Chemistry	ESCPI	Laboratory leader of a group of 30 researchers
ESPCI-PARISTECH	**PICHON**	Valérie	Professor	Analytical Chemistry	ESCPI	Laboratory leader of a group of 30 researchers
ESPCI-PARISTECH	**BOCKELMANN**	Ulrich	Director of Research	Solid State, Biophysics	ESPCI-PARISTECH/CNRS	Team Leader of a group of 5 researchers
ESPCI-PARISTECH	**VINH**	Joelle	Director of Research	Proteomics Mass Spectroscopy	ESPCI-PARISTECH/CNRS	Laboratory leader of a group of 10 researchers

CURIE	**VIOVY**	Jean-Louis	Director of Research	Microfluidics, Blotechnology	Curie/CNRS	Team leader of a group of 30 researchers. EQUIPEX Scientific Coordinator for Curie
CURIE	**PIEL**	Mathieu	Director of Research	Biotechnology	Curie/CNRS	Team leader of a group of 10 researchers
CURIE	**SILBERZAN**	Pascal	Director of Research	Microfluidics	Curie/CNRS	Team leader of a group of 10 researchers
CURIE	**BUGUIN**	Axel	Director of Research	Microfluidics	Curie/CNRS	Team leader of a group of 10 researchers
ENS	**FATTACCIOLI**	Jacques	Assistant Professor	Physico-chemistry, microfluidics	UPMC	EQUIPEX Scientific coordinator for ENS
ENS	**CHEN**	Yong	Director of Research	Physics nano-technology	CNRS	Group leader of a group of 20 researchers
ENS	**CROQUETTE**	Vincent	Director of Research	Single Molecule biophysics	CNRS	Team leader of a group of 15 researchers
ENS	**BENSIMON**	David	Director of Research	Single molecule biophysics	CNRS	Team leader of a group of 15 researchers
ENS	**DAHAN**	Maxime	Director of Research	Optics, quantum dots, neuronal cells	CNRS	Team leader of a group of 15 researchers
ENSCP	**TATOULIAN**	Michael	Professor	Surface chemistry, Plasma processing of materials	ENSCP	Team leader of a group of 10 persons, Scientific coordinator for ENSCP
ENSCP	**BEDIOUI**	Fethi	Director of research	Electro-chemistry, microactuators	CNRS	Team leader of a group of 10 researchers

5. FINANCIAL ASSESSMENT

5.1. FIRST PHASE: INVESTMENT

Element 1: Clean room (class 10 000)	Supplier name	Country	Cost (in k€)	Quotation number
Technical space				
Room layout	Vêpres construction	France	676	31
TOTAL			**676**	

Element 2: Equipment for the cleanroom				
8 Hot plates	SPS	France	14	1
Spincoater	Pi-KEM, hhvltd	England	84	2-3-21
Reactive Ion Etching	Corial	France	160	19
Deep Reactive Ion Etching	Corial	France	314	20
PECVD system	Plasmionique	Canada	195	32
Aligners	*Estimated*		274	
Microsonic multipurpose bonder	Metronelec	France	25	34
Wire bonding	Metronelec	France	54	35
Oven	Fischer Scientific	France	10	5-6
Oxygen plasma	IntCo	France	41	9-10
Direct lithography	Heidelberg Instruments	Germany	245	7-8
Profilometer	Veeco	France	38	33
Ellipsometer	Horiba Jobin Yvon	France	75	37
IR Spectrometer	*Estimated*		93	37
TOTAL			**1622**	

Element 3: Observation systems for the cleanroom				
reflection straight microscope	Nikon	France	11	15
Scanning Electron Microscope	Elexience	France	568	27
TOTAL			**579**	

Element 4: Grey room (class 1 000 000)				
UV Lamp	SPS	France	41	18
Aligner/Holder	*Estimated*		20	
Plasma system	Harrick Plasma	USA	8	23-24
Spin coater + Spin coater PDMS	Laurell, SPS	Wales, France	6	17
Hoods	ADS Laminaire	France	50	30
2 inverted microscopes	Nikon	France	28	14
Reflection straight microscope	Nikon	France	11	15
UV oven	Jelight Company	USA	7	16
Micromilling	Minitech Machinery corp.	USA	22	4
Hot embossing system	*Estimated*		10	
Roll embossing	*Estimated*		250	
Injection moulding	ENGEL	France	68	36
Room layout	Vêpres construction	France	685	31
TOTAL			**1206**	

Element 5: Observation room				
Confocal classic microscrope	Nikon	France	252	25
Spining disk confocal microscope	Nikon, Roper	France	244	11-12
Video-microscope	Nikon	France	84	13
3 biostations	Nikon	France	175	26
Room layout	*Estimated*		200	
TOTAL			**955**	

Element 6: biospaces				
3 hoods	*Estimated*		100	
3 incubators	VWR	France	155	28
3 microscopes	Nikon	France	84	14
Confocal macroscope	*Estimated*		170	
Centrifuge	*Estimated*			
Liquid nitrogen storage	*Estimated*			
3 sterilizers	*Estimated*			
3 thermostatic shaking baths	*Estimated*			
Cell culture	VWR	France	127	29
Room layout	*Estimated*		450	
TOTAL			**1086**	

Element 7: laboratories		
Team equipment	*Estimated*	200
Start-up package for hosted teams	*Estimated*	200
TOTAL		**400**

Other costs for investment	Cost (in k€)	Scientific justification
Procurement and achievement of market	140	Time of a non permanent project leader for procurement and achievement of market during a 2-year period
FPGG Network extension	35	Computing to ensure efficient collaborative work
HSE study to implant teams	30	Hygiene, Security and Environment study to optimize positioning of research teams
Travel costs	5	International meetings
TOTAL	**210**	

5.2. SECOND PHASE: FUNCTIONING COSTS

Element	Maintenance (in k€/year)	Operational costs (in k€/year)
Element 1: Clean room	4	
Element 2: Equipment for the cleanroom	36,4	
Element 3: Observation systems for the cleanroom	11	80
Element 4: Grey room	15,7	
Element 5: Observation room	25,8	
Element 6: Biospaces	16,5	
Element 7: Laboratories	8,5	5,7
TOTAL per year	117,9	85,7
TOTAL over 7 years	**825,3**	**600**

Data concerning the maintenance of the equipment comes from:
- supplier of the equipment for some of them;
- extrapolation of annual maintenance cost for existing equipment from ESPCI and Curie clean room;
- Average rate of 2.6% of the investment cost as maintenance cost per year.

Operational costs come from the current ESPCI clean room and its direct environment which cost 30 k€/year for a 30 sq m room.

4 engineers will be made available from the partners to ensure training for an efficient and safe use of the equipment. They will appear in the next section (5.3).

5.3. OTHER: PARTNER CONTRIBUTION

Personnel from partners	Investment phase: 24 months		Functional phase: 7 years	
	Person.month	Cost (in €)	Person.month	Cost (in €)
ESPCI				
Engineer	24	80 016	84	280 056
Research director	-	-	10	75 000
Part time researcher/part time teacher	-	-	10	27 080
Curie				
Engineers	30	176 880	168	990 528
ENS				
Researcher	4,8	28 584	16,8	100 044
ENSCP				
Part time researcher/part time teacher	2,4	15 600	10	65 000
Part time researcher/part time teacher	2,4	11 520	10	48 000
Technician	12	36 000	50	150 000
PhD	-	-	10	27 500
Post-doc	-	-	20	82 000
TOTAL	75,6	348 600	388,8	1 845 208
ETP	3,15		4,63	

Equipment from partner	Qtty	Supplier	Amortization remaining (k€)	Amortization duration	Total maintenance costs (k€)
ESPCI contribution					
Aligner MJB4	1	Karl Suss	55	5	30
Metal deposition system	1	Edwards	55	5	30
Metal sputtering system	1	Edwards	50	6	33
Mecanical profilometer	1	Dektak	150	9	116
Optical profilometer	1	Veeco	10	5	6
Oxygen plasma system	1	Harrick	18	8	14
UV cleaning system	1	Leica	10	6	7
UV lamp LC8	1	Hamamatsu	15	7	12
UV lamp	1	Hamamatsu	18	8	14
Characterization microscope and macroscope	1	Zeiss and Leica	20	7	15
		TOTAL	**401**		**276**
Curie contribution					
Inverted microscope	2	Nikon	65	6	46
Nikon Imagery system	3	Nikon	31	4	22
Roper imagery system + software	2	Roper	38	6	26
Flow controller MFCS 4/8voies	2	Fluigent	17	6	12
Flow controller MFCS 4/8voies	3	Fluigent	13	3	9
Laminar flow hoods	2	ADS Laminaire	6	4	5
Antivibration optical table	3	TMC	15	6	11
Laminoir	1	Bernier	2	2	1
Spin coater + Pump	1	SPS Europe	3	5	2
Oxygen plasma system + Pump	1	Harrick US	1	1	1
Optical profilometer	1	Veeco	27	5	6
Straight microscope	1	Olympus	13	4	9
Platine Translation PI	1	Phisik Instrumente	2	3	1
Accurate push-syringe	1	Cetoni	7	4	5
Infra-red camera	1	FLIR Systèmes	13	4	9
Microscope Nikon	1	Nikon	25	5	18
8 channel high voltage generator	1	Mengel	4	3	3
high voltage alimentation	1	Condatas	5	4	3
Environmental systems	2		17	6	12
Inverted microscope	1	Olympus	6	3	4
Software Comsol	1	COMSOL	4	6	3
		TOTAL	**314**		**208**
ENS contribution					
Inverted microscope	2	Leica	60	7	46
		TOTAL	**60**		**46**
ENSCP contribution					
PECVD Reactor	1	Plasmionique	110	9	85
Spectrometer	1	Pfeiffer	30	5	17
Optical emission spectroscope	1	EGG Princeton	50	5	28
Digidrop goniometer	1	GBX	15	7	12
		TOTAL	**205**		**140**

These equipments already contribute to partners' research in their current facilities. They will move into the IPGG building located rue Jean Calvin.

5.4. PARTNER CONTRIBUTION TO RESEARCH PROJECTS

Here we emphasize that the groups are strongly involved in the project. The Table below provides details on the level of human resources that the three larger teams will dedicate to the project.

It appears that throughout Phase 1 and 2, the overall contributions of the teams will stand above ten millions of Euros.

	Investment phase: 24 months		Functional phase: 7 years	
Human ressources from ESPCI	Person.month	Cost (in €)	Person.month	Cost (in €)
P Tabeling team				
Research director	24	270 720	26	296 100
Researcher	29	135 635	101	337 748
Ingeneer			11	66 365
Other (administrative work)	6	35 376	21	89 649
PhD			338	998 857
PhD			281	1 322 017
TOTAL	59	441 731	779	3 110 737

	Investment phase: 24 months		Functional phase: 7 years	
Human ressources from Curie	Person.month	Cost (in €)	Person.month	Cost (in €)
JL Viovy team				
Research director	24	270 720	26	296 100
Researcher	43	202 440	151	504 101
Ingeneer			17	99 053
Technician	6	25 476	17	126 000
Other (administrative work)	12	70 752	42	179 298
PhD			504	1 490 832
PhD			420	1 973 160
M. Piel team				
Researcher	19	114 336	67	400 176
Researcher	19	89 971	67	314 899
Ingeneer	24	102 456	84	358 596
PhD			252	745 416
Post-doc			336	1 578 528
Ingeneer (non permanent)			84	495 264
TOTAL	148	876 151	2 067	8 561 423

5.5. JUSTIFICATION OF THE PLATFORM ACCESS FEES

As written in the section 4.1.2, fees charged for the access of the equipment are based on the following model:

Number of effective days	200 days			
Time repartition				
Equipex partner	50%	100 days		
Other users	50%	100 days		
Average number of researchers during 1 day		10 researchers		
Annual costs				
Running costs	85,7 k€/year			
Personnel costs	263 k€/year			
Maintenance costs	117,9 k€/year			
User contributions				
Flat fees	50 €/day/user			
Equipex partner's contribution	50 k€/year		500 €/day	**50** €/day/user
Other users' contribution	283,3 k€/year		2833 €/day	**283,3** €/day/user

Other users' contributions will cover 50% of running, personnel and maintenance costs. The aim is to ensure attractiveness of the foreseen platform toward external users and thus, to limit entry fees.

6. ANNEXES / APPENDICES

6.1. STATE OF ART REFERENCES

[1] see recent developments of this technology in http://www.chem.agilent.com/cag/feature/08-01/feature.html
[2] A.D.Manz, A.,J.Harrison, E. Verpoorte, H. M. Widmer, *Adv. Chromatogr.* **33**, 1 (1993).
[3] http://www.abbottpointofcare.com/; see also MM.Stephan, *The Scientist* **18** (11) 38
[4] C. Chin, V.Linder, S.K.Sia, Lab Chip, **7**, 41 (2007).
[5] P. Tabeling, *Introduction to Microfluidics*, Oxford Univ. Press (2005)
[6] G. Whitesides, *Nature* **442**, 368 (2006).
[7] A Günther, KF Jensen, *Lab on a Chip*, **6**, 1487 (2006).
[8] Hessel, V., Hardt, S., Löwe, H. *Chemical Micro Process Engineering - Fundamentals, Modelling and Reactions,* Wiley-VCH, Weinheim (2004).
[9] KF Jensen - Chemical Engineering Science,**56**, 293 (2001).
[10] *Chemical Micro Process Engineering - Fundamentals, Modelling and Reactions, ed by* Hessel, V., Hardt, S., Löwe, H. , Kluwer Acad. Publishers, Wiley-VCH, Weinheim (2004).
[11] The Laboratory of the Future, including more than 100 researchers, was created in Bordeaux for this objective.
[12] H Song, DL Chen, RF Ismagilov**, 7**, 768 (2003).
[13] Unilever has developed a laboratory for microfluidic applications to food industry
[14] Capsum, a company developed by a team (J. Bibette) of the Institute, uses microfluidics for synthesizing multiple droplets dedicated to cosmetic application.
[15] F.Malloggi, N. Pannacci, R. Attia, F. Monti, P.Mary, H. Willaime and P. Tabeling, B . Cabane, P. Poncet, *Langmuir,* **26** (4), 2369 (2010)
[16]See http://www.eink.com/
[17] M. Majumder *et al.*, *Nature* **438,** 44 (2005)
[18] Holt, J. K., H. G. Park, Y. Wang, M. Stadermann, A. B. Artyukhin, C. P. Grigoropoulos, A. Noy, and O. Bakajin, *Science* **312**, 1034 (2006).
[19] Cleary J, Slater C, McGraw C, et al. IEEE SENSORS JOURNAL , **8**, 5-6, 508 (2008).
[20] T. Perkins, Quake SR, D. Smith, and *S Chu Science* **264**, 822 (1994).
[21] A. Groisman,M. Enzelberger, S. R. Quake, *Science* **9, 300**. 5621, 955 (2003).
[22] Nghe P, Degre G, Tabeling P, et al. App. Phys. Lett., **93**, 204102 (2008)
[23] P. Nghe, S. Fielding, A.Ajdari, P.Tabeling, *Phys.Rev.Lett*, **104**, 24, 248303 (2010).
[24] J. Maurer, P. Tabeling, P. Joseph, H. Willaime Phys. Fluids., **15** (9), 2613-2621 (2003)
[25] D. Beebe, Annual Review of Biomedical Engineering, **4**, 261 (2002)
[26] N. Lions et al, **24**, 21, 3533 (2003)
[27] Daniel Figeys and Devanand Pinto*Anal. Chem.*, **72** (9), 330 A (2000).
[28] C.Hansen et al, *PNAS**, 99**, 26 16531 (2002)*
[29] L. Mitnik, C. Heller, J. Prost, J.L. Viovy, *Science,* **267,** 219, (1995)
[30] H. Isambert, J. Prost, A. Ajdari, J.L. Viovy, *Physical Review Letters***, 78,** 5, 971 (1997)
[31] B.Ladoux, J-F. Léger, H. Isambert, J-L. Viovy, *Physical Review Letters, **17***, 3793 (1998)
[32] S.Magnusdöttir, H. Isambert, Ch. Heller, J-L Viovy, B*iopolymers*, **49,** 385 (1999)
[33] Doyle PS, Bibette J, Bancaud A, Viovy JL *Science,* **295** (5563) 2237 (2002).
[34] J. Leng, M.Joanicot, A.Ajdari, P. Tabeling, *Phys. Rev. Lett.* **96**, 084503 (2006)
[35] Kraus T, Malaquin L, Schmid H, Riess W, Spencer ND, Wolf H. *Nature Nanotechnology*, ***2**, 570*
[36] Thery M, Racine V, Piel M, Pepin A, Dimitrov A,Chen Y, Sibarita JB,Bornens M. *PNAS***, 103**(52), 1977 (2006)
[37] J. Rolland, R. Van Dam, D. Schorzman, S. Quake, and J. DeSimone, *J. Am.Chem. Soc.,* **126,** 2322 (2004).
[38] SM Moghimi, AC Hunter, *Pharmaceutical Res.,* **18,** 1 (2001)
[39] T Yanagishita, Y Tomabechi, K Nishio, H Masuda *Langmuir*, **20,**3, 554 (2004).
[40] Saliba et al., *Proc. Natl Acad Sci.* USA, **107**, 14524 (2010)
[41] Peyrin, Brugg, Vignes, Viovy patent WO2010040920

6.2. PARTNERS' REFERENCES

We show here a selection of papers published by the partners between 2002 to 2010. The selection includes 19 **Physical Review Letters**, 9 **Proceedings of National Academy of Science USA**, 8 **Nature**, 3 **Science**, 1 **Cell**, several **Angewandte Chemie**, **Anal Chem, Langmuir,** etc.. Most of the journals showed in the list below have the highest impact factors that can be found in the domains of expertise of the partners. This selection underlines the outstanding scientific level of the teams gathered in the Institute and involved in the Equipex project.

Partner 2 : ESPCI

1. *Instabilities of shear banded fluids in straight channels*. P. Nghe, S. Fielding, A. Ajdari, P. Tabeling, **Phys.Rev.Lett,** 104, 24, 248303 (2010).
2. *Total on-line analysis of a target protein from plasma by immunoextraction, digestion and liquid chromatography-mass spectrometry*. A. Cingöz, F. Hugon-Chapuis, V. Pichon.. **J. Chromatogr. B**, 878 213-221 (2010).
3. *Formation of liquid-core capsules having a thin hydrogel membrane: liquid pearls,* N. Bremond, E. Santanach-Carreras, L.-Y. Chu, J. Bibette, **Soft Matter** 6, 2484 (2010).
4. *Distinct proteomic features of two fibrogenic liver cell populations : hepatic stellate cells and portal myofibroblasts.* N. Bosselut, C. Housset, P. Marcelo, C. Rey, T. Burmester, J. Vinh, M. Vaubourdolle, A. Cadoret, B. Baudin, **Proteomics,**10(5):1017-28 (2010 Mar).
5. *Bubble phononic crystals*. A. Bretagne, A. Tourin, P. Tabeling, V. Leroy, N. Pannacci, H. Willaime, M. Fink, **The Journal of the Acoustical Society of America**, A110, 5, 3040 (2009).
6. *Determination of Cocaine in Human Plasma by Selective Solid-Phase Extraction Using an Aptamer-Based Sorbent.* B. Madru, F. Chapuis-Hugon, E. Peyrin, V. Pichon. **Anal. Chem**. 81, 7081-7086 (2009).
7. *Integrated microdevice for preconcentration and separation of a wide variety of compounds by electrochromatography.* G. Proczek, V. Augustin, S. Descroix, M.C. Hennion, **Electrophoresis** 30, 515-524 (2009).
8. *Selective sample pretreatment by molecularly imprinted polymer for the determination of LSD in biological fluids.* F. Chapuis-Hugon, M. Cruz-Vera, R. Savane, W. H. Ali, M. Valcarcel, M. Deveaux, V. Pichon, **Journal of Separation Science**, 32 (2009).
9. *Breaking of an Emulsion under an ac Electric Field.* A.R. Thiam, N. Bremond, J. Bibette, **Phys. Rev. Lett.**, 188304 102 (2009).
10. *Regional brain metabolism with cytochrome c oxidase histochemistry in a PS1/A246E mouse model of autosomal dominant Alzheimer's disease : correlations with behavior and oxidative stress.* C. Strazielle, R. Jazi, Y. Verdier, S. Qian, R. Lalonde, **Neurochem Int.** 55(8):806-14 (2009).
11. *Microfluidic droplet-based liquid-liquid extraction*. P. Mary, V. Studer, P. Tabeling, **Anal. Chem**., 80, 2680 (2008).
12. *Nanofluidics in the Debye layer at hydrophilic and hydrophobic surfaces.* C.I. Bouzigues, P. Tabeling, L. Bocquet, **Phys. Rev. Lett.,**114503 (2008).
13. *Equilibrium and Nonequilibrium States in Microfluidic Double Emulsions.* N. Pannacci, H. Bruus, D. Bartolo et al**., Phys. Rev. Lett.,** 101**,** 16 (2008).
14. *Role of molecularly imprinted polymers for the selective determination of environmental pollutants.* V. Pichon, F. Chapuis-Hugon, **Anal. Chim. Acta**, 622, 48-61 (2008).
15. *Microelectrochemical Patterning of Surfaces with Polymer Brushes*. C. Slim, Y. Tran, M. Chehimi, N. Garraud, J.P. Roger, C. Combellas, F. Kanoufi, **Chem. Materials,** 20, 6677-6685 (2008).
16. *Chiral Colloidal Clusters.* D. Zerrouki, J. Baudry, D. Pine, P. Chaikin, J. Bibette, **Nature**, 455, 7211, 380-382 (2008).
17. *Decompressing Emulsion Droplets Favors Coalescence.* N. Brémond, A. R. Thiam, J. Bibette, **Physical Review Letters** 100, 024501 (2008)

18. *Kinetics of biorecognition: the capture range of tethered biomolecules,* L. Cohen-Tannoudji, E. Bertrand, J. Baudry, C. Robic, C. Goubault, M. Pellissier, A. Johner, F. Thalmann, N.K. Lee, C.M. Marques, J. Bibette. **Physical Review Letters**, 100, 108301 (2008).
19. *Ligand-Receptor Interactions in Chains of Colloids: When Reactions Are Limited by Rotational Diffusion.* N-K. Lee, A. Johner, F. Thalmann, L. Cohen-Tannoudji, E. Bertrand, J. Baudry, J. Bibette, C. M. Marques, **Langmuir** 24, 1296 -1307 (2008).
20. *Interference and crosstalk in double optical tweezers using a single laser source.* P. Mangeol, U. Bockelmann, **Rev. Sci. Instrum.** 79, 083103 (2008)
21. *T7 RNA Polymerase Studied by Force Measurements Varying Cofactor Concentration*. P. Thomen, P. J. Lopez, U. Bockelmann, J. Guillerez, M. Dreyfus, F. Heslot, **Biophys. J**. 95, 2423 (2008).
22. *On-line preconcentration using monoliths in electrochromatography capillary format and microchip*. V. Augustin, G. Proczek, S. Descroix, J. Dugay, M.C. Hennion, **J. Sep. Sci**. 45, 2858-67 (2007).
23. *Selective sample treatment using molecularly imprinted polymers.* V. Pichon, **J. Chromatogr***, A* 1152, 41-53 (2007).
24. *Arnold tongues in microfluidic systems.* H. Willaime, V. Barbier, P. Tabeling, **Phys. Rev. Lett.,** 96, 054501 (2006).
25. *Slippage of water past superhydrophobic carbon nanotube forests in microchannels.* P. Joseph, C. Cottin Bizonne, J.-M. Benoît, C. Ybert, C. Journet, P.Tabeling, L. Bocquet **Phys. Rev. Lett.** 97*, 156104 (2006).*
26. *Microevaporators for kinetic exploration of phase diagrams.* J. Leng, M. Joanicot, A. Ajdari, P. Tabeling**,** **Phys. Rev. Lett.** 96**,** 084503 (2006).
27. *Single molecule study of DNA conductivity in aqueous environment*. O. Legrand, D. Côte, U. Bockelmann **Phys. Rev. E**, 73, 031925 (2006).
28. *PDMS-based microfluidics for proteomic analysis.* A. Dodge, E. Brunet, S. Chen, J. Goulpeau, V. Labas, J. Vinh, P. Tabeling, **The Analyst,** 131(10):1122-8 (2006).
29. *Microscopic artificial swimmers*. R. Dreyfus, J. Baudry, M.L. Roper, M. Fermigier, H.A. Stone, J. Bibette, **Nature** (London, United Kingdom), 437(7060), 862-865 (2005)
30. *Spatio-temporal resonances in mixing of open viscous fluids.* F. Okkels, P. Tabeling, **Phys.Rev.Lett**. 92 (3), 038301 (2004).
31. *Single molecule manipulation of nucleic acids,* U. Bockelmann, **Curr. Op. Struct. Biol.** 14, 368 (2004).
32. *Dynamics of the DNA duplex formation studied by single molecule force measurements.* U. Bockelmann, P. Thomen, F. Heslot**, Biophys. J**. 87, 3388 (2004).
33. *DNA detection on transistor arrays following mutation-specific enzymatic amplification*. F. Pouthas, C. Gentil, D. Côte, U. Bockelmann, **Appl. Phys. Lett**. 84, 1594 (2004).
34. *Ordered and disordered patterns in two phase flows in microsystems*. R. Dreyfus, P. Tabeling, H. Willaime, **Phys Rev Lett.,** 90, 144505 (2003).
35. *Second order slip laws for Helium and Nitrogen.* J. Maurer, P. Tabeling, P. Joseph, H. Willaime, **Phys. Fluids.,** 15 (9), 2613-2621 (2003).

Partner 3 : Institut Curie

1. *Direct observation of twisting steps during Rad51 polymerization on DNA.* H. Arata, A. Dupont, J. Miné-Hattab, L. Disseau, A. Renodon-Cornière, M. Takahashi, J.L. Viovy, G. Cappello, **Proc Natl Acad Sci USA**, 106, 19239-19244 (2010).
2. *Confinement-optimized three-dimensional T cell amoeboid motility is modulated via myosin IIA–regulated adhesions.* J. Jacobelli, R. S. Friedman, M.A. Conti, A.M. Lennon-Dumenil, M. Piel, C. M. Sorensen, R. S. Adelstein, M.F. Krummel, **Nature Immunology**, in press.
3. *Physical model of the dynamic instability in an expanding cell culture***,** S. Mark, R. Shlomovitz, N.S. Gov, M. Poujade, E. Grasland-Mongrain, P. Silberzan, **Biophys. J.,** 98, 361 (2010).
4. *Right-handed nucleosome: myth or reality? C.* Lavelle, P. Recouvreux, H. Wong, A. Bancaud, J.L. Viovy, A. Prunell, J.M. Victor, **Cell,** 139(7):1216-7; author reply 1217-8 (2009).

5. *Microfluidic high-throughput encapsulation and hydrodynamic self-sorting of single cells.* M. Chabert, J.L. Viovy, **Proc Natl Acad Sci USA**, 105(9):3191-6 (2009).
6. *Stepping Mechanism.* G. Cappello, P. Pierobon, C. Symonds, L. Busoni, J.C.M. Gebhardt, M. Rief, J. Prost, V. Myosin, **Proc. Natl. Acad. Sci. USA,** 104 : 15328-15333 (2009).
7. *Adaptive force transmission in amoeboid cell migration.* J. Renkawitz, K. Schumann, M. Weber, T. Lämmermann, H. Pflicke, M. Piel, J. Polleux, J. P. Spatz, M. Sixt. **Nat. Cell Biol**., (12):1438-43 (2009 Dec 11).
8. *A nanostructure made of a small non-coding RNA.* B. Cayrol, C. Nogues, A. Dawid, I. Sagi, P. Silberzan, H. Isambert, **J. Am. Chem. Soc**., 131, 1727 (2009).
9. *E. Coli and Oxygen: A Motility Transition.* C. Douarche, A. Buguin, H. Salman, A. Libchaber **Phys. Rev. Lett.,** 102, 198101 (2009).
10. *Nanoparticle printing with single-particle resolution.* T. Kraus, L. Malaquin, H. Schmid, W. Riess, N.D. Spencer, H. Wolf, **Nature Nanotechnology,** 2, 570 (2008).
11. *Regulation of dendritic cell migration by CD74, the MHC class II-associated invariant chain.* G. Faure-André, P. Vargas , M.I. Yuseff, M. Heuzé, J. Diaz, D. Lankar, V. Steri, J. Manry, S. Hugues, F. Vascotto, J. Boulanger, G. Raposo, M.R. Bono, M. Rosemblatt, M. Piel, A.M. Lennon-Duménil, **Science,** 322(5908):1705-10. (2008 Dec 12)
12. *Physical mechanisms redirecting cell polarity and cell shape in fission yeast.* C.R. Terenna, T. Makushok, G. Velve-Casquillas, D. Baigl, Y. Chen, M. Bornens, A. Paoletti, M. Piel, P.T. Tran, **Curr Biol**, 18(22):1748-53. (2008 Nov 25).
13. *Collective migration of an epithelial monolayer in response to a model wound.* M. Poujade, E. Grasland-Mongrain, A. Hertzog, J. Jouanneau, P. Chavrier, B. Ladoux, A. Buguin, P. Silberzan, **Proc. Nat. Acad. Sci**. USA, 104, 15988 (2007).
14. *Rigidity-driven growth and migration of epithelial cells on microstructured anisotropic substrates.* A. Saez, M. Ghibaudo, A. Buguin, P. Silberzan, B. Ladoux, **Proc. Nat. Acad. Sci.** USA, 104, 8281 (2007).
15. *Structural plasticity of single chromatin fibers revealed by torsional manipulation. A.* Bancaud, N. Conde e Silva, M. Barbi, G. Wagner, J.F. Allemand, J. Mozziconacci, C. Lavelle, V. Croquette, J.M. Victor, A. Prunell, J.L. Viovy, **Nature Struct. Mol. Biol,** 13, 444-450 (2006).
16. *Tracking Individual Kinesin Motors in Living Cells Using Single Quantum-Dot Imaging.* S. Courty, C. Luccardini, Y. Bellaïche, G. Cappello, M. Dahan, **Nanoletters**, 6:1491-1495 (2006).
17. *Broad-spectrum biofilm inhibition by a secreted bacterial polysaccharide.* J. Valle, S. Da Re, N. Henry, T. Fontaine, D. Balestrino, P. Latour-Lambert, J.M. Ghigo, **PNAS**, 103, 12558-12563 (2006).
18. *Traction forces developed by myogenic cells at cadherin contacts.* A. Ganz, M. Lambert, A. Saez, P. Silberzan, A. Buguin, R.M. Mège, B. Ladoux, **Biology of the Cell,** 98, 721 (2006).
19. *Micro-muscles : When artificial muscles made of nematic liquid crystal elastomers meet soft lithography. A.* Buguin, M.H. Li , P. Silberzan, B. Ladoux, P.J. Keller, **Am. Chem. Soc.,** 128, 1088 (2006).
20. *Non-Markovian Transport of DNA in Post Arrays.* N. Minc, J.L. Viovy, K.D. Dorfman, **Physical Review Letters**, 94(19): 198105 (2005).
21. *Closing the gap between self-assembly and microsystems using Self-assembly, Transfer, and Integration (SATI) of particles.* T. Kraus, L. Malaquin, E. Delamarche, H. Schmid, N.D. Spencer, H. Wolf, **Advanced Materials (Cover),** 17 (20):2438 – 2442 (2005).
22. *The extracellular matrix guides the orientation of the cell division axis*. M. Théry, V. Racine, A. Pépin, M. Piel, Y. Chen, J.B. Sibarita, M. Bornens, ***Nat Cell Biol***, (10):947-53 (2005 Oct 7).
23. *Directing cell migration with asymmetric micropatterns*. X. Jiang, D.A. Bruzewicz, A.P. Wong, M. Piel, G.M. Whitesides, ***Proc Natl Acad Sci U S A***., 102(4):975-8 (2005 Jan 25).
24. *Force mapping in epithelial cell migration. O.* Roure, A. Saez, A. Buguin, R.H. Austin, P. Chavrier, P. Silberzan, B. Ladoux, **Proc Nat. Acad. Sci.** USA, 102, 2390 (2005).
25. *Model of RecA-mediated homologous recognition,* K.D. Dorfman, R. Fulconis, M. Dutreix, J.L. Viovy, **Phys. Rev. Lett.,** 93(26) 268102 (2004).

26. *ATM germline mutations in women with familial breast cancer and a relative with haematological malignancy*. L.L. Paglia, A. Laugé, J. Weber, J. Champ, E. Cavaciuti, A. Russo, J.L. Viovy, D. Stoppa-Lyonnet, **Breast cancer research and treatment,** 119(2):443-52.
27. *Self-assembled magnetic matrices for DNA separation chips.* P.S. Doyle, J. Bibette, A. Bancaud, J.L. Viovy, **Science,** 295, (5563), 2237 (2002).
28. *Microtubule release from the centrosome in migrating cells.* M. Abal, M. Piel, V. Bouckson-Castaing, M. Mogensen, J.B. Sibarita, M. Bornens M, ***J Cell Biol***, 159(5):731-7 (2002 Dec 9).
29. *The Rho-associated protein kinase p160ROCK is required for centrosome positioning*. V. Chevrier, M. Piel, N. Collomb, Y. Saoudi, R. Frank, M. Paintrand, S. Narumiya, M. Bornens, D. Job, ***J Cell Biol***, May 27;157(5):807-17 (2002).

Partner 4: ENS

1. *Covalent monofunctionalization of peptide-coated semiconductor quantum dots for single molecule assays.* S. Clarke, F. Pinaud, O. Beutel, C. You, J. Piehler, M. Dahan, **Nanolett**, 10 (6) 2147–2154 (2010).
2. *Probing cellular events, one quantum dot a time.* F. Pinaud, S. Clarke, A. Sittner, and M. Dahan, **Nature Methods** 7, 275-85 (2010).
3. *Active and passive mechanisms of helicases*. M. Manosas M, X.G. Xi, D. Bensimon, V. Croquette, **Nucleic Acids Res** (2010 Apr 27).
4. *Microfluidic stickers for cell and tissue-based assays in microchannels.* M. Morel, D. Bartolo, J. C. Galas, M. Dahan, V. Studer, **Lab on Chip** 9, 1011-1013 (2009).
5. *High-affinity quantum-dot labeling of histidine-tagged proteins for multiplexed targeting and single-molecule tracking in live cells.* V. Roullier, S. Clarke, C. You, F. Pinaud, G. Gouzer, D. Schaible, V. Marchi-Artzner, J. Piehler, M. Dahan, **Nanolett. 9**, 1228-1234 (2009).
6. *Velocity, processivity and individual steps of single myosin V molecules in live cells*, P. Pierobon, S. Achouri, S. Courty, A. Dunn, J.A. Spudich, M. Dahan, G. Cappello, **Biophys. J** 96(10):4268-75 (2009).
7. *Measurement of the torque on a single stretched and twisted DNA using magnetic tweezers*. F. Mosconi, J.F. Allemand, D. Bensimon, V. Croquette, **Phys Rev Lett**., 102(7):078301 (2009 Feb 20).
8. *Mechanisms of chiral discrimination by topoisomerase IV*. K.C. Neuman, G. Charvin, D. Bensimon, V. Croquette, **Proc Natl Acad Sci U S A**, 106(17):6986-91 (2009 Apr 28).
9. *Coupling DNA unwinding activity with primer synthesis in the bacteriophage T4 primosome.* M. Manosas, M.M. Spiering, Z. Zhuang, S.J. Benkovic, V. Croquette, **Nature Chem Biol**, (12):904-12 (2009 Dec 5).
10. *Asymmetric redistribution of GABAA receptors during GABA gradient sensing by nerve growth cones.* C. Bouzigues, M. Morel, A. Triller, M. Dahan, , **Proc. Natl. Acad. Sci. USA** 104, 11251 (2007).
11. *Real-time observation of bacteriophage T4 gp41 helicase reveals an unwinding mechanism.* T. Lionnet, M.M. Spiering, S.J. Benkovic, D. Bensimon, V. Croquette, **Proc Natl Acad Sci U S A,** 104(50) :19790-5 (2007 Dec 11).
12. *Fourier analysis to measure diffusion coefficients and resolve mixtures on a continuous electrophoresis chip.* A. Estévez-Torres, C. Gosse, T. Le Saux, J.F. Allemand, V. Croquette, H. Berthoumieux, A. Lemarchand, L. Jullien, **Anal Chem,** 79(21) :8222-31 (2007 Nov 1).
13. *The manipulation of single biomolecules*. J.F. Allemand, G. Charvin, V. Croquette, G. Lia, D. Bensimon, **Interdisciplinary Science Reviews,** 32-2 p : 149-161 (2007).
14. *Tracking individual kinesin motors in living cells using single quantum dot imaging.* S. Courty, C. Luccardini, Y. Bellaiche, G. Cappello, M. Dahan, **Nanolett. 6**, 1491-1495 (2006).
15. *Wringing out DNA.* T. Lionnet, S. Joubaud, R. Lavery, D. Bensimon, V. Croquette, **Phys. Rev. Lett**., 96(17) :178102 (2006 May 5).
16. *Mechanically controlled DNA extrusion from a palindromic sequence by single molecule micromanipulation.* A. Dawid, F. Guillemot, C. Breme, V. Croquette, F. Heslot, **Phys Rev Lett**., 96(18) :188102 (2006 May 12).

17. *Structural plasticity of single chromatin fibers revealed by torsional manipulation.* A. Bancaud, N. Conde e Silva, M. Barbi, G. Wagner, J.F. Allemand, J. Mozziconacci, C. Lavelle, V. Croquette, J.M. Victor, A. Prunell, J.L. Viovy, **Nat Struct Mol Biol,** (5) :444-50 (2006 May 13).
18. *Direct observation of DNA distortion by the RSC complex.* G. Lia, E. Praly, H. Ferreira, C. Stockdale, Y.C. Tse-Dinh, D. Dunlap, V. Croquette, D. Bensimon, T. Owen-Hughes, **Mol Cell,** 21(3) :417-25 (2006 Feb 3).
19. *Friction and torque govern the relaxation of DNA supercoils by eukaryotic topoisomerase IB*, D.A. Koster, V. Croquette, C. Dekker, S. Shuman, NH. Dekker, **Nature**, 434-7033 p.671 (2005).
20. *Tracking topoisomerase activity at the single-molecule level.* G. Charvin, T.R. Strick, D. Bensimon, V. Croquette, **Annu Rev Biophys Biomol Struct,** 34 :201-19 (2005).
21. *Measurement of the radiative and non-radiative decay rates of single CdSe nanocrystals through controlled modification of their spontaneous emission.* X. Brokmann, L. Coolen, M. Dahan, J.P. Hermier, **Phys. Rev. Lett. 93**, 107403 (2004).
22. *Statistical Aging and Non-ergodicity in the fluorescence of single nanocrystals.* X. Brokmann, J.P. Hermier, G. Messin, P. Desbiolles, J.P. Bouchaud, et M. Dahan, **Phys. Rev. Lett. 90**, 120601-1 (2003).
23. *Diffusion dynamics of glycine receptors revealed by single quantum dot tracking*. M. Dahan, S. Lévi, C. Luccardini, P. Rostaing, B. Riveau and A. Triller, **Science 302**, 442 (2003).

Partner 5: ENSCP

1. *Separation of a-lactalbumin grafted- and non-grafted maghemite core/silica shell nanoparticles by capillary zone electrophoresis.* J. Petr, B. Teste, S. Descroix, J.-M. Siaugue, P. Gareil, A. Varenne, **Electrophoresis**, 31, 2754–276 (2010).
2. *Automated synthesis of a 96 product-sized library of triazole derivatives using a solid phase supported copper catalyst.* I. Jlalia, C. Beauvineau, S. Beauvière, E. Onen, M. Aufort, A. Beauvineau, E. Khaba, J. Herscovici, F. Meganem, C. Girard, , **Molecules**, 15, 3087-3120 (2010).
3. *Microfluidics in Inorganic Chemistry.* A. Abou-Hassan, O. Sandre, V. Cabuil, **Angewandte Chemie,** International Edition, 49 (36), 6268 (2010).
4. *Fluorescence Confocal Laser Scanning Microscopy for pH Mapping in a Coaxial Flow Microreactor: Application in the Synthesis of Superparamagnetic Nanoparticles.* A. Abou-Hassan, J.R. Dufreche, O. Sandre, G. Meriguet, O. Bernard , V. Cabuil, **J. Phys. Chem. C**, 113(42) 18097 (2009).
5. *Multistep Continuous-Flow Microsynthesis of Magnetic and Fluorescent gamma-Fe2O3@SiO2 Core/Shell Nanoparticles.* A. Abou-Hassan, R. Bazzi, V. Cabuil, **Angewandte Chemie**, 48(39), 7180 (2009).
6. *Synthesis of Goethite by Separation of the Nucleation and Growth Processes of Ferrihydrite Nanoparticles Using Microfluidics.* A. Abou-Hassan, O. Sandre, S. Neveu, V. Cabuil, **Angewandte Chemie**, 48(13), 2342 (2009).
7. *Synthesis of iron oxide nanoparticles in a microfluidic device: preliminary results in a coaxial flow millichannel.* A. Abou Hassan, O. Sandre, V. Cabuil, P. Tabeling, **Chem. Com**, 15, 1783 (2008).
8. *Stable Modification of PDMS surface properties by plasma polymerization: Application to the formation of double emulsions in microfluidic systems.* V.Barbier, M.Tatoulian, Hong Li, F. Arefi-Khonsari, A. Ajdari, P. Tabeling**, Langmuir**, 22, pp 5230 – 5232 (2006).

6.3. COMMITMENT LETTERS AND ESTIMATE FOR THE EQUIPEMENT

Here is a copy of an email from CNRS which proves the commitment of this entity toward the IPGG project. The official letter has been delayed for the electronic submission but it will be attached in the final paper document.

Cher Jacques,

Jusqu'à réception du dossier en cette toute fin de semaine, il était assez difficile d'exprimer une opinion de soutien sur cette intention de projet. Nos DAS ont pu le regarder dans le week-end et une lettre de soutien du CNRS devrait te parvenir.

Amicalement
Bertrand

Pr. Bertrand GIRARD

Directeur Scientifique

Institut de Physique du CNRS

3 rue Michel Ange

75016 Paris

Tél : (33) 1 44 96 42 50

Fax : (33) 1 44 96 53 20

bertrand.girard@cnrs-dir.fr
http://www.cnrs.fr/inp/

MAIRIE DE PARIS

Jean-Louis Missika

Adjoint au Maire de Paris
Chargé de l'Innovation
de la Recherche et des Universités

Nos Réf. : JLM/JBH/MRM_d80

Paris, le 13 SEP. 2010

Objet : Lettre de recommandation
Création de l'Institut Pierre Gilles de Gennes pour la microfluidique

La Ville de Paris soutient la démarche initiée par plusieurs établissements scientifiques d'excellence (ESPCI, ENS, Institut Curie, ENSCP) consistant à créer, dans le cadre de la procédure du grand emprunt, un institut international de recherche en microfluidique.

Afin de permettre la création de cet institut, la Ville de Paris est prête à lui affecter un bâtiment situé au 6/8 rue Jean Calvin, dans le cadre d'un accord avec l'Etat (courrier du Recteur en date du 17 mai 2010).

L'institut international de recherche en microfluidique contribuera à structurer la recherche et l'innovation dans cette discipline nouvelle, au cœur du grand quartier scientifique de Paris.

Cet apport de la ville de Paris est estimé à environ 26 M€. Le coût de l'adaptation et de la mise aux normes du bâtiment est estimé à environ 12 M€.

Jean-Louis MISSIKA

Hôtel de Ville - 75196 Paris RP
Tél : 01 42 76 51 31 - Fax : 01 42 76 54 75

académie Paris

MINISTÈRE DE L'ÉDUCATION NATIONALE

MINISTÈRE DE L'ENSEIGNEMENT SUPÉRIEUR ET DE LA RECHERCHE

Liberté • Égalité • Fraternité
RÉPUBLIQUE FRANÇAISE

Jean-Louis MISSIKA
Adjoint au Maire de Paris

31 MAI 2010

COURRIER ARRIVÉE

426.

Le Recteur de l'académie
Chancelier des universités
de Paris

Paris, le 17 mai 2010

Helene.gobert@ac-paris.fr
Tél : 01.40.46.21.06.
N/Réf. : VCU / HG 2010- 108

Monsieur le Maire,

J'accuse réception de votre courrier en date du 3 mai dernier par lequel vous reprenez les termes des échanges intervenus lors de notre entretien du 1er avril 2010 concernant différents projets ou immeubles, objets de négociations entre la Ville et l'État.

RECTORAT
DE L'ACADÉMIE
DE PARIS

☒ CHANCELLERIE
DES UNIVERSITÉS
En Sorbonne
47, rue des Écoles
75230 Paris cedex 05
Tél. : 01 40 46 22 11
Fax : 01 40 46 20 10

☐ ENSEIGNEMENT
SCOLAIRE
94, avenue Gambetta
75984 Paris cedex 20
Tél. : 01 44 62 40 40
Fax : 01 44 62 12 72

Site internet
www.ac-paris.fr
www.sorbonne.fr

Ainsi, vous rappelez, conformément à votre courrier du 15 avril 2010, votre demande relative à l'implantation de l'Institut Langevin au sein du bâtiment prochainement livré par l'EPA Jussieu sur l'îlot Cuvier, en confirmant que la prise en charge des travaux, dont le coût estimatif avant études d'APD et avant chiffrage par l'entreprise est évalué à 3,4 M€, s'effectuera au coût réel de l'opération, au vu des factures correspondantes.

Vous proposez également une base de discussion pour la définition d'engagements réciproques entre la Ville et le Rectorat, lesquels ont vocation à fonder un accord global équilibré.

Ces propositions, formulées dans les termes suivants, recueillent mon accord, sous réserve des résultats des estimations que je demande à France Domaine :

- ✓ la Ville de Paris consent à une occupation à titre gratuit par l'Université Paris IV du lycée Championnet jusqu'à la livraison de locaux construits dans le cadre du contrat de partenariat public-privé Paris IV - Clignancourt ;
- ✓ la non restitution des locaux de Garancière pourra être compensée par la cession des locaux du 6/8 rue Jean Calvin ;

Monsieur Jean-Louis MISSIKA
Adjoint au Maire de Paris
Chargé de l'Innovation, de la Recherche
et des Universités
Hôtel de Ville de Paris
Place de l'Hôtel de Ville
75 196 PARIS Cedex 04

- ✓ les locaux de la rue Charles V continuent d'être occupés par l'université Paris VII jusqu'à la livraison des locaux construits dans le cadre du contrat de partenariat public-privé relatif à la 2ème phase d'implantation de Paris 7 sur la zac PRG, date à laquelle leur cession à la Ville sera effective ;
- ✓ s'agissant du relogement du CNOUS, les services de la Ville de Paris effectueront les démarches nécessaires afin d'accompagner les recherches de locaux disponibles dans la capitale.

Comme je vous l'ai indiqué, l'État demande que cet accord soit accompagné d'une bienveillance de la Ville concernant le versement des pénalités dues par l'EPCJ concernant l'occupation de l'ancien hôpital Boucicaut jusqu'à la fin 2010. La Ville, comme l'État, rencontre d'inévitables retards de chantier pour lesquels la compréhension des acteurs devrait permettre une meilleure coopération.

Enfin, je souhaite rappeler que les décisions relatives à la mise à disposition de locaux aux établissements publics de l'État pour l'accueil de leurs différentes activités d'enseignement supérieur et de recherche relève de la responsabilité de l'État.

Si vous en êtes d'accord, nos services respectifs pourront se rapprocher afin de mettre au point un projet de convention État-Ville de Paris qui reprenne ces différentes propositions.

Dans cette perspective, je vous prie d'agréer, Monsieur le Maire, l'assurance de ma considération la plus distinguée.

Patrick GÉRARD

FLUIGENT

A l'attention de Monsieur Gilles Rubinstenn
Fondation Pierre-Gilles de Gennes
29 rue d'Ulm
75005 Paris

Paris, 1st September 2010

Our re: 2010-63/PKo

To whom it may concern,

I am pleased to write this letter in support of your project of Pierre Gilles de Gennes Institute for Microfluidics, and of the Labex proposal associated with it.

Fluigent is a "Startup" company issued from Curie Institute's research, located in Paris Santé Cochin incubator. Our mission is to develop microfluidic technologies, integrated systems based on these technologies for the life sciences, environment and medicine, and diagnosis kits and equipment. We currently hire about 20 persons, for a gross revenue in 2010 expected to 2M€, and 120 Fluigent instruments sold so far (1/3 international sales).

We are convinced that microfluidics will bring in life sciences a revolution comparable to the advent of microprocessors in the microelectronics and computer industry, and harness efforts to be pioneers and become leaders in this revolution.

Our experience has taught us that access to the optimal technology is a key to success in this field. Because it is an emerging field, this access is not easy: the technologies available in microelectronic foundries are not well adapted to our applications, and much too expensive. "Soft lithography" techniques currently used in academic laboratories are not productive enough for industrial research and clinical validation. At the other end of the industrial development chain, technologies like injection molding are suitable for mass production, but the fabrication of moulds is prohibitively long and expensive during the R&D and early validation stages. In addition, some microfluidic applications just cannot be implemented with the technologies currently available for mass production. This is an emerging field still in strong need for innovation. We thus believe that the developments proposed in the Pierre Gilles de Gennes Institute for Microfluidics are very timely and foreseeing: they have the potential to bridge the gap between current laboratory techniques and industrial production, and thus to bring to

FLUIGENT
Siège social : Pépinière Paris Santé Cochin -29 rue du Faubourg Saint Jacques – 75014 Paris - France
Tel : +331 71 18 20 55 – Fax : +331 46 33 16 68
www.fluigent.com

SA à Directoire et Conseil de Surveillance au capital de 58164,70 € - Siret : 487 636 409 00020 – N°TVA UE/EU VAT Number : FR 53 487 636 409

FLUIGENT

Companies lucky enough to benefit from this expertise and infrastructures, a dramatic competitive advantage in our R&D.

Finally, it appears that the Institute would also involve some space dedicated to Industrial collaboration, and we would be extremely interested in applying to this programme.

Yours faithfully,

Patrick KORMAN
CEO

FLUIGENT
Siège social : Pépinière Paris Santé Cochin -29 rue du Faubourg Saint Jacques - 75014 Paris - France
Tel : +331 71 18 20 55 – Fax : +331 46 33 16 68
www.fluigent.com

SA à Directoire et Conseil de Surveillance au capital de 58164,70 € - Siret : 487 636 409 00020 – N°TVA UE/EU VAT Number : FR 53 487 636 409

10 Septembre 2010

Monsieur Patrick TABELING
ESPCI
Laboratoire Gulliver
10 Rue Vauquelin
75008 PARIS

Cher Monsieur Tabeling,

Vous m'avez fait part de votre intention de déposer, dans le cadre des initiatives d'excellence, un projet d'Institut dédié à la microfluidique.sur le site parisien.

Je suis totalement en accord avec cette idée de fédérer les multiples activités de microfluidique sur la place de Paris, et c'est d'ailleurs une des recommandations que j'avais effectuées à l'occasion de ma participation au Comité d'évaluation AERES du Laboratoire PASTEUR de l'ENS.

La ville de Paris possède en son sein des équipes d'excellence en microfluidique, un peu dispersées toutefois. La réunion sur un même lieu des outils de fabrication, des compétences scientifiques, l'accueil de jeunes équipes, sont autant d'éléments qui peuvent donner une ambition réelle pour la création d'un des plus importants centres de microfluidique en Europe et dans le Monde

Je soutiens donc sans réserves ce projet, auquel Rhodia pourra d'ailleurs être associé à terme au travers de collaborations, soit directes, soit mettant en œuvre nos équipes du Laboratoire du Futur à Pessac.

Bien sincèrement,

Patrick MAESTRO
Directeur de la Recherche Avancée
178 avenue du Docteur Schweitzer
33608 Pessac - France