THE UNIVERSITY of TEXAS
HEALTH SCIENCE CENTER AT HOUSTON

Division of Nanomedicine, Biomedical Engineering Department,
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Decoupling Diffusive Transport Phenomena in Microgravity

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The emergent properties of materials and devices fabricated with critical dimensions in the nanoscale present significant opportunities in the fields of medicine and biology for engineering of pharmaceutical delivery vehicles, therapeutic and imaging agents, and biological sensors. Despite the increasing focus on nanofluidics in many of these applications, the laws governing molecular transport through nanoscale fluidic channels have not been fully realized. As the size of the channel is reduced to the molecule size, classical continuum theories fail to predict even basic characteristics of fluid transport. New transport mechanisms are observed whereby channel surface properties begin to dominate over volume properties. At the theoretical level the major challenge in analyzing these systems arises from the difficulty in decoupling the interactive effects of charge distribution, space constraints and molecular adsorption. At the experimental level this decoupling becomes nearly impossible.

We propose an experiment capable of analyzing nanoscale confinement on molecular diffusion through simulation at the microscale. The objective of this study is to provide insight into the aforementioned decoupled interaction effects by overcoming experimental limitations specific to the nanoscale. In the absence of significant gravitational forces, micron sized particles should constitute a reliable substitute for molecules at nanoscale once the appropriate microscale channel size is determined. This substitution allows for greater control of the geometric design, size distribution, and surface modification of the diffusing constituents and decreases the complexity of quantifying the experimental results. The analysis will focus on understanding how particle and channel properties, such as surface charge, coupled with particle-to-particle and particle-to-channel interactions affect the diffusive transport.

The insight into nanoscopic diffusive transport gleaned from this study will be relevant for "on-Earth" applications including drug delivery, molecular sieving and particle filtration. Moreover, the study will provide an understanding of microparticle diffusive transport in view of future technological applications for space exploration.

Participating Organization and Key Personnel

Organization:
The participating institution is The University of Texas Health Science Center at Houston (UTHSC-H) located in the Texas Medical Center in Houston, Texas. UTHSC-H is a graduate university that has a Graduate School of Biomedical Sciences, Medical School, School of Health Information Sciences, School of Public Health, School of Nursing, and a Dental Branch. The Principal Investigator is located in the Department of Biomedical Engineering, Division of Nanomedicine. UTHSC-H will house and support the proposed research effort.

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Experimental Objective

Nanotechnology, as generally accepted, is concerned with structures, properties, and processes involving materials having organizational features on the spatial scale of 1–300 nm. Being much smaller than the wavelength of visible light, but much larger than simple molecules, it is difficult to characterize the structure of and to control the processes involving nanomaterials. However, the phenomena occurring at this scale provide opportunities for new levels of sensing, manipulation, release and control; hence, nanodevices may lead to dramatically enhanced performance, sensitivity, and reliability with considerably decreased size, weight, and cost. Considerable progress has been seen in the development of microfabricated systems for use in the domains of health, medicine, and agriculture; nanoengineered devices have been realized for drug delivery, nanoporous membranes for biosensing applications, lab-on-a-chip systems, and for controlled chemical release in various ambits from farming to industrial processing [Chin et al., 2007; Desai et al., 1999; Han et al., 2008; La Van et al, 2003; Whitesides, 2003]. In addition the low costs of mass producing microchips and the automation of reaction systems have allowed for the adoption of microfluidic systems for commercial use. All these systems are based upon mixing, separation, diffusion, interface contact and kinetics at the nanoscale, but, despite the widespread adoption of these technologies, the evolution of the transport phenomena within these systems has not been investigated locally nor the theoretical description developed sufficiently.

A tangible effect of miniaturization is that fluid properties become increasingly dominated by viscous forces rather than inertial forces. Reynolds numbers (Re) are typically $<10^2$, flow is laminar with mixing accomplished only through diffusion, and cross-sectional velocity profiles are parabolic as a result of zero fluid velocity at the channel walls. This causes a residence-time distribution and a significant variation in the yield that is not easy to control. Generally, the confined transport at the nanoscale is driven and improved by means of passive methods, such as specifically designed channel geometry, and active methods, via externally applied forces such as electrokinetic, electrophoresis and electroosmotic pumping, that are not yet analytically described. Since it is difficult to follow what occurs at the nanoscale, there are very few experimental measurements preformed within nanosystems described in the literature.

Analytes within nano- or microstructures are acted upon by a range of different driving forces at ambient conditions due to nanoscale confinement. The relative importance of these forces is given by the following relations: buoyancy < inertial forces ≈ gravitational < viscous force << interfacial force [Eijkel et al., 2005]. Interfacial forces start to dominate when systems are reduced in scale, affecting the transport of analytes and fluids. The interface influences the density of particles in a fluid despite the size of the channel or any other microscale volume. Therefore, fluid stratification can take place. This stratification can occur, for example, if any channel contains several immiscible/low-miscible liquids or if big heavy particles are suspended in fluid. Such effects can stratify the solution and create laminar flow of different densities. Although gravitational force is negligible when considering a single solute, it can affect the laminar flow of stratified fluids, as described above. An analogically the situation can happen in a reservoir of solution, where different local densities of liquid are possible due to interface effects or concentration depletion (density decrease) at reservoir/channel boundaries. The standard gravity the buoyancy of a liquid can play a significant role, as found in protein crystallization experiments [Qi et al., 2000]. It was revealed that microgravity diminishes convective flows. Crystal growth is governed by pure diffusion only causing slowdown of the crystals significantly. As the size and mass of particles increases, the rate of particle diffusion drops. The typical diffusion rates of micro-size particles is approximately 10^{-10} – 10^{-9} cm^2/s, which is ~ 10^4 – 10^5 times lower than for small drug like molecules and ~ 10^2 – 10^3 times lower than that of proteins. Therefore the movement of big particles would be affected significantly more by interfacial forces than by passive diffusion. On this basis, the microgravity environment should eliminate several possible effects that render analysis of nanofluidic phenomena more difficult at standard gravity.

Experimental studies performed by our group reveal that diffusion at nano- and microscale is affected by channel dimensions. As particle size approaches channels size constrained diffusion is observed [Martin et al., 2005]. Diffusion is affected by the close proximity of the interface with reduced freedom of diffusion inside the channels. The surface presents electrostatic forces that act as far as the electrical double layer extends, which is from 1 nm up to 100 nm. Electrostatic forces depend on electrolyte concentration and wall charge, and can be repulsive or attractive. At the same time Van der Waals forces are only attractive and extend up to 2 nm at the

most. Therefore, diffusion of any analyte can be significantly affected by the interface directly, or by the organized structure of the buffer solution at the interface that shrinks the "effective" size of the channels. The majority of novel properties at the nanoscale associated with nanofluidics and transport in general are tightly bound to the length scales of the problem. Although the diffusion of particles or other analytes is strongly affected by the aforementioned factors, it is necessary to understand the nature of nano- and microscale transport to rationalize and develop novel biomedical nano/micro devices.

In the liquid or gas phase, increasing particle size renders those particles less susceptible to Brownian diffusion and more strongly driven by gravity [Dailey et al., 2007]. However other studies suggest that solutions containing relatively small particles, with sizes less than 1 μm such as proteins, can be affected by gravity. The study of tubulin polymerization into microtubules revealed that gravity controls the growth of polymeric species along the axis of a microtubule [Papaseit et al., 2000]. The study was performed with the help of the European Space Agency, and suggests that gravity modifies the orientation of microtubules and affects the concentration distribution around heavier oligomers. The interpretation of the phenomena in a reaction-diffusion system is that the interaction of concentration fluctuations with gravity results in a small directional transport term that destabilizes the equilibrium state at the bifurcation point and thus favors the formation of a macroscopic pattern [Papaseit et al., 2000]. This clearly illustrates that gravitational forces cannot be discarded absolutely from a general or macroscopic point of view of the system. Although the tubulin is a protein with a typical size, it shows that oligomeric tubulin structures and different tubulin concentrations can be affected. Therefore the results of nano- or microconfinement studies might be affected by subtle effects of gravity (stratified and/or laminar flow of liquid in channels; analyte particle in reservoir) through the positioning of nano- or microdevices.

Another important fact is that experimental studies are quite restricted at the nanoscale. The microscale can give an additional boost to apply conventional techniques to analyze the transport in microchannels. Frequently scientists face analyzing the "macro" outcome of nano- or micro experiments, like measuring the total flux of analytes through nanochannels. Microgravity yields a valuable gift for scientists to study larger particles transported over microchannels, which in

standard gravity would sediment in the reservoir without any flux through the microchannels. Moreover, the ability to use large particles would allow for optical analysis that would entail direct visualization of the distribution of the particles over a chosen dimension of the microchannels. This unique scale-up of systems would bring a penalty of lower diffusivities of the particles that can be resolved by specific tuning of the microchannel dimensions.

In this framework it would be of great benefit to perform studies of the transport of micro and nano particles within microsystems in space. At the microscale all geometrical and chemical proprieties can be controlled to a much greater extent, and measurements can be performed more easily. A particular advantage of having experimental data of free diffusion not affected by gravity at the microscale is the possibility to correlate these data with similar results obtained on Earth at the nanoscale. Moreover, with this experiment it will be possible to quantify the effect of size, charge and chemistry on diffusive transport and even lead to a theoretical relationship able to describe diffusion at nanoscale as well. This finding would allow for predictions of nanosystem performance and, hence, to design, adjust and refine them so as to obtain the optimal properties before the arduous experimental task of synthesis and characterization.

There are significant challenges in finding a theory to predict accurate transport properties for nanoscale materials. In fact, as the size of the membrane pores approaches the molecular hydrodynamic radius unexpected effects, which cause substantial deviations from classic diffusion theory described by Fick laws, can occur [Aggarwal et al., 2007; Mackay et al., 2003]. It has been already observed that in nanochannels the basic principle of diffusion, a mixing process with solutes free to undergo Brownian motion in three dimensions, does not apply, since in at least one dimension molecular movement within the nanopore is physically constrained by the channel walls. In this frame, the transport phenomena may be classified as anomalous diffusion or processes in which particles move coherently for long times with infrequent changes of direction. This model describes motility characterized by the average mean-squared displacement of the diffusing particle, $\left\langle \Delta x^2(t) \right\rangle$, proportional to t^y with $y \neq 1$, where the linear dependence with time found by the classic theory is lost. The anomalous behavior may also be due to a molecular diffusion mechanism that depends on the nature, shape and size of the diffusing molecule. In the literature this has been widely observed and theoretically studied

providing many theoretical models that describe molecular transport in solution, gel and flux, depending on molecular size, shape and flexibility; these models delineate the experimental observations but are not as valid within nanodevices. These are the reasons why, despite the tremendous advances made in the modeling of the structural, thermal, mechanical and transport properties of materials at the macroscopic level (i.e., finite element analysis of complex structures or continuum simulations), there remains a remarkable uncertainty about how to predict many critical properties related to final performance at the nanoscale.

A promising possibility to fill this lack in knowledge of phenomena occurring at the nanoscale is to perform experiments on microscale systems in space. The experimental results could also provide the as yet unknown values of chemical kinetics, diffusivity and velocity of each specific molecule within constrained systems in the absence of weight. Correlations between the same parameters for nanosystems and microsystems will help in understanding diffusion mechanisms, fluid dynamics and chemical kinetics at the nanoscale that is currently lacking.

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Commercial Potential

The results of the proposed experiment will have a direct impact on the development of drug delivery systems for medical applications. Dr. Ferrari's group (in which this experiment will be developed) is focused on the development of the science and technology for implantable devices for controlled, long-term drug release. The research is focused on understanding the transport phenomena at the nano- and microscale. The understanding will enable us to develop better nanoscale drug-delivery systems, and more accurate predictive models of drug delivery. The major commercial potential of this experiment in relation to systems developed by our laboratory is the development an efficient and unique drug delivery system. The planned pathway toward commercialization is as follows:

1. Obtain better understanding of transport phenomena
2. Design optimized drug delivery system.
3. *in vivo* animal studies.
4. Successful clinical trials.
5. Sale of drug delivery systems to pharmaceutical companies, hospitals, and other relevant medical organization.

Dr. Ferrari's group is collaborating with NanoMedical System, Inc. (NMS) for the development of drug delivery devices and their application in the clinic. After the flight experiments are complete, we will need to apply the experimental results to Dr. Ferrari's group's drug delivery system in the next step toward commercialization. Additionally, many more years of research and resources including clinical research are needed in the commercialization pathway. The support of such research and resources should come from other grant giving organizations. Beyond the primary advantages to drug delivery, microgravity studies will provide extremely valuable insight into the relative behavior of large biomolecules, micro- and nanoparticles, and living cells. A better understanding of the parameters affecting transport phenomena will have a significant impact of the development of a variety of technologies employing multichambers, engineered viscosities, electro-osmosis, etc. In particular, the results of the analysis performed in

microgravity will provide the know-how to manipulate contained media, facilitate mobility, mixing and diffusion of micro- and nano-objects in a fluid environment.

Beyond the primary advantages to drug delivery, the following industrial application opportunities exist:

- Micro-Nanorobotics: better understanding of small object transport phenomena occurring at the nanoscale and their implications on micro- and nanorobot distribution on target surface, storage and deployment of micro-nanorobots and nanoprobes.
- Nanoreactors: understanding kinematics, dynamics, and catalysis of non-gravity driven (unconventional flow), micro- and nano-synthesizers; applications in biotechnology as well as power generation in embedded microsystems.
- Rational surface functionalization: better understanding of transport phenomena as related to surface properties and modifications.
- Nanopropulsion: understanding the material storage, mixing, stability, chemical reactivity of engineered nano-particulate dispersion in fuel media in moving vehicles, high-pressure fuel lines, miniature power systems, etc.

Few possible areas for use in space:

- Nanoparticles that can modify properties, including storage and transportation attributes of fuel, water, and other liquid supplies on spaceships.
- Delivery of drug or functionalized microparticles in human or animals (multistage microparticle delivery), especially for long term missions.

The experiment here proposed will give a unique gift to analyze transport phenomena at nano- and microinterface in microgravity. The further research in microgravity environment is desired to study the drug delivery device performance and function in cell culture, tissues, and small mammals. This phase is crucial, for the approval of the developed drug delivery systems for in

humans application at microgravity conditions, for example in long term missions. This step cannot be duplicated on Earth. The further experiments would tackle drug release characteristics, drug dispersion in tissues or cell cultures. Also, further fictionalization or property tuning of drug delivery devices is another important goal.

Experiment

Objective of the experiment

The objective of this study is to provide insight into the decoupled effects of space constraints and charge distribution over diffusive molecular and particle transport. At the nanoscale this decoupling becomes experimentally impossible. Here, we propose an experiment capable of analyzing nanoscale confinement and charge interaction effects on molecular diffusion through simulation at the microscale.

We hypothesize that, in the absence of significant gravitational forces, micron sized particles should constitute a reliable substitute for molecules once the appropriate microscale channel size is determined. This substitution allows for greater control of the geometric design, size distribution, and surface modification of the diffusing constituents and decreases the complexity of quantifying the experimental results. The analysis will focus on understanding how particle and channel properties, such as surface charge, coupled with particle-to-particle and particle-to-channel interactions, affect the diffusive transport.

Summary of the Experiment

In order to perform this study the concentration-driven diffusion of fluorescent spherical silica microparticles will be investigated by employing silicon microchanneled diffusion devices (MDDs). To analyze the decoupled effect of size constrain and charge interaction on the diffusive transport, particles and microchannels of different size will be employed. Custom MDDs will be microfabricated in our group in an academic cleanroom (Microelectronics Research Center, The University of Texas at Austin, TX, and The Cleanroom Laboratory, The University of Texas at Dallas). Each MDD will house two reservoirs separated by a parallel set of microchannels (see Figure 1). One reservoir will be loaded with silica microparticles dispersed in agarose water solution. The second reservoir will be filled with agarose water solution. At a temperature lower than +45°C the agarose solution gelifies to a solid media in which the particle diffusion is negligible. By increasing the temperature of the system to +65° the agarose gel liquefies allowing the motion of the particles. Driven by a gradient of concentration the

microparticles will diffuse across the microchannels toward the sink reservoir. By controlling the temperature of the devices it will be possible to maintain the system in a stable condition pre- and post-flight and to perform and control the diffusion experiment in microgravity conditions. The analysis of the diffusion of the florescent microparticles will be performed by measurement of the fluorescence in the microchannels.

Description of the Experimental Setup

MDD Description

The MDD consists of two reservoirs separated by a bank of parallel microchannels. The reservoirs and microchannels, along with the inlet and outlet ports from which the reservoirs will be filled prior to sealing, will be formed by machining trenches directly into the surface of a 500 micron thick silicon wafer (Figure 1A) and capping them with an anodically bonded Pyrex wafer 150 microns thick (Figure 1B). The thickness of the top Pyrex glass layer should allow for the analysis of the particle distribution by means of optical or fluorescence microscopy. Due to the required depths of the trenches these features will be etched using a Bosch process in an inductively coupled plasma (ICP) reactive ion etcher (RIE). This etch process uses a chemically deposited polymer to protect the walls of the etched feature during deep etches to achieve very high aspect ratios.

The etching of the silicon will have to be performed in two steps, starting with the microtrenches, due to the differential depths of the features. First, a layer of chemical vapor deposition (CVD) oxide will be deposited and the microtrenches lithographically patterned on top. Once the pattern has been transferred into the oxide etch mask, the ICP RIE will be used to create microtrenches of the appropriate depth. The remaining oxide mask will then be removed and the wafers thoroughly cleaned. The process will be repeated for the large reservoirs which will be etched to a much greater depth than the microtrenches. In order to insure sufficient bond strength and good structural integrity, a series of support pillars will be included interspersed throughout the reservoir (Figure 1A). Once the etching of both sets of features is complete, the

150 micron Pyrex wafer will be anodically bonded on top. The wafer stack will then be diced into individual units, or die, ready for testing.

Each device presents 240 rectangular microchannels (width 20 µm, length 500 µm). The device will be fabricated in 3 microchannel depth configurations (2, 5, 10 µm).

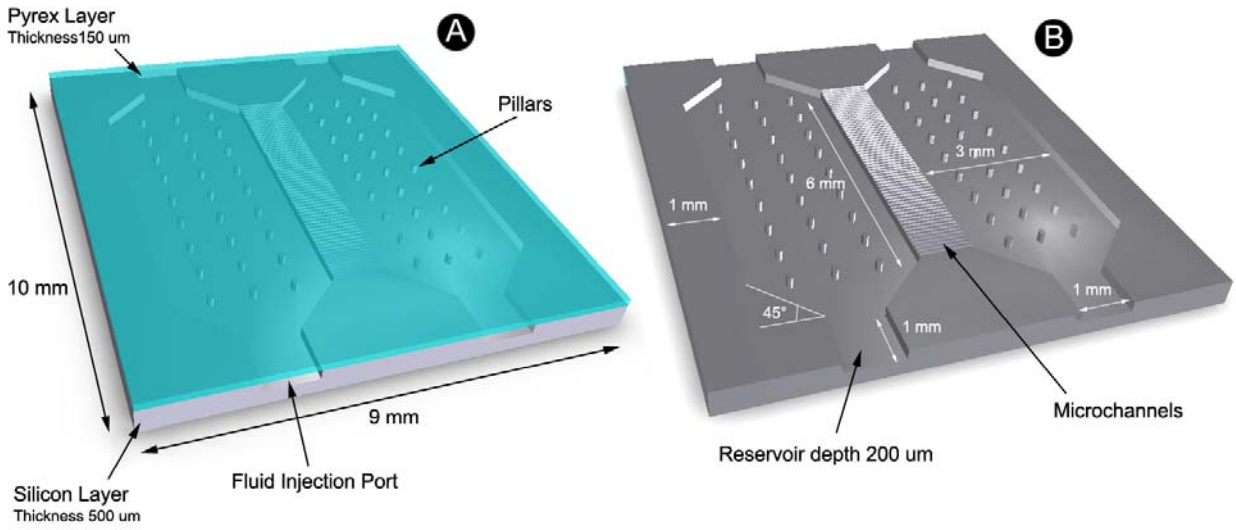


Figure 1. schematics of the MDD structure. Complete device (A), silicon layer (B).

Description of the Experiment Setup

The Experimental Setup will be composed of an electronic control circuit, back-up power supply (solid state battery), independent temperature and acceleration sensing devices and the silicon diffusion chambers coupled with electrical heating elements and thermostats. All components are assembled on an aluminum alloy frame. 9 silicon devices will be interposed in between a heating element and the sensing unit of a thermostat. The heating element and the thermostat will be connected in series to a control unit. The sandwich assembly of silicon diffusion chambers (set) will allow for control of the temperature of the sets. Five device set assemblies (multiple sets in each assembly) will be connected to independent ports of the control unit. The control unit, connected to the power supply of the spacecraft will control the power supplied to the five lines of devices. A back-up battery is connected to the control unit to supply power in case of an

interruption to the spacecraft power supply. The experiment houses an independent temperature sensor and a data acquisition unit which will monitor the temperature of the system during the flight. Additionally, a 3-axis accelerometer will sense and record acceleration data in all three directions, providing important control data for the final analysis of the experiment results. Figure 2 shows the schematic of the experimental setup.

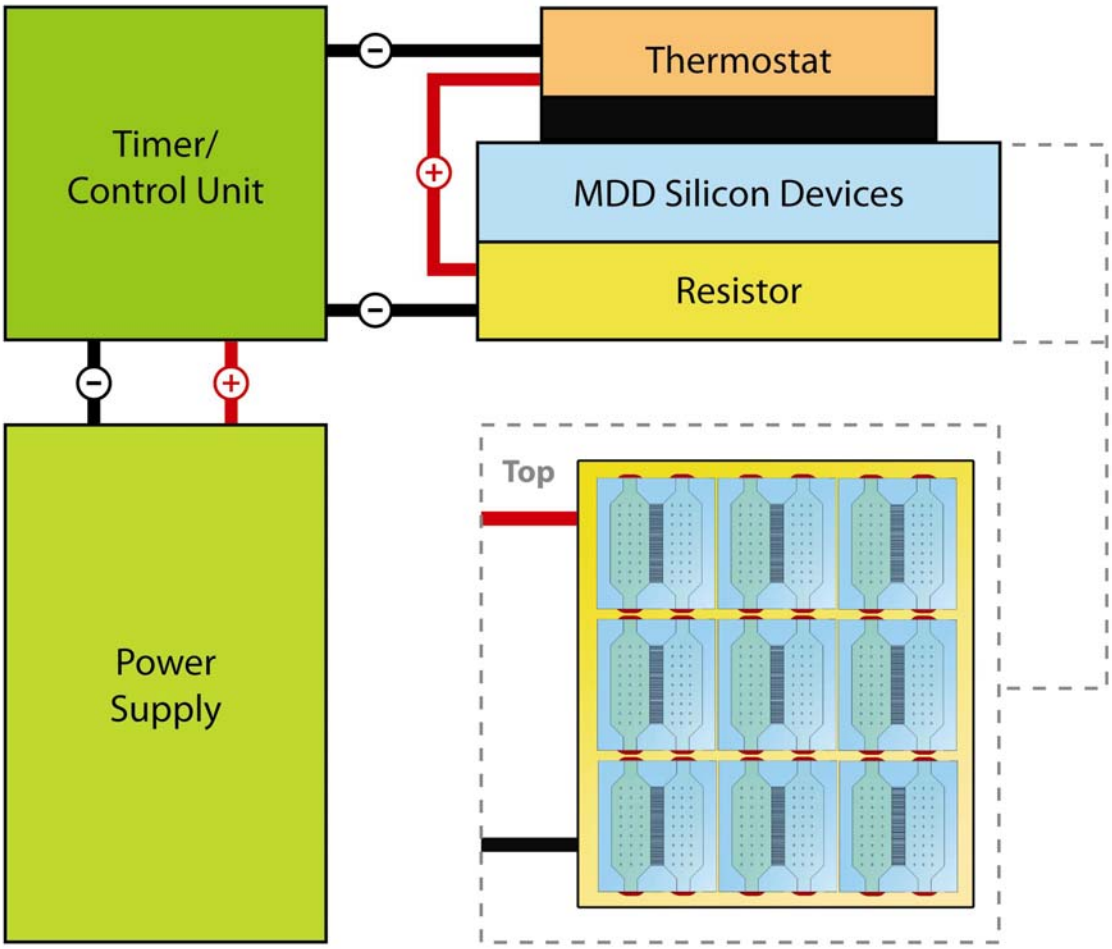


Figure 2. Conceptual scheme of the Experimental setup.

List of Material.

All materials and instrumentation employed in the experiments will be prepared and assembled in-house prior to the shipping of the payload to the launch location. No additional material will

be required to further support the experiment. Materials and instrumentation will be assembled in a rigid structure with the experiments requiring no movable parts. Additionally, no biological materials will be used. The list of the essential materials and instrumentation to perform the study is presented here:

- Spherical silica microparticles, size 0.1, 0.3, 1 μm (Polysciences, Inc.)
- Water solution of agarose (Bio-Rad Laboratories, Inc), approximate total amount 1 mL
- Microfabricated silicon MDDs (90)
- Flat resistors (10)
- High precision thermostats (10)
- Thermoconductive paste
- 5 channel control switch unit
- Temperature monitor and recording unit
- 3-axis acceleration monitor and recording unit
- Back-up battery
- Electrical wiring
- Aluminium alloy frame and chassis.

Approximate total weight: 20-25 kg

Preparatory Steps

Preparation of the experiment will be performed completely in our laboratory. The frame and mounting parts will be assembled onto a Middeck Locker, creating the firm structure holding the experimental components. The frame will hold the electronic control circuit, back-up power supply (solid state battery), independent temperature and acceleration sensing devices, and the silicon MDDs coupled with the electrical heating elements and thermostats.

Device Preparation.

The study will be performed in 9 different experimental configurations according to the size and charge of the employed particle and depth of the microchannels. Fluorescent silica particles presenting 3 different sizes (0.1, 0.3, 1 μm) and surface charge states (positive, negative and neutral) will be employed. MDDs will be fabricated with 3 different microchannel depths (2, 5, 10 μm). Table 1 summarizes the 9 experimental configurations. Additionally the experiment will be performed in duplicate for each testing configuration.

Table 1. Experimental Configurations. *The analysis of the charge interaction effect will be performed with 0.3 μm particles (positive, negative, neutral charge) in 10 μm channels.

Microparticle Size (μm)	**Microchannel Depth (μm)**		
0.1		5	
0.3*	2	5	10*
1	2	5	10

Water solutions of agarose (0.25%wt) will be prepared at +65°C and loaded into one of the reservoirs of the MDD's chamber. The loading will be performed through the bottom injection port allowing the air to escape through the top opening. The fluid will wet the microchannels by capillary filling. Fluorescent silica microparticles dispersed in the agarose solution will be loaded into the second chamber by promoting complete air evacuation. The volume of agarose solution loaded in each reservoir will be approximately 4 μL. The loaded MDDs will be cooled to room temperature causing the agarose solution to gelify. Under this condition the dispersed microparticles will be stable in the gel unable to sediment or diffuse. Finally, the injection ports will be sealed with epoxy glue. A set of 9 silicon devices, corresponding to the 9 experimental configurations, will be bonded on one side to a flat resistor and on the other side to the temperature sensor of the thermostat. A thermoconductive paste will be used to maximize the

heat exchange. A schematic of the assembled set of MDDs is shown in Figure 2. 10 assemblies of MDD sets will be prepared as described. The assembled devices will be connected to the electric control unit as shown in Figure 2 and mounted onto the structure frame. Finally the experimental setup will be closed into a rigid chassis.

Experiment Operation in Microgravity

Once assembled, the system will be in stable conditions without requiring any supplied power. By keeping the temperature of the system in the range of +10 to +35 ºC the agarose gel will preserve the particles in a steady state during the pre-flight period. Additionally, during the launch the gel will help to avoid significant particle displacement due to the acceleration of the spacecraft. At the loading of the payload the experiment will be connected to the power line available on the space craft. As the microgravity condition is met, the control unit will automatically start the experiment by providing power to the heating elements of each set. The temperature of the MDDs will be quickly increased (<10 minutes) and maintained at ~+65±1°C. At this temperature agarose gel liquefies enabling the microparticles to diffuse. The target temperature will be maintained at ~+65±1°C by means of high precision thermostats connected in series with the heating elements. This setup will avoid overheating and will minimize power consumption. During the microgravity flight the temperature of the environment will be recorded by the independent temperature monitoring device. Every 21 hours, the control unit will switch off the power to 2 sets of devices. By the end of the 4.5 days of flight in microgravity all sets of MDDs will be switched off. By removing the power source, the set of devices will cool down to the cabin air (+10 - +46°C). As the active volume of the MDD's chambers under test are exceptionally small, the heating and cooling processes will occur very quickly. The agarose solution will gelify preserving the position of the diffusing particles. For cabin temperature exceeding +46°C but lower than +55°C the gel will still preserve the position of particles with negligible movement of the particles. In case of a blackout during the flight the back-up power supply will allow to the experiment to proceed.

Post-Flight Analysis

After the flight the experiment will be preserved in a stable condition without the need of supplied power. By keeping the experiments in the preferred range of +10 to +35 ºC the microparticle position in the silicon devices will be preserved.

The static diffusion chambers will be analyzed by fluorescent microscopy, optical microscopy and spectrofluorimetry. By measuring the fluorescence in the microchannels it will be possible to determine the gradient of the concentration of particles along the length and the width of the channels. The microparticle concentration and gradient data will be collected and averaged over all microchannels of the same device (240 microchannels per device). The data collected at different time points will give information over the dynamic of the diffusive transport. By comparing the results related to the different experimental configurations the evaluation of the effect of size constrains and charge interactions will be analyzed. Additionally, the collected data will allow for calculating the diffusivity of the microparticles. Finally the analysis of the microparticle distribution in proximity to the channel walls will allow for the evaluation of interface interactions between the particles and the channels.

Potential Hazards

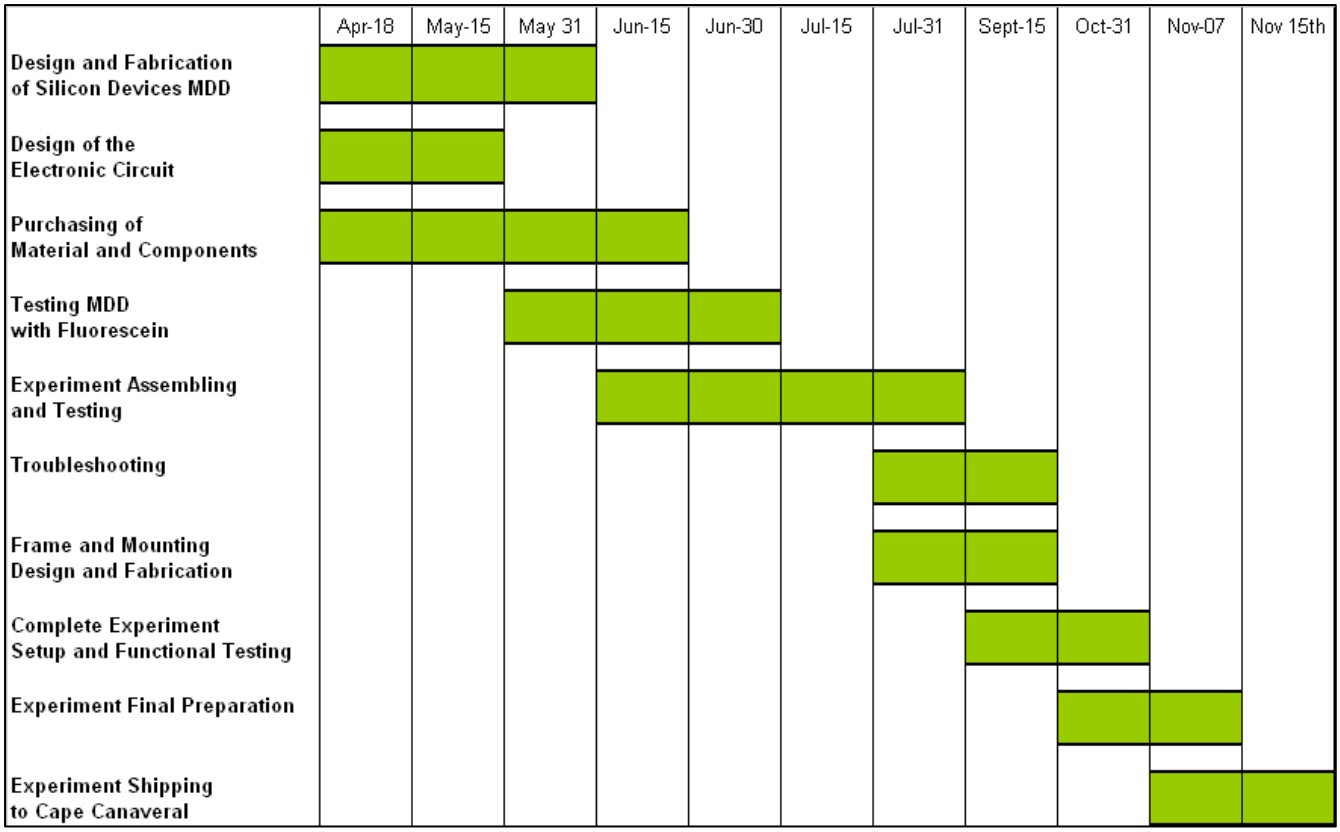
The Experiment setup does not present any potential hazard to ground personnel. Additionally, the experiment does not require pressurized vessels, hazardous materials or biological samples.

Pre-and Post Flight Handling

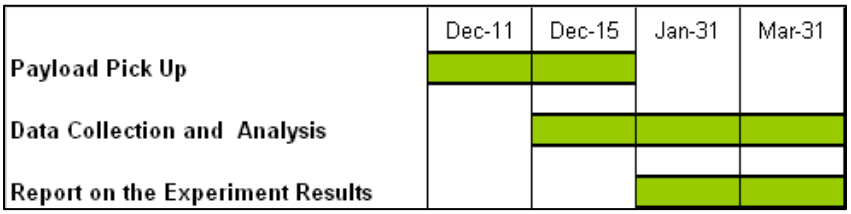
The only requirement is the storage of the experiment in the temperature range of +10 to +35°C. No other requirements need to be considered for pre- and post-flight operation and for transportation and loading.

Experiment Schedule

Pre-Flight Schedule



Post-Flight Schedule



Project Budget

Silicon Fabrication	
Device Processing	
Bonding	$400,00
Dicing	$40,00
Facility fees	
Etching (2 to 4 days)	$300,00
Material	
2 Masks	$800,00
Silicon Wafer + Pyrex	$100,00
Subtotal Silicon Fabrication	$1.640,00
Instrumentation	
Temperature Moritor Recording Unit	$2.200,00
10 Surface Temperature Probes	$1.200,00
Acclerometer Monitor Unit	$2.000,00
Power supply Back-up Battery	$1.500,00
Control Unit	$2.000,00
Resistors	$1.000,00
Thermostats	$1.800,00
Subtotal Instrumentation	$11.700,00
Chemicals and General Lab Supplies	
Agarose	$200,00
Microparticles	$800,00
Alexafluor Conjugates	$500,00
General Lab Supplies (pipettes, gloves, etc.)	$1.000,00
Subtotal Chemicals and General Lab Supplies	$2.500,00
Service Fees	
Machining of Mechanical Frames	$2.000,00
Subtotal Service Fees	$2.000,00
Consultant	
Design Consultant	$5.000,00
Subtotal Consultant	$5.000,00
Travel	
Fabrication in Dallas	$2.000,00
Subtotal Travel	$2.000,00
TOTAL	**$24.840,00**

Data Restrictions.

There is no restriction regarding public disclosure of sections 3 to 6.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME: **Mauro Ferrari, PhD**	POSITION TITLE **Professor– The University of Texas Health Science Center at Houston** **President – Alliance for NanoHealth**
eRA COMMONS USER NAME: **mferrari**	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(S)	FIELD OF STUDY
Universita' di Padova, Italy	Dottore	1985	Mathematics
University of California, Berkeley, CA	M.S.	1987	Mechanical Engineering
University of California, Berkeley, CA	Ph.D.	1989	Mechanical Engineering
The Ohio State University, Columbus, OH		2002-2004	Medical School

A. MAIN POSITIONS AND HONORS

Positions and Employment:

University of California, Berkeley, CA

1991 – 1996 Assistant Professor, Materials Science and Civil Engineering
1994 – 1998 Faculty, Bioengineering Program UC San Francisco/Berkeley, and Biophysics Program
1996 – 1998 Associate Professor with Tenure, Materials Science and Civil Engineering;
1996 – 1998 Director, Biomedical Microdevices Center

The Ohio State University, Columbus, OH

1999 – 2005 Professor, Biomedical Engineering and Mechanical Engineering
1999 – 2005 Professor, Internal Medicine, Division of Hematology and Oncology
1999 – 2002 Director, Biomedical Engineering Center
2000 – 2005 Associate Director, Dorothy M. Davis Heart and Lung Research Institute
2001 – 2005 Edgar Hendrickson Designated Chair in Biomedical Engineering
2002 – 2005 Scientific Founder and Scientific Advisor, the Ohio MicroMD Lab

Texas Medical Center, Houston, TX

2006 – present Professor and Division Head, Division of NanoMedicine; Professor, Department of Internal Medicine, Division of Cardiology; Chairman, Department of Biomedical Engineering The University of Texas Health Science Center at Houston
2006 – present Professor, Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center
2006 – present Professor, Department of Bioengineering, Rice University
2006 – present President, Alliance for NanoHealth
2007 – present Adjunct Professor, Department of Biochemistry and Molecular Biology, University of Texas Medical Branch at Galveston

Main Honors and Professional Service:

1993 - 1998 National Science Foundation: National Young Investigator Award.
1998 – 2000 National Institute of Health – James A. Shannon Director's Award
1999 Wallace H. Coulter Award for Innovation and Entrepreneurship
2006 Texas Emerging Technology Fund Research Superiority Award Recipient, $2.5 Million
2007 Bestowed the Honor "Knight of the Order of Merit of the Italian Republic" from the President of Italy Giorgio Napolitano
2008 Session Chair, "Nanotechnology and Cancer". AACR Annual Meeting 2008 - Methods Workshop
2008 Elected to the College of Fellows of The American Institute for Medical and Biological Engineering (AIMBE)

2008 Speaker for Session “Molecular Basis of Nanomedicine” and Co-Chair for Session “Nanotechnology - Path to the Clinic: Promises and Hurdles”. The 1st Joint U.S.-China Symposium on Nanobiology and Nanomedicine- Cancer Nanotechnology & Nanomedicines, organized by Chinese Academy of Science and NIH, Beijing, China

Selected State and Federal Advisory Service:

1999 National Cancer Institute: Novel Technologies for Noninvasive Detection, Diagnosis, and Treatment of Cancer, Special Emphasis Panel (Chair); Executive Office of the President of the United States of America: Nanotechnology Research Directions: National Science and Technology Council, Committee on Technology, Interagency Working Group on Nanoscience, Engineering and Technology.

1999 – 2002 National Research Council’s Board on Army Science and Technology: Committee on Opportunities in Biotechnology for Future Army Applications; Materials Research for Defense After Next.

2002 – 2003 Chairman, Planning Committee and Working Committee of the National Institute for Heart, Lung, Blood and Sleep (NHLBI), National Initiative on Nanotechnology.

2003 – 2005 Member, Integration Committee, Congressionally mandated Army Breast Cancer Research Program, US Department of Defense

2003 – 2005 Special Expert on Nanotechnology and Eminent Scholar, The National Cancer Institute.

2007 Member, External Advisory Board Committee to Nanobiology Program (CCR) recommended from the Board of Scientific Counselors of the NCI.

2007 Invited Speaker, President’s Council on Bioethics, Washington, D.C.

2007 Invited Reviewer, Bioengineering Sciences and Technologies Integrated Review Group Study Section, the National Institute of Health (NIH)

2008 Invited Panel Member, DoD Congressionally Directed Medical Research Programs (CDMRP) Breast Cancer Innovator Research Project Award Panel, Washington, D.C.

2009 Recipient of the DoD CDMRP Breast Cancer Research Program Innovator Award

B. SELECTED RECENT PUBLICATIONS (from over 186 peer-reviewed articles and 6 books)

1. Liotta, LA, Ferrari, M, and Petricoin, E, “Clinical Proteomics: Written in Blood”, Nature 425, 2003, p. 301. (PMID: 14586448)
2. Decuzzi, P, Lee, S, Decuzzi, M, and Ferrari, M, “Adhesion of Micro-Fabricated Particles on Vascular Endothelium: A Parametric Analysis”, Annals of Biomedical Engineering, Vol.32, Issue6, 2004, p. 793-802. (PMID: 15255210)
3. Sullivan, D, and Ferrari, M, “Nanotechnology and Tumor Imaging: Seizing an Opportunity”, Molecular Imaging, Vol. 3, No. 4, 2004, p. 364. (PMID: 15802054)
4. Decuzzi, P, Lee, P, Bhushan, B, and Ferrari, M, “A Theoretical Model for the Margination of Particles within Blood Vessels”, Annals of Biomedical Engineering, Vol. 33, No. 2, 2005, pp. 179-190. (PMID: 15771271)
5. Ferrari, M, “Cancer Nanotechnology: Opportunities and Challenges”, Nature Reviews Cancer, Vol. 5, No.3, 2005, pp.161-171. (PMID: 15738981)
6. Martin, FJ, Melnik, K, West, T, Shapiro, J, Cohen, M, Boiarski, AA, and Ferrari, M, “Acute Toxicity of Intravenously Administered Microfabricated Silicon Dioxide Drug Delivery Particles in Mice: Preliminary Findings”, Drug Research and Development, Vol. 6, No. 2, 2005, pp. 71-81. (PMID: 15818779)
7. Ferrari, M, “Nanovector Therapeutics”, Curr. Opin. Chem. Biol., Vol. 9, No. 4, 2005, pp. 343-346. (PMID: 15967706)
8. Cheng, MC, Cuda, G, Bunimovich, Y, Gaspari, M, Heath, JR, Hill, HD, Mirkin, CA, Nijdam, AJ, Terracciano, R, Thundat, T, and Ferrari, M, “Nanotechnologies for Biomolecular Detection and Medical Diagnostic”, Curr. Opin. Chem. Biol., Vol. 10, Issue 1, 2006, pp. 11-19. (PMID: 16418011)
9. Decuzzi, P, Causa, F, Ferrari, M, and Netti, PA, “The Effective Dispersion of Nanovectors Within the Tumor Microvasculature”, Annals of Biomedical Engineering, Vol. 34, No. 4, 2006, pp. 633-641. (PMID: 16568349)
10. Decuzzi, P, and Ferrari, M, “The Adhesive Strength of Non-Spherical Particles Mediated by Specific Interactions”, Biomaterials, 2006; 27(30): pp. 5307-1534. (PMID: 16797691)
11. Robertson, FM, Mallery, SR, Bergdall-Costell, VK, Cheng, MC, Pei, P, Prosperi, JR, and Ferrari, M, “Cyclooxygenase-2 Directly Induces MCF-7 Breast Tumor Cells to Develop into Exponentially Growing,

Highly Angiogenic and Regionally Invasive Ductal Carcinoma Xenografts", Anticancer Research, 2007, 27(2): 719-727. (PMID: 17465194)
12. Decuzzi, P, and Ferrari, M, "The Role of Specific and Non-Specific Interactions in Receptor-Mediated Endocytosis of Nanoparticles", Biomaterials, 2007, 28(18):2915-2922. (PMID: 17363051)
13. Sakamoto, J, Annapragada, A, Decuzzi, P, and Ferrari, M, "Anti-Biological Barrier Nanovector Technology for Cancer Applications", Expert Opinion on Drug Delivery, 2007, 4(4):359-369.(PMID: 17683250)
14. Decuzzi, P, and Ferrari, M, "Design Maps for Nanoparticles Targeting the Diseased Microvasculature", Biomaterials, 2008, 29(3):377-384. (PMID: 17936897)
15. Smith, BR, Heverhagen, J, Knopp, M, Schmalbrock, P, Shapiro, J, Shiomi, M, Moldovan, NI, Ferrari, M, and Lee, SC, "Localization to Atherosclerotic Plaque and Biodistribution of Biochemically Derivatized Superparamagnetic Iron Oxide Nanoparticles (SPIONs) Contrast Particles for Magnetic Resonance Imaging (MRI)", Biomedical Microdevices, 2007, 9(5):719-727. (PMID: 17562181)
16. Gentile, F, Decuzzi, P. and Ferrari, M, "The Transport of Nanoparticles in Blood Vessels: The Effect of Vessel Permeability and Blood Rheology", Annals of Biomedical Engineering, 2008, 36 (2):254–261. (PMID: 18172768)
17. Ferrari, M, "Nanogeometry: Beyond Drug Delivery", Nature Nanotechnology, 2008 March; 3(3):131-132. (PMID: 18654480)
18. Tasciotti, E, Liu, X, Bhavane, R, Plant, K, Leonard, A, Price, B, Cheng, MC, Decuzzi, P, Tour, J, Robertson, F, and Ferrari, M, "Mesoporous Silicon Particles as a Multistage Delivery System for Imaging and Therapeutic Applications", Nature Nanotechnology, 2008, 3(3):151-157. (PMID: 18654487)
19. Sanhai, WR, Sakamoto, JH, Canady, R, and Ferrari, M, "Seven Challenges for Nanomedicine", Nature Nanotechnology, 2008, 3(5):242-244. (PMID: 18654511)
20. Tanaka, T, Decuzzi, P, Cristofanilli, M, Sakamoto, J, Tasciotti, E, Robertson, FM, Ferrari, M Nanotechnology for Breast Cancer Therapy, Biomedical Microdevices, 2008, (EPub ahead of print) (PMID: 18663578)

PATENTS (from 29 issued and 5 pending)

1. Ferrari M. Therapeutic Microdevices and Methods of Making and Using Same, U.S. Patent No. 6,107,102, 8/22/00.
2. F. Martin and M. Ferrari, "Microfabricated Particles and Methods for Treating Solid Tumors", Pub App. No. 20030114366; June 2003.

C. RESEARCH SUPPORT – FROM A CAREER TOTAL OF OVER $46 MILLION

Ongoing Research Support

N/A (Ferrari) 8/23/2006 – 8/31/2010
State of Texas Governor's Emerging Technology Fund
Acquisition of Scientific Superiority in Biomedical Nanotechnology
This funding is for development of a biomedical nanotechnology research program within the Texas Medical Center in Houston and in concert with the Alliance for NanoHealth of which Dr. Ferrari is the President.

NNJ06HE06A (Ferrari) 9/01/2006 - 8/31/2009
NASA NSPIRES
Nanotechnology for Space Medicine
This projects' goal is to develop the diagnostic and therapy tools for long-term clinical care for space missions.

W81XWH-07-2-0101 (Ferrari) 8/29/2007 - 8/28/2009
DoDArmy/TATRC
The Medical Nanovector Research and Development Center of The Alliance for NanoHealth
This project's goal is to design and refine the 1st stage nanovector to enhance the ability of targeting to diseased vascular endothelial cells by using mathematical modelling and microfluidic, endothelialized flow chambers which will be designed and manufactured to mimic each pathological condition.

W81XWH-07-01-0596 (Serda) 9/15/2007 – 10/14/2010
DoD Army/Multidisciplinary Postdoctoral Fellow Award
Nanovectors for Targeting and Delivery of Therapeutics to Her-2 Neu Positive Breast Cancer Cells
The goal of this project is to develop a system to deliver therapeutic drugs and contrast agents specifically to breast cancer cells.
Role: PI Mentor

R01CA128797 (Ferrari) 9/28/2007 – 7/31/2011

NIH/BRP
Nanovectors for Characterization and Destruction of Breast Tumor Vasculature
The aim of this project is to identify molecular signatures of breast tumors and their associated vasculature to enable targeting and destruction of breast tumors and blood vessels using nanovectors.

ECCS-0725886 (Zhang) 10/1/2007 – 9/30/2010
NSF
Nano-scale Light Emitting Diode on Silicon Cantilever for Sub-diffraction-limit Near-field Microscopy of Single Molecules on Living Cells
This project's goal is to direct fabricate nanometer sized light source (light emitting diode, LED) on patterned silicon probe tip using micro-electro-mechanical system (MEMS) technology to detect individual fluorescent proteins as part of multi-molecular complexes on the surface of fixed cells in vitro.
Role: Co-PI

R33CA122864 (Ferrari) 8/01/2008 -- 7/31/2011
NIH R33 Skin Cancer
Nanoparticles for Harvesting and Targeting Angiogenic Proteins
This project's role is to achieve the goal of developing and refining tools for detection of angiogenic proteins and for selective targeting and destruction of tumor-associated blood vessels. These studies may also provide strategies to selectively target tumor vessels for destruction using nanotechnology approaches.

NSF 08-503 (Litvinov) 9/1/2008 – 8/31/2010
NSF
MRI: Consortium Proposal: Acquisition of a Dual Beam to Support Basic Device and Materials Research in the Greater Houston Area
This project's role is to acquire shared equipment
Role: Co-PI

Komen Foundation Promise Grant (Cristofanilli and Robertson) 3/1/2008—2/28/2013
Komen Foundation
Novel Targets for Treatment of and Detection of Inflammatory Breast Cancer
This project's role is to develop nanoporous proteomics chips and particles for the detection and therapy for inflammatory breast cancer.
Role: Subcontract PI

FDA RFQ #1048351-1 (Ferrari) 1/1/2009 – 12/31/2009
FDA: "Bridging Scientific and Translational Gaps in Nanotechnology and Nanomedicine
Safety of Nano-Engmeered Materials
This project's role is to assemble an experienced management team comprised of Alliance for NanoHealth representatives to coordinate and manage future priority projects that are focused upon the safety of nano-based medical projects.

DOD/DARPA W911NF-09-1-0044 (Ferrari) 1/01/2009-12/31/2010
DOD/DARPA
BioNanoScaffolds (BNS) for Post-Traumatic Osteoregeneration
The goal of this project is to develop BioNanoScaffolds for post-traumatic osteoregeneration, which is designed to actively promote and enable the self-healing of the bone and surrounding soft tissue, so that 6 months post injury, their architecture and function are fundamentally restored.

DOD/BCRP W81XWH-08-BCRP-INNOV (Ferrari) 3/01/2009-2/28/2014
DOD/DARPA
Towards individualized breast cancer therapy: Leveraging molecular medicine with multi-stage vector technology
The goal of this project is to develop a multistage nanovector system for the delivery of therapeutic and imaging agents for individualized treatment of breast cancer.

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME	POSITION TITLE
Alessandro Grattoni	Senior Research Assistant

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Wichita State University, Wichita, Kansas, USA		2003	Intensive English Language
Politecnico di Torino, Torino, Italy	B.S	2006	Mechanical Engineering
Politecnico di Torino, Torino, Italy	M.S	2006	Mechanical Engineering with Biomedical training
Politecnico di Torino, Torino, Italy	Ph.D.	2006 – 2008	Biomedical Engineering

A. Positions and Honors.

Aug 06 – July 08 Research Technician 2 at Division of Nanomedicine, Department of Biomedical Engineering, The University of Texas Health Science Center at Houston, Houston, TX.

July 08 - present Senior Research Assistant at Division of Nanomedicine, Department of Biomedical Engineering, The University of Texas Health Science Center at Houston, Houston, TX.

Honors and Awards

- None

B. Selected peer-reviewed publication or presentation (in chronological order).

- **Grattoni, A.**, Canavese, G. Osmotic pressure measurement device and measurement method. IT Patent T02006A000508, (2006).
- Canavese, G., **Grattoni, A**. Dispositivo perfezionato di misura della pressione osmotica e relativo procedimento di misura. IT Patent TO2007A000177. (2007).
- **Grattoni, A.,** Merlo, M., Ferrari, M. Osmotic Pressure Beyond Concentration Restrictions. *J. Phys. Chem B.* **40**, 11770 – 11775, (2007).
- **Grattoni, A.**, Canavese, G., Montevecchi, F.M., Ferrari, M. Membrane Osmometer as Alternative to Freezing Point and Vapor Pressure Osmometry. *Anal. Chem.* **80** (7), 2617-2622, (2008).

- **Grattoni, A.** Ferrari, M., Liu, X**.** *Quality control method for micro- nano-channels silicon devices*. US Patent Application No. 61/049,287 (April 2008).

- **Grattoni, A.**, Ferrari, M. Reply to "Comment on Osmotic Pressure Beyond Concentration Restrictions". *J. Phys. Chem, B.* **112** (49), 15943, (2008).

- De Rosa, E., **Grattoni, A.**, Ferrati, S., Liu, X., Ferrari, M. "How to control the molecular transport throughout nanochanneled delivery system." BMES October 2nd – 4th 2008, St. Luis, MO (USA).

- Ferrari, M., Liu, X**., Grattoni, A.** Cheng, M.M., Hosali, S., Goodall, R., Medema, R., Hudson, L. *Nanochanneled Device and Method of Fabrication* US Patent Application No. No.61/114687 (November 2008).

- **Grattoni, A.**, De Rosa, E., Ferrati, S., Wang, Z., Gianesini, A., Liu, X., Hussain, R. Goodall, F., Ferrari, M. Novel method for quality control of complex design nano-channels devices. *J. Micromec. Microeng.*. Submitted (March 2009).

- **Grattoni, A.**, De Rosa, E., Ferrati, S., Liu, X., Ferrari, M. Effect of concentration and channel size on release rate of nanochannel delivery system: measurements and predictions. *Anal. Chem*. In Preparation (2009).

- De Rosa, E., **Grattoni, A.**, Liu, X., Ferrari, M. "Controlled Drug Delivery through Nanochanneled Devices" HSEMB conference March 19th and 20th 2009, Houston, TX (USA). (Accepted)

- De Rosa, E., **Grattoni, A.**, Ferrati, S., Liu, X., Ferrari, M. "Nanochanneled implantable device for sustained controlled cancer treatment." AACR April 18th-22nd 2009, Denver, CO (USA). (Accepted)

C. Pending Research Support

None

Arturas Ziemys

Postdoctoral fellow
Institute of Molecular Medicine
The University of Texas Health Science Center at Houston
1825 Pressler St., Houston, TX-77030

E-mail: Arturas.Ziemys@uth.tmc.edu
URL: http://www.ziemys.org/
Office phone: 713 500 2311
Fax: 713 500 2462

Education. B.S. Biology, Vytautas Magnus University, Lithuania, 1996; M.S. Molecular Biology and Biotechnology, Vytautas Magnus University, Lithuania, 1998; Ph.D. Molecular Biophysics, Vytautas Magnus University & Institute of Biochemistry, Lithuania, 2002.

Professional Experience. Assist. prof. and staff researcher, Vytautas Magnus University, Lithuania, 2003-2005; staff researcher, Institute of Biochemistry, Lithuania, 1996-2005; postdoctoral fellow, The Ohio State university, Dept. of Chemical and Biomolecular Eng. 2005-2007; postdoctoral fellow, School of Health Information Sciences, UTH, 2008, Jan 1 – Dec 31; postdoctoral fellow, Institute of Molecular Medicine, UTH, 2009-present.

Awards. The Lithuanian Academy of Sciences, student award, 1998; The Lithuanian Academy of Sciences, young scientist award, 2002.

Research Interests. The main interests are related to protein function and structure at ambient conditions and close to interface. Currently studying how nanoconfinement affects diffusivities of biomolecules. The research is focused on nanochannel transport phenomena. Additional research is related to the binding of peptides to the protein with the active site fully exposed to solvent. The later research tried to analyze entropy-enthalpy compensation in the free energy of binding.

Synergistic Activities and Service. Reviewer for National Awards, the Lithuanian Academy of Sciences, 2008, Lithuania;

Five Selected Publications.

- A.Ziemys, M.Ferrari, C.Cavasotto. Molecular modeling of glucose transport in silica nanochannels. (*in preparation*).
- A. Ziemys, J. Kulys. An experimental and theoretical study of Coprinus cinereus peroxidase-catalyzed biodegradation of isoelectronic to dioxin recalcitrants. Journal of Molecular Catalysis B: Enzymatic, 2006, 44: 20-26
- A. Ziemys, A. Toleikis, D.M. Kopustinskiene, Molecular modeling of KATP channel blockers-ADP/ATP carrier interactions. IEE Proceedings - Systems Biology, 2006, 153/5: 390-393
- A. Ziemys, J. Kulys. Heme peroxidase clothing and inhibition with polyphenolic substances revealed by molecular modeling. Computational Biology and Chemistry, 2005, 29/2: 83-90

- Kulys J., Ziemys A., A role of proton transfer in peroxidase-catalyzed process elucidated by substrates docking calculations. BMC Structural Biology 2001, 1:3.

Five Most Relevant Publications.

- Monti MC, Casapullo A, Cavasotto CN, Tosco A, Dal Piaz F, Ziemys A, Margarucci L, Riccio R. The binding mode of petrosaspongiolide M to the human group IIA phospholipase A(2): exploring the role of covalent and noncovalent interactions in the inhibition process. Chemistry. 2009; 15(5):1155-63.
- L.Tetianec, M. Dagys, J. Kulys, A. Ziemys, R. Meskys. Study of the reactivity of quinohemoprotein alcohol dehydrogenase with heterocycle-pentacyanoferrate(III) complexes and the electron transfer path calculations. Central European Journal of Biology, 2007, DOI: 10.2478/s11535-007-0033-y.
- A. Ziemys, J. Kulys. An experimental and theoretical study of Coprinus cinereus peroxidase-catalyzed biodegradation of isoelectronic to dioxin recalcitrants. Journal of Molecular Catalysis B: Enzymatic, 2006, 44: 20-26
- J. Kulys, L. Tetianec, A. Ziemys, Probing Aspergillus niger glucose oxidase with pentacyanoferrate(III) aza- and thia-complexes. Journal of Inorganic Biochemistry, 2006, 100/10: 1614-1622
- Kulys J., Krikstopaitis K., Ziemys A., Kinetics and thermodynamics of peroxidase- and laccase-catalyzed oxidation of N-substituted phenothiazines and phenoxazines, JBIC, 2000, 5: 333-340.

Students Advised. 3 bachelor students, Vytautas Magnus University, Lithuania; 2 master students, Vytautas Magnus University, Lithuania;

Teaching. 6 semester courses (Lithuania): Bioinformatics (undergraduate); Biotechnology for Health (*in silico* methods for drug design, graduate); molecular biology (undergraduate);

Collaborators in Last Four Years.

Advisors. Juozas Kulys (Institute of Biochemistry, Lithuania); Michael Paulaitis (OSU), Claudio Cavasotto (SHIS/UTH); Mauro Ferrari (IMM/UTH).

Daniel Fine

10100 Burnet Rd., MER Bldg. 160, Austin, TX 78758
(512) 475-8483 dan.fine@gmail.com

Education

Ph.D. Electrical Engineering & Certification in Nanotechnology, the University of Texas at Austin, August 2007.
M.S. Electrical Engineering, the University of Texas at Austin, June 2002.
B.S. Electrical Engineering, Cornell University, June 2000.

Positions

Post Doctoral Fellow – University of Texas Health Science Center at Houston, Division of NanoMedicine, August 2007 – present.

Research

8/07 – present

Nanoscale Drug Delivery System,
NASA, The Texas Emerging Technology Fund
* Designed and executed the process flow for the fabrication of nanopatterned semipermeable membranes to be incorporated into implantable drug delivery capsules
The University of Texas Health Science Center at Houston, Division of NanoMedicine and the Microelectronics Research Center, the University of Texas at Austin
Supervisor: Prof. Mauro Ferrari

9/01 -6/07

Biologically interfaced ion channel sensors
Defense Advanced Research Projects Agency (DARPA) project
* Designed and fabricated bipolar junction transistors (BJTs) with high current-gain and low cut-off frequency for the purpose of amplifying the small electrical signals of ion channels
* Designed ion channel simulation apparatus to produce pico-ampere currents at kHz frequencies with high signal-to-noise ratio
* Successfully detected simulated ion channel pico-ampere level currents at kHz frequencies using those BJTs
* Successfully fabricated ultra-flat gold surfaces to interface the ion channels with solid-state electronic devices
National Science Foundation NIRT grant on Nanoscale Organic Circuits and Sensors
* Successfully fabricated nanoscale organic field effect transistors down to sub 10 nm with electron beam lithography
* Fabrication of organic and conjugated polymer thin film transistor sensors utilizing small molecule receptors for enhanced selectivity and sensitivity
* Designed a hybrid inorganic/organic dual channel device with capability to detect analyte species with high sensitivity and to enable the study of charge trapping effects in organic semiconductors due to analyte interactions
Microelectronics Research Center, the University of Texas at Austin
Advisor: Prof. Ananth Dodabalapur

8/27/06 – 9/17/06 **Attended the European School for Nanoscience and Nanotechnology**
* Two weeks of lectures covering topics in nanoscience as they related to biophysics such as the mechanical properties of molecules and biological structures, immunochemistry, fluorescent labeling, single molecule microscopy, microfluidics, biological applications of microelectrodes, AFM studies of surfaces such as cell membranes, and neuroelectronics,
* One week of practicals covering topics including, using AFM for nanoparticle manipulation, electron beam lithography, fluorescent labeling of DNA, and Surface Plasmon Resonance (SPR) spectroscopy

Skills

Processes performed in class 100 cleanroom:

* AFM, four point probe measurements, surface step profilometry, ellispometry, SEM, TEM and STEM, sectioning
* electron beam lithography, photolithography, deep reactive ion etching, electron beam evaporation, thermal evaporation, lift-off, wet etching, lapping, chemical mechanical polishing, electroplating
* electrical characterization techniques at room and low temperatures, chemical sensing measurement
* semiconductor parameter analyzer, lock-in amplifier, oscilloscope, signal generator
* L-Edit layout, Labview, Origin, Matlab

Experience

Fall 1998, Summer 1999, Summer 2000 — Intern at Digital Equipment Corporation, which transitioned to a division of Compaq Computer Corporation, doing circuit design and circuit schematic verification

Publications

1. Planar nanoscale architecture for organic thin-film field-effect transistors
Daniel Fine, Liang Wang, Deepak Sharma, and Ananth Dodabalapur,
Appl. Phys. Lett.,89(20), article no. 203118, pp. 1-3 (Nov. 13th, 2006)

2. Tethered bilayer lipid membranes with giga-ohm resistances
Inga Vockenroth, **Daniel Fine**, Ananth Dodabalapur, A. Toby A. Jenkins, and Ingo Köper,
Electrochemistry Communications, 10(2), pp. 323-328 (Feb. 2008)

3. Voltage-induced gating of the mechanosensitive MscL ion channel reconstituted in a tethered lipid bilayer membrane
Martin Andersson, George Okeyo, Danyell Wilson, Henk Keizer, Paul Moe, Paul Blount, **Daniel Fine**, Ananth Dodabalapur, and Randolph S. Duran
Biosensors and Bioelectronics, 23(6), pp. 919-923 (Jan. 18th, 2008)

4. Detection of single ion channel activity on a chip using tethered bilayer membranes
Martin Andersson, Henk Keizer, Chenyu Zhu, **Daniel Fine**, Ananth Dodabalapur, and Randolph S. Duran

Langmuir, 23(6), pp. 2924-2927 (Mar. 13th, 2007)

5. Functional ion channels in tethered bilayer membranes – Implications for biosensors
   Henk Keizer, Brian R. Dorvel, Martin Andersson, **Daniel Fine**, Rebecca B. Price, Joanna R. Long, Ananth Dodabalapur, Ingo Köper, Wolfgang Knoll, Peter A. V. Anderson, and Randolph S. Duran
   Chembiochem, 8(11), pp. 1246-1250 (Jul. 23rd, 2007)

6. Tethered bilayer lipid membranes with giga-ohm resistances
   Inga Vockenroth, **Daniel Fine**, Ananth Dodabalapur, A. Toby A. Jenkins, and Ingo Köper
   Electrochemistry Communications, 10(2), pp. 323-328 (Feb. 2008)

7. Formation of tethered bilayer lipid membranes on gold surfaces: QCM-Z and AFM study
   Brian R. Dorvel, Henk M. Keizer, **Daniel Fine**, Jorma Vuorinen, Ananth Dodabalapur, and Randolph S. Duran
   Langmuir, 23(13) pp. 7344-7355 (Jun. 19th, 2007)

8. Electric-field-dependant charge transport in organic thin-film transistors
   Liang Wang, **Daniel Fine**, Debarshi Basu, Ananth Dodabalapur
   J. Appl. Phys., 101(5), article no. 054515, pp. 1-8 (Mar. 1st, 2007)

9. Organic and hybrid organic/inorganic transistors for chemical and bio sensing
   Deepak Sharma, Liang Wang, Cynthia Burham, **Daniel Fine**, Ananth Dodabalapur
   IEEE International Electron Devices Meeting (IEDM) Technical Digest., Dec. 2005 (invited)

10. Pentacene field-effect transistors with sub 10 nm channel lengths
    Liang Wang, **Daniel Fine**, Taeho Jung, Debarshi Basu, Heinz von Seggern, Ananth Dodabalapur
    Appl. Phys. Lett., 85(10), 1772 (Sep. 6th, 2004)

11. Nanoscale chemical sensor based on organic thin film transistors
    Liang Wang, **Daniel Fine**, Ananth Dodabalapur
    Appl. Phys. Lett., 85(26), 6386 (2004)

12. Nanoscale Polymer Field-Effect Transistors
    Liang Wang, Taeho Jung, **Daniel Fine**, Saiful I Khondaker, Zhen Yao, Heinz von Seggern, Ananth Dodabalapur
    Proceedings of the 3rd IEEE Conference on Nanotechnology, 2003, vol. 2, page 577-580

13. Nanoscale chemical sensors based on conjugated polymer transistors
    Liang Wang, **Daniel Fine**, Taeho Jung, Ananth Dodabalapur
    Proceedings of SPIE, volume 5522, 81-88 (2004)

14. Sub 10 nm conjugated polymer transistors for chemical sensing
    Liang Wang, **Daniel Fine**, Saiful I Khondaker, Taeho Jung, Ananth Dodabalapur
    Sensors and Actuators B: Chemical, Volume 113, Issue 1, 17 January 2006, Pages 539-544

15. Nanoscale organic and polymeric field-effect transistors as chemical sensors (critical review)
    Liang Wang, **Daniel Fine**, Deepak Sharma, Luisa Torsi and Ananth Dodabalapur
    Anal Bioanal Chem., 384(2), page 310-21, (Jan. 2006)

16. High-performance solution-deposited n-channel organic transistors and their complementary circuits
    Byungwook Yoo, Brooks A. Jones, Debarshi Basu, **Daniel Fine**, Taeho Jung, Siddarth Mohapatra, Antonio Facchetti, Klaus Dimmler, Michael R. Wasielewski, Tobin J. Marks, Ananth Dodabalapur

Advanced Materials, 19(22), pp. 4028-4032 (Jan. 18th, 2008)

17. Organic thin-film transistor sensors: Interface dependent and gate bias enhanced responses
    Maria Cristina Tanese, **Daniel Fine**, Ananth Dodabalapur and Luisa Torsi
    Microelectronics Journal, Volume 37, Issue 8, August 2006, Pages 837-840

18. Interface and gate bias dependence responses of sensing organic thin-film transistors
    Maria Cristina Tanese, **Daniel Fine**, Ananth Dodabalapur and Luisa Torsi
    Biosensors and Bioelectronics, Volume 21, Issue 5, 15 November 2005, Pages 782-788

19. High-performance organic thin film transistor sensors
    Maria Cristina Tanese, **Daniel Fine**, Nicola Cioffi, Ananth Dodabalapur and Luisa Torsi
    Proceedings of SPIE, volume 5522, 22-26 (2004)

Presentations

1. Integration of Immobilized Ion Channels with Bipolar Junction Transistors to Realize Portable, Highly Sensitive Biosensors
   Daniel Fine, Henk M. Keizer, Debarshi Basu, Liang Wang, Wolfgang Knoll, Ingo Köpper, Joanna Long, Peter Anderson, Randolph S. Duran, and Ananth Dodabalapur
   International Conference on Microelectronics and Interfaces, March 6-8, 2006

2. A New Architecture for Nanoscale Field-Effect Transistors
   Daniel Fine, Liang Wang and Ananth Dodabalapur
   Materials Research Society Spring Meeting, March 31, 2005, abstract #I7.4

3. Design Considerations of Solid State Devices for Integration with Immobilized Ion Channels
   Daniel Fine, Debarshi Basu, Liang Wang, Wolfgang Knoll, Ingo Koepper, Joanna Long, Peter Anderson, Randolph Duran and Ananth Dodabalapur
   Materials Research Society Spring Meeting, March 29, 2005, abstract #HH3.4

4. The Effects of Grain Boundaries and Small Molecule Receptors on Organic Thin Film Transistor Chemical Sensors
   Daniel Fine, Liang Wang, David Cauble, Taeho Jung, Debarshi Basu, Heinz von Seggern, Michael J. Krische, Ananth Dodabalapur
   AIChe 2004 Annual National Meeting, Austin, Nov. 7-12, 2004

5. Organic FET Chemical Sensors with Small Molecule Receptors
   Daniel Fine, David F. Cauble, Taeho Jung, Heinz von Seggern, Michael J. Krische, Ananth Dodabalapur
   American Physical Society, Annual APS March Meeting, March 3-7, 2003, abstract #V16.001

BIOGRAPHICAL SKETCH Provide the following information for the key personnel on page 1 of the Detailed Cost Estimate form for the initial budget period.			
NAME Enrica De Rosa	POSITION TITLE Postdoctoral Fellow		
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Universita' degli Studi di Napoli "Federico II"	Master in Chemical Engineering	1996-2001	Transport Phenomena, Material engineering, Fluorescence microscopy
Universita' degli Studi di Napoli "Federico II"	PhD in Chemical, Material and Production Engineering (Biomaterial subsector)	2001-2004	Tissue Engineering, Polymeric systems

Research and professional experience

Enrica De Rosa

- **in March 1998** won the Erasmus Program Scholarship and during the academic year 1998/99 took classes and gave exams in Transport Phenomena, Water Treatment and Environmental Pollution at the ***Katholieke Universiteit of Leuven in Belgium***.
- **in March 2002** won the Scholarship for the PhD in Chemical, Materials and Production Engineering in Biomaterial - cycle XVII (2001-2004) at the ***University of Naples "Federico II"***.
- **in September 2002** awarded the qualification to the profession of engineer with full marks and by January 2006 is put on the engineers register of Naples.
- **from December 2004 to June 2005** based on her experience was asked to work as research assistant on "Transport properties in micro and nano porous systems" at the Department of Material and Production Engineering (DIMP) in Engineering Faculty of the ***University of Naples "Federico II"***.
- **from July 2005 to September 2007** winning a Post Doctoral Scholarship for Research worked on "Remodelling of bio-hybrid tissues *in vitro*" and "Biomolecular transport in three-dimensional cellular constructs" at the Interdepartmental Research Centre of Biomaterials (CRIB) in Engineering Faculty of the ***University of Naples "Federico II"*** financed by IMBIOTOR EU projects (contract G1RDCT-2000-00293) and DERMAGENESIS EU project (contract COLL-CT-2003-500224-2).
- **since October 2007** is a Post Doctoral Fellow at the ***University of Texas in Huston*** in the Division of Nanomedicine of the Department of Biomedical Engineering to develop implantable nanodevice for drug delivery, within a project financed by NASA (contract SA23-06-017).

Research activity

Enrica De Rosa started her research activity in **May 2000** at the Department of Material and Production Engineering (DIMP) carrying on her master thesis on "A new experimental technique to determine the transport parameters in polymeric gel and solutions". During her thesis work (**2000-2001**) she has realized and set up a Fluorescence Recovery After Photobleaching (FRAP) apparatus at the Laboratory of Molecular and Cellular Engineering of DIMP, and the first results achieved with this apparatus in water solutions of hyaluronic acid solutions helped the comprehension of the peculiar properties of biologic fluids due to this biopolymer (publication #1 in the hereafter Publications list). During this activity she has widened her knowledge of transport phenomena and their mathematical models. She has gained know-how on optical physics and fluorescence techniques. She had experience of programming in matlab and C++. During her PhD (**2001-2004**) she has made further studies on transport mechanisms in complex materials and on polymeric physics, by

analysing structural changes of several biopolymeric systems (water solutions of hyaluronic acid, collageneous cellular constructs, pluronic water solutions) due to the variation of a physical parameter, with different transport measurements techniques, traditional and optical, such as reometrics, FRAP, Fluorescence Correlation Spectroscopy (FCS) and Dynamic Light Scattering (DLS). The work developed during these three years, also collaborating with Biologist and Physicists, has enabled the successful defence of the thesis "Transport mechanisms of macromolecules in complex biopolymers", and the writing of many publications. In particular the results achieved from in vitro experiments carried on 3D constructs were object of several oral presentation at international conferences. In **2005-2006** on the basis of these results the research was directed towards the comprehension of the transport regulation mechanisms of the extracellular matrix, studying especially the effects on its transport properties, of presence, concentration and assembly of the its components, by mean of similar collageneous constructs produced in vitro (works #3-5 and few oral and poster presentations at conferences). Among these, a result of great interest in design and control of *in vitro* 3D cellular culture is the mathematical relation found between the extracellular matrix produced and the transport properties of the engineered scaffolds proposed in the publication #3. In **2007** the research was aimed to the comprehension of the mechanisms of transport and biological functions regulation of the HA within natural tissues. In this context a worthwhile observation was that the hyaluronic acid (HA) obstruction effect on different diffusing probe motion is selective and depends on nature and dimension of the probe (publication #6). On the one hand this research lead to the understanding of the conformational and structural changes occurring in HA water solutions and their theoretical description that was in great agreement with the experimental results and allowed to quantify the structural parameter experimentally evaluated (publication #5). On the other hand it was also studied the retard and inhibition of the cellular bioactivity that the HA induces within collageneous scaffolds on endothelial cells spheroids and mouse embryonic fibroblasts (presented at conferences). **Since October 2007** she is applying her knowledge of molecular diffusion to the study of non-fickian diffusion at nanoscale though nanochanneled Delivery System (nDS) in the division for Nanomedicine at Houston. Within this study a theoretical predictive model to describe the release of small molecules has been found (presented at conferences) and a quality control method for nDS device has been proposed (publication #7). Recently theoretical and experimental studies, performed also in vitro and in vivo, are focused on nDS controlled release for cancer treatment (presented at AACR conference). This work has lead to 3 ***invention disclosures*** entitled "Implantable Smart Multi-Drug Controlled Release nano-Device", "Long term constant release of molecules from super-saturated solutions" and "Intravaginal nanochanneled drug delivery device".

Publications

on peer reviewed journals

1. Enrica De Rosa, Assunta Borzacchiello; "Hyaluronic Acid Rheology: role and importance in biological fluids properties" παντα ρει Publication of the Italian Rheology Society, B. di M - 3 (**2005**) 20-27.
2. Enrica De Rosa, Cristina Borselli, Paolo A. Netti; "Transport of large molecules in hyaluronic acid - based membranes and solution." **Journal of Membran Science,** Elsevier 273 (**2006**) 84-88.
3. Enrica De Rosa, Francesco Urciuolo, Cristina Borselli, Diego Gerbasio, Giorgia Imparato, Paolo A. Netti; "Time and space evolution of transport properties in agarose-chondrocyte constructs." **Tissue Engineering,** Mary Ann Liebert 12:8 (**2006**) 2193-2201.
4. Cristina Borselli, Olimpia Oliviero, Enrica De Rosa, Luigi Ambrosio, Paolo A Netti "Spatio-temporal distribution of matricellular cues regulates endothelial cell function" **Cytotherapy** Taylor & Francis As. 8(2) (**2006**) 18
5. Enrica De Rosa, Francesco Urciuolo, Cristina Borselli, Paolo A Netti "Temporal and spatial transport properties evolution and extracellular matrix production in tissue engineered cartilage constructs" **Cytotherapy** Taylor & Francis As. 8(2) (**2006**) 19
6. D. Guarnieri, S. Battista, A. Borzacchiello, L. Mayol, E. De Rosa, D.R. Keene, L. Muscariello, A.Barbarisi, P.A. Netti; "Effects of fibronectin and laminin on structural, mechanical and transport

properties of 3D collageneous network." **Journal of Materials Science: Materials in Medicine,** 18 (**2007**) 243-251.

7. Grattoni, E. De Rosa, S. Ferrati, Z. Wang, A. Gianesini, X. Liu, F. Hussain, R. Goodall, M. Ferrari "Defect detection in complex nanonochannel membranes." **Journal of Membrane Science** (submitted Dec.**2008** – currently under review)

on congresses and conferences proceedings (21)

Oral (14) and poster (7) presentations at international conference both in Europe and USA. (selected recent ones are listed)

Oral

- Enrica De Rosa, Francesco Urciuolo, Cristina Borselli, Paolo A Netti "Temporal and spatial transport properties evolution and extracellular matrix production in tissue engineered cartilage constructs", Strategies in Tissue Engineering May 30th -June 2nd 2006, Würtzburg (Germany).
- Cristina Borselli, Olimpia Oliviero, Enrica De Rosa, Luigi Ambrosio, Paolo A Netti "Spatio-temporal distribution of matricellular cues regulates endothelial cell function", Strategies in Tissue Engineering May 30th - June 2nd 2006, Würtzburg (Germany).
- Enrica De Rosa, Carmen Palmiero, Paolo A Netti "Diffusivity and self-assembly within ECM analogue composite: role of HA and cells presence during culture", 20th European Conference on Biomaterials ESB Septmber 27th - October 1st 2006, Nantes (France).
- D. Guarnieri, S. Battista, A. Borzacchiello, E. De Rosa, L.Muscariello, A.Barbarisi, P.A. Netti "Effect of laminin and fibronectin on structural properties of 3D collageneous network", 20th European Conference on Biomaterials ESB September 27th - October 1st 2006, Nantes (France).
- Enrica De Rosa, Susi Borzacchiello, Paolo Netti, "Structure and dynamics of semidilute polyelectrolyte solutions" AERC 2007 4th Annual European Rheology Conference - April 12-14, Napoli (Italy).
- Enrica De Rosa, Carmen Palmiero, Paolo A Netti "Transport regulation in ECM analogue obtained by cellular remodeling", 21st European Conference on Biomaterials ESB September 9th - 13th 2007, Brighton (UK).
- Enrica De Rosa, Assunta Borzacchiello, Paolo A Netti "Hyaluronan Molecular Dynamic by self and probe diffusivity", 8th World Biomaterial Congress May 28th– June 1st 2008, Amsterdam (Holland).
- Enrica De Rosa, Alessandro Grattoni, Silvia Ferrati, Xuewu Liu, Mauro Ferrari "How to control the molecular transport throughout nanochanneled delivery system." BMES October 2nd – 4th 2008, St. Luis, MO (USA).
- Enrica De Rosa, Alessandro Grattoni, Xuwue Liu and Mauro Ferrari "Controlled Drug Delivery through Nanochanneled Devices" HSEMB conference March 19th and 20th 2009, Houston, TX (USA)

Posters

- Enrica De Rosa, Carmen Palmiero, Paolo A Netti "Role of HA on bioactivity and transport regulation within cellular collagenous networks", International Conference On Advances In Biomaterials For Drug Delivery And Regenerative Medicine ICAB June 11th-16th 2006, Capri (Italy).
- Cristina Borselli, Olimpia Oliviero, Enrica De Rosa, Laura Majol, Sabrina Battista, Luigi Ambrosio, Paolo A Netti "The spatial distribution and the time evolution of the matrix regulate sprouting angiogenesis", International Conference On Advances In Biomaterials For Drug Delivery And Regenerative Medicine ICAB June 11th-16th 2006, Capri (Italy).

- D. Guarnieri, S. Battista, A. Borzacchiello, L. Mayol, E. De Rosa, L. Muscariello, A. Barbarisi, P.A. Netti "Effect of extracellular matrix proteins on structural properties of 3D collagen gels", International Conference On Advances In Biomaterials For Drug Delivery And Regenerative Medicine ICAB June 11th-16th 2006, Capri (Italy).
- Enrica De Rosa, Alessandro Grattoni, Xuewu Liu, Mauro Ferrari "Nanochanneled implantable device for sustained controlled cancer treatment." AACR April 18th-22nd 2009, Denver, CO (USA).

in progress

- Enrica De Rosa, Assunta Borzacchiello, Paolo A. Netti "Structure and dynamics of hyaluronic acid semidilute solutions with no added salt"
- Enrica De Rosa, Alessandro Grattoni, Xuewu Liu, Arturas Zyemis, Claudio Cavasotto, Mauro Ferrari "Controlled release throughout nanochanneled delivery systems: measurements and predictions."

Mentorship activities

Since January 2002 Enrica De Rosa has tutored 7 master thesis in chemical engineering, material science and engineering, and bioengineering.

In September 2003 she was appointed expert in the topic of Polymer Technology by the Faculty Council of the University of Naples "Federico II".

In the academic year 2002/2003 She taught the course of "Polymer Technology" for the master degree of chemical engineering for three years, of "Technological and physical properties of polymers" for the master degree of Material Engineering, of "Interstitial Transport" for the master degreee of Bioengineering, of "Material Technology" for the master course of Material Science and Engineering, and of "Physical and technological properties of polymers" for the master course of Material Engineering.

Master Credits

Schools and Courses Attended

- **INFM 2nd National School of Biophysics**, Genova; December 1st-7th 2003.
- **National School of Transport Phenomena**, Pacognano; February 9th-14th 2003.
- **National School of Applied Thermodynamics**, Abano Terme; March 29th-April 3rd 2004
- **4th Course of Principles in Fluorescence Spectroscopy**, Genova; June 19th-22nd 2006
- "**Confocal use and FCS (*Fluorescence Correlation Spectroscopy*) measurements course**" hold by Dr. Manfred Brich (Zeiss); September 17th-20th 2002.
- "**Use methodologies and measurements techniques of Confocal microscope and FCS (*Fluorescence Correlation Spectroscopy*)**" hold by Zeiss; March 26th-28th 2002.
- "**Use and measurements of Dynamic and Static Light Scattering**" hold by Malvern Instruments; May 17th-20th 2004.
- "**Protecting Human Research Participants**" web based course by the National Institutes of Health (NIH) Office of Extramural Research; June 2nd 2008.

Organizing activities

she was member of the Organizing Committee of the following congresses

- 19th European Conference on Biomaterials ESB September 11th-15th 2005, Sorrento
- International Conference On Advances In Biomaterials For Drug Delivery And Regenerative Medicine ICAB June 11th-16th 2006, Capri.