Dear Colleagues,

We warmly welcome you to the workshop titled as “Novel Fluidic Technologies and Applications with an Emphasis on Collaboration” in Izmir, Turkey during April 21-22, 2014.

The workshop is organized within the framework of the German-Turkish Year of Research, Education and Innovation 2014 with the motto "Science Bridging Nations" which is a joint initiative of the BMBF and the Turkish Ministry of Science, Industry and Technology. The celebratory opening event took place on 23 January 2014 in Berlin.

Amongst the objectives of the German-Turkish Year of Science are increasing the visibility of the diversity and excellence of German-Turkish activities in research, education and innovation, establishing new partnerships and making better use of joint innovation potential. This should help develop the next generation of young scientists in both countries, leading to greater qualitative progress in terms of cooperation.

Therefore, the organized workshop not only focuses on technical aspects but also collaboration possibilities among the researchers of both countries. The workshop aims to gather researchers from the field of microfluidic systems in order to discuss manufacturing techniques, immobilization of biological materials such as enzymes, DNA, cancer cells both from clinical and early research perspectives.

We warmly welcome the researchers and graduate students who would like to present their studies in poster session.

We look forward to the scientific exchange and the profile you bring to this meeting.

On behalf of the Organizing Committee,

Assoc. Prof. Dr. Ozlem YESIL-CELIKTAS

Workshop chair,
Ege University
Department of Bioengineering

Preface

Researches on microfluidic systems have attracted growing interest over the past decade due to their advantages such as size reduction, low cost, efficient conversion, efficient heat and mass transfer. This technology is a promising field which enables usage in different areas such as chemical, biotech, pharmaceutical industries, life sciences, clinical and environmental diagnostics. Microfluidic devices themselves are concomitantly of small dimensions, from some mm to micrometers. Microfluidic reactors consist of a network of miniaturized channels, embedded in a flat surface, commonly called "chip". Along with this chip type of microreactors, simpler microcapillary devices are also extensively used, where the microchannel is the reaction space, and thus no control of microfluidics is required. On the other hand, they do not allow for the integration of different processes into one reaction device, unlike chip microreactors.

To date the greatest research effort in the field of microscale devices has been in the analytical arena. One of the major focuses of this research is to develop a miniaturized total analytical system (μ-TAS). Optimally, such devices would automatically perform sampling, sample preparation, separation, detection and data processing in a fully integrated manner. In addition to this advantage of high automated throughput and low reagent consumption with increased safety of operation resulting from low reagent quantities, these devices offer potential as remote control systems. To date most popular area of μ-TAS has been in the biomedical field covering DNA and proteomics, whereas various bioconversions have been investigated using microreactors.

Instrumentation and automation in microdevices have been one of the major issues that researchers are focusing on intensively. Microfluidic systems could be designed by assembly and modification of microcapillaries that offers numerous advantages such as rapid heat and mass transfer constituting the key reasons for the superiority of microfluidic systems over conventional bioprocess strategies. Depending on the material used, a range of channel microfabrication methods such as photolitography, hot embossing, etching, powder blasting, injection moulding and laser microforming are available. Designing low-cost and simple microbioreactors, instrumentation and automation in this device to perform high throughput bioprocesses in microscale is a major issue in order to deploy this technology on a wider spectrum.

The emergence of microreaction technology and process miniaturization has provided a potentially new platform for accelerating the development of bio-based microfluidic systems. The increasing number of granted patents and published papers indicate the upcoming applications in this field.

ORAL PRESENTATIONS

Microfluidics and fabrication techniques

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Keywords: microfluidics**,** materials, fabrication technology, smart system integration, MEMS[1]

Introduction: Microfluidics is the technology for processing fluids with volumes on the order of nanoliters or picoliters. The devices themselves have characteristic dimensions ranging from millimeters down to micrometers, designed on chip areas typically in the square centimeters range. When scaling down the dimensions of fluidic structures fluid behavior are dramatically altered. Due to an enormous increase in surface to volume ratio, surface effects are dominating making inertia effect neglectable. Capillary action changes the way in which fluids pass through microchannels resulting in well-defined laminar flow. Heat and mass transfer become more efficient with the benefit of minimum material consumption. Unsurprisingly, microfluidics bears promises for so many application areas as medical diagnostics, chemistry, analytics, and biotechnology [1].

Different materials are used to manufacture microfluidic devices. Starting with silicon and glass [2] using well-known processes from MEMS technology in the 80's and 90's, replication techniques based on PDMS[2] experienced a strong growth starting 2000, followed by the use of thermoplastics [3]. A review of the approximate numbers of annual publications referencing different materials for microfluidics reveals that silicon, silica and glass are mostly used, followed by PDMS and thermoplastics [4].

The capability of the different materials with their corresponding fabrication technology has been demonstrated in plenty of devices developed for the various application areas [5-10]. Mostly designed for liquids, devices for micro analytics in gas phase also have been realized [11,12].

Discussion & Conclusions: After more than three decades of R&D in microfluidics this area is becoming an emerging technology with an expected swiftly growing market [13] – however, still being far away from getting fully established. The efforts result in a variety of technologies with a mix of different materials in use and corresponding fabrication techniques.

Considering the fabrication of passive microfluidic components such as microchannels and microcavities with chip areas above 1 cm² polymer replication technology is the only solution which can meet the demand of low cost for mass production. For point-of-care applications paper-based devices also provide an alternative [14]. Depending on the application, materials have to be carefully selected taking into account among others good solvent and chemical compatibility, or pressure stability. Microfluidic chip fabrication using semiconductor technology provides integrated functionality [15,16,17]. The cost factor will become less dominating if chip areas can be scaled down to 10 mm² or even smaller. Scaling down the microfluidic chip requires the design of microstructures in micrometer and submicrometer range, potentially merging into the domain of nanofluidics. Furthermore, microfluidic packaging approaches with minimum space requirements have to be established. Hybrid systems [18,19] made of polymer and silicon are expected for the development of smart microfluidic systems.

The need for these smart devices results from the fact that when non-experts are targeted as end user, e.g. for POC[3] or quantitative analysis, the detection and signal conditioning units have to become parts of the integrated system.

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Abbreviations

1: MEMS – micro electro mechanical system, also synonym for microsystem

2: PDMS – Polydimethylsiloxane

3: POC – Point-of-Care

Immobilization of enzymes to microsystems

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Keywords: enzymes, microfluidics, immobilization, reactive distillation

Introduction: Enzymes are biological catalysts, which play an important role in industrial processes since they are versatile, regio-, chemo- and enantioselective. Since the isolation and purification of enzymes is an expensive procedure, the reusability of enzymes is important for industrial applications. Often the immobilization technique is used to fix the enzymes in the technical apparatus. Typical immobilization techniques are physical adsorption, immobilization via ionic interactions, covalent binding and encapsulation into polymeric gels. During encapsulation the enzyme is enclosed by a polymeric matrix which protects it from aggregation and denaturation by unfolding. Therefore it is not necessary to attach the enzyme molecules to the gel walls by adsorption or other ionic or covalent bonds. These interactions could affect negatively the performance of the enzymes [1-3]. In this paper the immobilization of enzymes by encapsulation in mesoporous gels via the sol–gel method is discussed.

Discussion & Conclusions:

The immobilization of the enzymes is carried out in microreactors since they offer advantages like high surface to volume ratio and the possibility to separate the enzymes into compartments where optimal conditions for enzyme activity prevail. The sol-gel process is preferred over other immobilization methods, since it allows the easy loading of the enzyme doped materials inside the microreactors. The final goal is the development of a monolithic enzyme carrier which offered high enzymatic activity and stability after encapsulation

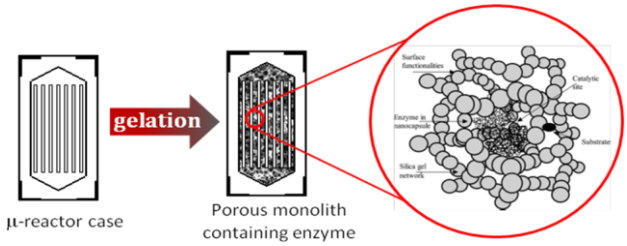

Figure 1. Illustration of the sol-gel based enzyme immobilization in microreactors.

Simultaneously the gel should bear high permeability and good mechanical properties to withstand flow-through. Different silica precursors, aging media, buffers and additives are used and their effect in the activity and stability of the immobilized enzyme is discussed. The effect of the addition of water-soluble polymers to the gels on microreactor performance is discussed. The possibility of reducing enzymatic leaching by functionalization of the gel surface is also presented [4,5].

Two different applications are targeted:

(1) Enzymatic reaction in the continuously operated microsystems
(2) Screening system for novel application of the enzymatic reactions

For the first application enzymatic reaction involving G6PDH from *L. mesen-teroides* in silica-based gels from different silica precursors are presented. Here the reaction yield and conversion in dependence on the process conditions are discussed. For the second application lipase CALB was immobilized in silica-based gels and loaded into the microreactors. The reaction was used to find the optimal conditions for the enzymatically catalyzed reactive distillation.

In case of reactive distillation the attachment of enzymes to the column internals plays the crucial role. Since the gel composition should be adjusted to provide this characteristic, the activity and stability of enzymes in corresponding gels should be investigated. The use of microfluidic devices were proven to be very promising for the screening of different enzymes and reaction condition for this purpose.

Acknowledgements:

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Immobilization of biological materials to microsystems

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Keywords: microfluidics, microreactor, cells, DNA, enzyme

Introduction: The capabilities of micro- and nanotechnologies have been exploited considerably leading to the progression of novel microfluidic applications. The first reported use of a microchip was in 1979 by fabrication of gas chromatograph air analyzer on a silicon wafer [1]. Miniaturized instrumentation has gained attention, particularly by performing flow through analysis on a chip [2] and rapidly grown with the introduction of integrated microfluidic devices which are typically referred to as lab-on-a-chip or micro total analysis systems (μTAS). The design of highly efficient microfluidic devices (**Fig. 1**) have been applied in biochemical analysis, medical analysis, environmental monitoring, fermentation and life science applications such as detection kits, animal cell culture studies, enzymatic bioconversions, DNA analysis and polymerase chain reactions.

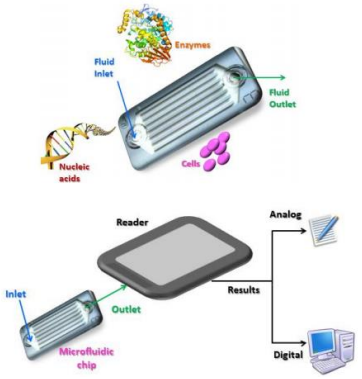

Fig. 1. Integrated microfluidic components

The aim of this study was to analyze the contribution of patents to the advancement of bio-based microfluidic applications.

Discussion & Conclusions: A significantly increasing trend was observed in terms of both scientific and patent disclosures from 2000 and onwards (**Fig. 2**). Patents originating from United States (65.7%) originating from United States were dominating, followed by those from Japan (17.1%) and the European Union (17.2 %). Disclosures according to assignees were analyzed to identify the contribution of industrial and academic research to patented innovations. The results showed that 54.3 % contribution arised from universities and research institutes and 45.7 % from companies.

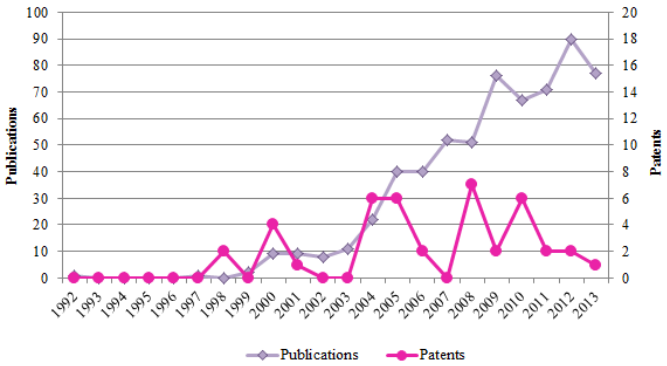

Fig. 2. Publication and patent disclosures between 1992 and 2013.

The mapped patents were grouped in three categories in order to provide a holistic overview, where the majority of the patent disclosures (45.7 %) were related to providing methods for immobilization of biological materials to microreactors, followed by fabrication of microsystems (31.4 %) and microreactor design (22.9 %). The increasing trend is expected to continue and the current knowledge and know-how will provide basis for further applications.

Acknowledgements:

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Cancer cells from a clinical perspective

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Keywords: Cancer, cell, chemotherapy, stem, prognosis

Introduction: For a long time, cancer has been proposed to develop from a cell that contains mutations on some critical (driver) genes. However, the origin of cancer cell (any differentiated cell in the organ or stem cells or their progenitors) was not clear. Recently, "cancer stem/initiating cell" hypothesis was postulated. This is a relatively new concept that has emerged over the last almost 10 years in solid tumors. This hypothesis means that tumors arise from cells termed cancer stem/initiating cells that have properties of adult stem cells.

These special cells have abilities to self-renew and differentiate into multiple cell types. More importantly, these cells persist in tumors as a distinct population in the bulk of tumor tissue that likely leads to recurrence of disease sometime after the therapy. It is also believed that metastasis is managed by these cells. In addition, they are the only cells capable of giving rise to development of new tumors when they are injected into the mice. In other words, it is thought that the bulk of the tumor tissue is not able to develop new tumors. These cancer stem cells are also found to be resistant to chemotherapy as well as radiotherapy.

There is accumulating evidence that the resistance of cancer stem cells to many classical chemotherapies may account for the inability of these therapies to cure the metastatic cancers. Therefore, complete knowledge of this evolutionary process may be crucial for the development of novel effective therapies that influence patient prognosis. Stem cell subcomponents have now been identified in a number of human malignancies, including hematologic malignancies as well as solid tumors of the breast, prostate, brain, pancreas, head and neck, and colon.

Discussion & Conclusions: In cancer stem cells, these pathways are thought to be deregulated, causing uncontrolled self-renewal of cancer stem cells which generate tumors that are resistant to conventional therapies. Current anti-cancer agents may target and kill differentiated tumor cells, which compose the bulk of the tumor, while untouching this rare cancer stem cell population. The cancer stem cell hypothesis suggests that the design of new cancer therapeutics targeting cancer stem cells is urgently required for better treatment of cancer. Therefore, it is necessary to design new strategies based on a better understanding of the signaling pathways controlling self-renewal and survival in cancer stem cells in order to discover novel chemotherapeutic genes/proteins in these cells.

Sorting of stem cells with microfluidic chips

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Keywords: Small bowel transplantation, stem cell sorting, microfluidic chips

Introduction: Intestinal transplantation is the most effective treatment for patients with short bowel syndrome and small bowel insufficiencies. We evaluated epithelial chimerism after infusion of autologous bone marrow mesenchymal stromal cells (BMSC) in patients undergoing cadaveric donor isolated intestinal transplantation (I-ITx). BMSCs were isolated from patients' bone marrow via iliac puncture and expanded *in vitro* prior to infusion. Two out of the three patients were infused with autologous BMSCs and analyzed small intestine tissue biopsies collected post-operatively and analyzed for epithelial chimerism using XY fluorescent in situ hybridization and short tandem repeat polymerase chain reaction. We observed epithelial chimeric effect in conditions both with and without BMSC infusion.

Results: Although our results suggest a higher epithelial chimerism effect with autologous BMSC infusion in I-ITx, the measurements in multiple biopsies at different time points that demonstrate the reproducibility of this finding and its stability or changes in the level over time would be beneficial.

Discuss & Conclusion: These approaches may have potential implications for improved graft survival, lower immunosuppressant doses, superior engraftment of the transplanted tissue, and higher success rates in I-ITx.

Biochemical assays from a clinical perspective
"Tiny Particles / Big Results "

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Keywords: Clinical chemistry, microfluidics, point of care testing

Laboratory test results are usually pivotal to critical care decisions. Testing provides physicians with valuable knowledge about the criticality of the patient so that appropriate therapeutic interventions can be made promptly. There has been growing interest in decentralized laboratory testing, especially point-of-care-testing (POCT) in critical care settings [1].

Introduction: Medical biochemistry seeks to advance the understanding of chemical structures and processes that constitute health and disease, and underlie transformations between these two states. Its applicative arm is clinical chemistry, a field that focuses on the methodology and interpretation of chemical tests performed to support diagnosis and treatment and monitoring of disease [2].

There is increasing pressure to provide cost-effective healthcare based on "best practice". Consequently new biomarkers and new techniques are only to be introduced into routine clinical biochemistry departments if they are supported by a strong evidence base and if the results will improve patient management and outcome [3].

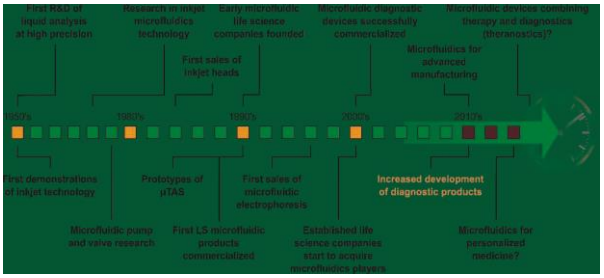

Fig. 1 Timeline of the evolution of microfluidic technology.

Taking a new method from the research laboratory successfully into the routine clinical laboratory or clinical use ideally requires a four-way collaboration, involving i) the research laboratories (which develops the fundamental concept), ii) the diagnostics industry (which turns the concept into a practical reliable tool), iii) the clinical laboratory (which evaluates the tool in real-life practice) and iv) clinicians [3].

Discussion & Conclusions: The research community now has a great opportunity to define the materials, chemicals and analytical techniques that will shape the future of diagnostics. A recent manifestation of this potential is in the emergence of microfluidic bioanalysis. It is important to evaluate where microfluidics can be applied and how they can be developed for specific needs. What gaps in current diagnostics can microfluidics fill? What kind of benefits can microfluidics provide to the detection of analytes in biological samples?

In many ways the intrinsic features of microfluidics are a natural fit for point-of-care (POC) diagnostic devices. Low consumption of reagents and sample, miniaturization of device, and fast running time for analysis [4]. Yet there are concerns debated by users/medical staff to be prudent with POCT devices.

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Lab-on-a-chip as rapid test kits

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Keywords: lab-on-a-chip, biosensors, diagnostics, nanotechnology

Introduction :

Once viewed solely as a tool to analyze biomolecular interactions, biosensors are gaining widespread interest for diagnostics, biological defense, environmental and quality assurance in agriculture/food industries. With a $42 billion yearly worldwide in vitro diagnostics (IVD) market (which has been believed to reach $56 billion in 2012) [1], medical diagnostics is one of the key areas where biosensors can make a life changing difference for patients and doctors. Diagnostic applications include the detection of disease-related biomarkers, e.g., metabolites, proteins or nucleic acid in human body fluidics. Biomarker concentrations in body fluids can be used to define disease type, state, or progress as well as the patient's response to therapy. Research on disease-related biomarkers is an ongoing process and more than one biomarker has to be determined to allow efficient diagnosis/prognosis, leading to biomarker profiles [2,3]. The recent advances in next generation genome sequencing have started to create vast amount of data that can be used to discover novel disease biomarkers which have potential to be used for personalized medicine. Currently, testing for biomarkers is typically performed in centralized laboratories using large automated clinical analyzers [4,5]. This process requires sample transportation, increased waiting time, high medical costs and trained staff. Therefore, there is a need to develop a detection system that is cheap, quick to process, uses low sample and reagent volume and easily operated. Recent advances in the area of sensor technology and lab-on-a-chip applications have enabled the miniaturization of the devices and multiplex testing of a range of analytes.

Advanced micro fabrication techniques have facilitated integration of microfluidics with sensing functionalities on the same chip making system automation more convenient [6]. Development of an integrated sensing platform relies on the collaborative work of a multidisciplinary group that consists of scientists and engineers (Figure 1).

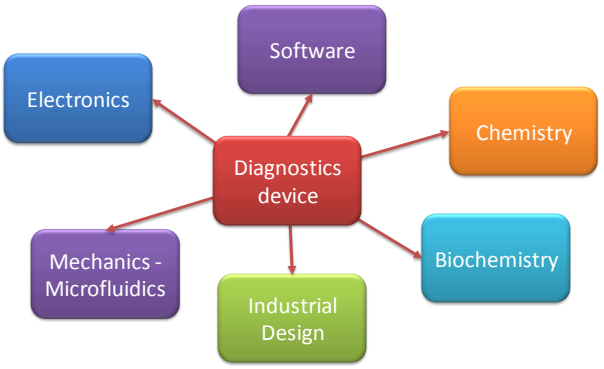

Fig. 1. Multidisciplinary dimension of biosensor based diagnostics device development is shown in the diagram.

Discussion & Conclusions: High sensitivity, selectivity, rapid analysis, the ability to operate in turbid solutions and the possibility of miniaturization enabled electrochemical biosensors to become the most widely used biosensors. Hence, in the literature numerous papers can be found that describe the electrochemical detection of DNA, proteins, microorganisms and etc. with very low detection limits. However, it is notable that these data were generated on "home-built" electrochemical detection systems and assay conditions are mostly in static with very few assays performed with fluidic systems.

In addition mostly, the assay procedures are long, labourous and not suitable for automation. In response to that, we have developed a novel detection technology, which we term Real-time Electrochemical Profiling™ (REP™). While this technology relies on the fundamental basics of amperometry, it has several key features including a novel electrode array, a microfluidic sensor cassette, microfluidics based assay and real-time amperometric measurements during the flow of enzyme substrate. This new sensing array with its sensor cassette allowed the assays to be performed in fluidics rather than static, that allowed not only faster assays due to minimal mass transport issues, but also enhanced the electrochemical response by allowing real-time chronoamperometric measurement. In short, REP™ technology may pave the way for easy to use, automated biosensing devices that could be used for a variety of applications from diagnostics to environmental monitoring, and studies will continue to move forward in this direction.

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Microfluidic bio-particle manipulation

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Keywords: Microfluidics, bio-particle manipulation

Introduction: The miniaturization trend of electronic components since 1970's, and the development of advanced fabrication techniques for micro and nano-scale devices since 1980's led to the usage of devices having the dimensions of micrometers and nanometers in many fields. This trend has helped nanotechnology become a new area of science at the intersection of chemistry, physics, biology and engineering. This intersection eliminated the boundaries between these disciplines. The elimination of these boundaries has posed many challenges and new directions for organization of education and research. One of the important challenges is the rapid development of biochips, miniaturized analysis systems or lab-on-a-chip (LOC) devices which are microfluidic platforms on which one can handle chemical and biological analyses, point-of-care testing, clinical and forensic analysis, molecular diagnostics and medical diagnostics for biological, biomedical and chemical applications. LOC devices can perform the same specialized functions as their room-sized counterparts. Chips can perform clinical diagnoses, scan DNA, run electrophoretic separations, act as microreactors, detect cancer cells and identify bacteria and viruses [1]. On a single chip, hundreds of different reactions and/or analyses can be performed at the same time through hundreds of different reactions and/or analyses can be performed at the same time through hundreds of parallel microchannels. Originally it was thought that the most significant benefit of these LOC devices would have been the analytical improvements associated with the scaling down of the size. Further developments revealed other significant advantages such as, **(i)** very small amount of sample (in the nano to picoliter range, opening the door to the possibility of analyzing components from single cells), **(ii)** small amount of reagents, **(iii)** very short reaction and analysis time compared to room-sized counterparts, **(iv)** reduced manufacturing costs, **(v)** increased automation, **(vi)** high portability, **(vii)** opportunity for massively parallel chemical analyses either on the same or multiple samples [2].

For chemical, biological and biomedical analysis in microfluidic systems, there are some fundamental operations such as separation, focusing, filtering, concentration, trapping, sorting, detection, counting, washing, lysis of bio-particles, and PCR-like reactions. The combination of these operations led to the complete analysis system or LOC system for a certain application. Manipulation of the bio-particles is the key ingredient for the many aforementioned processes. Therefore, microfluidic bio-particle manipulation has attracted a significant attention from the academic community. Considering the size of the bio-particles and the throughput of the practical applications, manipulation of the bio-particles is a challenging problem. Many research groups and scientists have proposed utilizing different techniques to manipulate bio-particles such as hydrodynamic-based, electrokinetic-based, acoustic-based, magnetic-based, optical-based etc.

In this talk, different techniques and the comparison among them will be discussed. Some recent biotechnology applications regarding the microfluidic bio-particle manipulation will also be presented. Challenges regarding the design, fabrication and integration of these systems will be discussed. The recent research projects within the Bilkent University Microfluidics and Lab-on-a-chip Research Group will also be presented.

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HORIZON 2020 - EU Funding Possibilities in Life Sciences

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Keywords: Calls in life sciences, Cooperation with Bavaria, Enterprise Europe Network, EU research funding for science and industry, HORIZON 2020

Introduction: Research is the most important prerequisite in order to combat diseases, one of the greatest threats to mankind. Even the most brilliant research idea requires an adequate framework and support in order to bring some benefit to society. The European Union offers various funding possibilities for research projects in life sciences. Therefore, it is important to find the optimal funding instrument for one's research activities.

HORIZON 2020: Horizon 2020 is the new framework programme for research and innovation of the European Union. From 2014-2020, it provides a funding of € 80 billion for innovative research and development projects. Horizon 2020 has the overall aim of creating new jobs and spurring economic growth in Europe. In order to achieve this goal, the programme combines three strategic priorities: boosting scientific excellence in Europe, increasing its industrial leadership in particular by removing barriers to innovation, and addressing societal challenges. One of the most challenging social problems are health issues. This is why the EU invests 9.7 % of Horizon 2020's total budget in the challenge "health, demographic change and wellbeing". [1]

Funding instruments and calls for proposals in life sciences: Horizon 2020 consists of a variety of funding instruments for innovative research projects in life sciences. The *SME Instrument* supports market-oriented development and innovation projects of small and medium-sized enterprises (SMEs) with the aim of product commercialization. [2] The *Eurostars-2 Programme* supports joint research and innovation activities of European SMEs. [3] Under the *Marie Skłodowska-Curie Actions*, two funding programmes help researchers enhance their career perspectives. *Initial Training Networks (ITN)* focus on the training of early-stage researchers while preparing them for their working life in academic and non-academic sectors. *Individual Fellowships* are aimed at experienced researchers willing to extend their skills by advanced training, international and intersectoral mobility. [4] *Future and Emerging Technologies (FET)* fund interdisciplinary collaborations creating synergies between advanced sciences and innovative engineering disciplines, which are able to create new future-oriented technologies. [5] Most of the current calls in life sciences could be found in societal challenge 1 "health, demographic change and wellbeing" or societal challenge 2 "food security, sustainable agriculture and forestry, marine and maritime and inland water research and the bioeconomy". However, due to the interdisciplinary character of Horizon 2020, some life science calls can also be found in the work programmes of other societal challenges.

BayFOR's services: When it comes to identifying the appropriate funding scheme for a project idea or applying for Horizon 2020 calls, the Bavarian Research Alliance (BayFOR) can provide substantial help. BayFOR supports and advises Bavarian scientists and stakeholders from the private sector **free of charge** on European research funding programmes. Scientific experts provide subject-specific information and offer strategic advice and active support for initiating projects, setting up international research consortia and submitting proposal applications. Upon successful evaluation, BayFOR is able to provide support during contract negotiations with the European Commission and, if required, BayFOR provides support with project management throughout the project duration as well as with dissemination of project results. BayFOR regularly organizes presentations and workshops where new EU funding programmes, details on EU application procedures and management of EU projects are explained.

BayFOR as a network and project partner: BayFOR is very well networked as it has established valuable contacts to a multitude of universities, research institutes and networks, small and medium-sized companies (SMEs) and EU bodies, and can establish contact to any of them. This network can be used to exchange experiences, to search for project partners, or to get the latest information. As a partner in the support network for SMEs "Enterprise Europe Network" (EEN), BayFOR provides specific advice to SMEs interested in EU research and innovation projects and helps them to identify appropriate project partners and funding instruments. The network comprises more than 600 organisations across Europe, with 4,000 employees in 54 countries.

BayFOR also acts as a long-term partner in several EU projects. Once an EU project is approved, BayFOR can take over the administrative handling of the project if it is coordinated in Bavaria. BayFOR's experienced project management department takes over tasks such as compliance with contractual specifications, financial and organisational management, and organisation of the communication within the project. BayFOR can also assume dissemination activities in a project such as press work or public relations.

Discussion & Conclusions: With its record budget, Horizon 2020 offers a great opportunity for ambitious researchers. However, the broad range of funding instruments makes an orientation sometimes difficult. Therefore, it is important to receive expert advice from an experienced partner like the Bavarian Research Alliance. With its Brussels office, BayFOR can also strengthen the visibility of the Bavarian universities and Universities of Applied Sciences on the European stage and functions as "door-opener" and contact to European institutions.

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[5] Future and Emerging Technologies
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Horizon 2020 with a focus on nanotechnology and advanced materials

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Keywords : Horizon 2020, NMP, nanotechnology, materials, manufacturing

Nanotechnology, Advanced Materials, Advanced Manufacturing and Processing Technologies (NMP) Theme

Introduction: NMP Theme is under the Horizon 2020 Program – Leadership in Enabling and Industrial Technologies Priority. NMP Theme indicative budget is around 3,5 Million EURO for 7 years.

NMP Theme 2014-2015 Work Programme covers totally 75 topics. The distribution of the topics according to corresponding fields is given below;

- 39 Topic for Nanotechnology and Materials
- 6 Topic for Biotechnology
- 14 Topic for Factories of the Future
- 8 Topic for Energy Efficient Buildings
- 8 Topic for Sustainable Process Industries and Resource Efficiency

The NMP Call for the years 2014-2015 is opened on 11 December 2013 and will be closed on different dates according to given deadlines

H2020-NMP-2014-two-stage
- 1st Stage:06.05.2014,2nd Stage: 07.10.2014

H2020-NMP-2015-two-stage
- 1st Stage:26.03.2015,2nd Stage: 08.09.2015

H2020-NMP-PILOTS-2014-2015
- 06.05.2014 – 26.03.2015

H2020-NMP-CSA-2015
- 06.05.2014

H2020-EeB-FoF-SPIRE-2015
- 09.12.2014

Discussion & Conclusions:

NMP Challenges

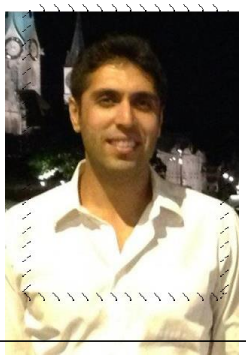
1. Bridging the gap between nanotechnology research and markets
2. Nanotechnology and Advanced Materials as enablers of applications in Health
3. Nanotechnology and Advanced Materials for low carbon energy technologies and Energy Efficiency
4. Tapping into the cross-sector potential of Nanotechnologies and Advanced materials to drive competitiveness and sustainability
5. Safety of nanotechnology-based applications and support for the development of regulation
6. Addressing generic needs in support of governance, standards, models and structuring in nanotechnology, advanced materials and production.

NMP Public Private Partnerships (PPPs):

1. Factories of The Future
2. Energy Efficient Buildings
3. Sustainable Process Industry and Resource Efficiency
4. Green Vehicles

POSTER PRESENTATIONS

Single particle loading and dispensing system



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Keywords: On-chip robotics, micro-nano robotics, Lab-on-a-chip systems

In this paper, on-chip particle loading and dispensing modules are presented with their results for the automation of a single particle retrieving from a microfluidic channel. Our proposed microfluidic chip has several modules. Each one of them has key functions as (a) loading micro-particles singly to main microfluidic flow by the aid of magnetically driven microtools (MMT); (b) finding particle position in a microfluidic channel by micro-capacitance sensors; (c) adjusting micro-channel height locally by pneumatic pressure valve; (d) dispensing particles out from the microfluidic chip to incubation environment. Novelty of this paper is summarized as follows: (1) Multi-photoresist combination technique for the pneumatic pressure valve; (2) Automatic on-chip particle dispensing with micro-capacitance sensors. We showed feasibility of automatic dispensing of a single polystyrene bead (about 100 µm) from the chip to atmosphere. The performances of each module (hybrid structure, sensor and dispensing parts) were evaluated individually. We succeeded in determination of the movement of micro-particles (about 50-100 µm) with the velocity of over 6 mm/sec. by the micro-capacitance sensors. The advantages of the proposed system are that composed of the reusable drive system such as xy-motorized stage, pumps and a disposable microfluidic chip

Introduction

Hydrogen in the biomedical field, automation of bio-manipulation by non-contact actuation is demanded using a disposable PDMS chip. Conventional PDMS disposable microfluidic chip have many functions such as loading, cutting and so on [1-3]. By using the PDMS disposable chips, on-chip particle manipulation has been studied with 3D magnetic particle loader to supply single particles [4].

However limited study is available on retrieving particles after they are manipulated on a chip. It is important to transport the particles that are continuously manipulated from the microfluidic chip to the incubation atmosphere. Generally it is ideal to inject particles immediately after the operation on the chip. Therefore automation system (the chip-world interface) of supplying particles from the microfluidic chip to the incubation atmosphere is highly required. The concept design of the entire system is illustrated in Figure 1.

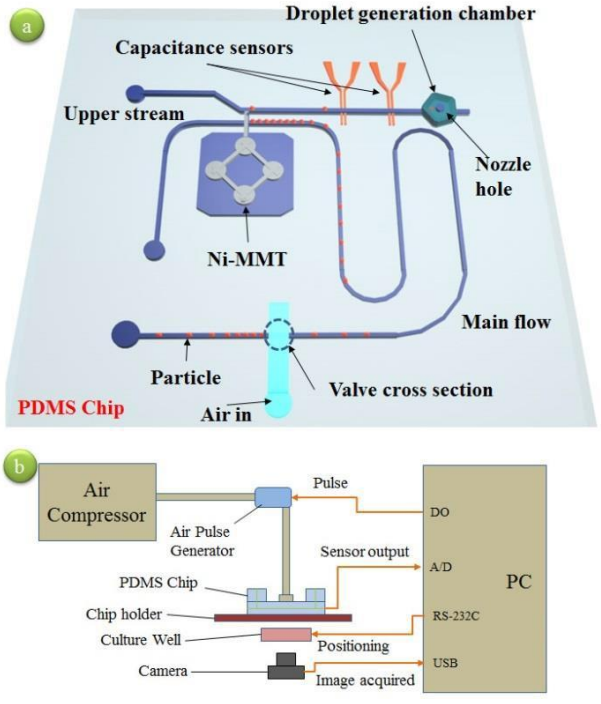

Figure 1, (a) Concept view of microfluidic particle loading and dispensing chip (b) Experimental system's components

The MMT particle loader is a non-contact magnetic loader module to manipulate particles in a microfluidic channel. It is capable to load micro- particles one-by-one by using its hook shape handles while moving up and down. Magnetic actuator located outside of the microfluidic chip controls it. Micro-controller control system accompanied by ultrasonic piezo vibrator drives magnets attached on a micro-stage [5]. The particle loader (Fig.1-A Ni- MMT), moves up and down, is controlled by magnet motion, which is laid under a glass substrate.

Conclusion

We successfully integrated magnetically driven particle loader onto a microfluidic chip. It has a vital importance to supply micro-particles to microfluidic channel one-by-one for different on-chip experiments. Two capacitance sensors were fabricated and synchronized with particle dispensing module. The sensing data was used to determine exact air-pulse generation in order to activate inkjet mechanism. The on-chip particle loading and dispensing immediately after an operation bring a significant advantage for the biomedical area. This system can be a breakthrough of a high throughput of accurate and effective particle manipulations in the field of cell culturing on a single particle. Even though we successfully achieved particle dispensing with current system, our future efforts will focus on that increasing the success ratio and load 100 or more particles singly to dispensing channel and automatically dispensing them.

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New applications of FTIR spectroscopy for process control and process development

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Keywords: FTIR-Spectroscopy, IR-transparent micro-reactors, multiphase-systems, biocatalysis

Infrared spectroscopy is a powerful method for qualitative and quantitative determination of substances. Infrared radiation causes molecular vibrations, the resulting absorption spectra give information about the molecular structure and the concentration. This enables online process control of biotransformations, even in multiphase reaction systems.

Materials & Methods:
Spectroscopy: Bruker Matrix-MF and Mettler Toledo React IR 45m with attenuated total reflectance and transmission.

IR-transparent microreactor: Plasma etched wafers. Technique: Eutectic bonding with a gold nanolayer.

Results & Discussion:
Due to the relatively high absorbance of samples in the mid-infrared range, a layer thickness of a few micrometer is required, hampering sample preparation. The limited applicability was extended by microsystem technology, e.g. IR-transparent microreactors and microtiter plates, which have been produced according to the experimental set-up [1].

Determination of substrate specificity, reaction parameters and enzyme kinetics were successfully carried out.
However beside the usage of the IR-transparent microreactor, even multiphase systems on industrial scale were monitored with a single probe [2,3]. By the use of Attenuated Total Reflectance (ATR) in combination with chemometrics, quantitative inline determination of all reactants was carried out simultaneously.

Conclusions:
In process development, local determination of characteristic key parameters is possible, e.g. mass transport coefficients of CO_2 in bubble columns or residence time distributions by means of IR-active tracers. The local determination of parameters creates new possibilities for the development and validation of scale independent models.

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A disposable instrument for molecular genetic analysis

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Keywords: molecular IVD, microfluidics, Real time PCR

Introduction: With adaptation of the microfluidics technology to the area of medical devices, a new era towards rapid, portable and affordable point of care (POC) analysis instruments has started. In here, we are presenting the ongoing RnD studies for developing a disposable instrument for molecular diagnostics.

Materials & Methods: In this study, a credit card sized disposable cartridge recruiting microfluidic fluid handling is developed for on board DNA analysis from full blood samples.

Blood sample is introduced and sealed to the cartridge which is designed to have all necessary reagents prefilled prior to use. Than the cartridge is inserted into the dedicated electrical instrument for further analysis.

The cartridge is designed for single use only and has on board reagent pumping, adsorption DNA purification and real time PCR with the aid of the hot air thermal cycling and fluorometric measurement performed in the complementary electrical instrument. Fluid movement is acquired through valveless diffusion PZT benders for pumping and paraffin phase change valves used for irreversible gating.

Results & Discussion: This project has started in the second half of 2013. Theoretical design is completed and the study continues with verification of design studies through building the first functional prototype.

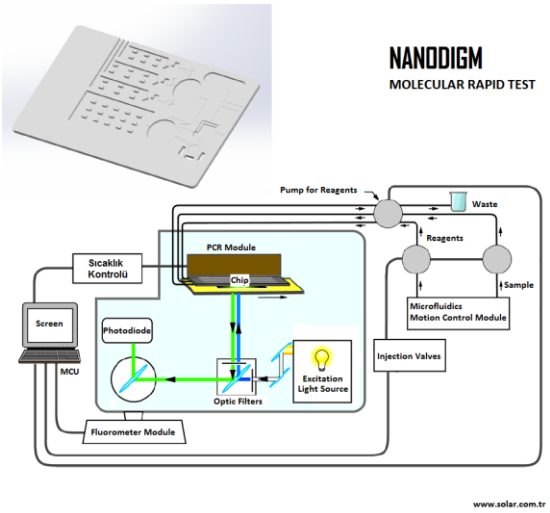

Fig. 1. The Design and Functional Schematic of the Disposable Instrument

Conclusions:

Developing POC devices using microfluidics technology will help to offer sensitive, rapid as well as low cost solutions for molecular IVD.

Acknowledgements: This project is supported by TUBITAK SME support program 1512/3

Sterilization requirements of microreactors fabricated by different materials

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Keywords : microreactor, sterilization, microfluidic device

Introduction: With advances in microreaction technology, microfabricated systems consist of multiple sub-millimeter channels in which fluid flows continuously and various bioprocesses can take place [1] including bioanalysis, pharmaceuticals, forensic and clinical applications [2]. Although sterility is required in most of the life science applications, contamination risk in microreactors is a significant limitation to realize these applications in aseptic conditions [3]. In medical practice the standard sterilization methods include steam, gamma-irradiation, ethylene oxide, and hydrogen peroxide sterilization. Each method has drawbacks in certain applications. Therefore, the sterilization of heat-sensitive or porous materials or devices poses a challenge to current technologies.

Materials & Methods: Sterilization techniques such as heat, UV, hydrogen peroxide and supercritical CO_2 are applied for sterilization of glass, metal and polymer microreactors (Fig. 1). The success of sterilization is determined by incubating the sterilized microreactors in tryptic soy broth (TSB) and thioglycollate broth (TGB) at two different temperatures. Furthermore, the sterilized microreactors are analyzed using Scanning Electron Microscope (SEM), differential scanning calorimetry (DSC) and Fourier Transform Infrared Spectroscopy (FTIR).

Fig. 1. Microreactors fabricated with PDMS and metal

Results & Discussion: After sterilization microreactors are incubated at 37^{o}C and 27 ^{o}C in TSB and TGB medium for 7 days.The applications are performed under steril conditions in order to assess the microbiological loads.

Conclusions: So far, heat and UV applications yielded promising results in terms of complete sterilization whereas a special emphasis should be on the property of the treated material. Especially, sterilization with heat seems to have an adverse effect on the characteristic of the material. Very interesting results were obtained using supercritical CO_2. Indeed, there has been a steady interest in using high-pressure carbon dioxide as a process medium for new sterilization technology. Among the potential advantages are that CO_2 may sterilize at low temperatures.

Acknowledgements: This project is supported by the Research Fund of Ege University.

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Dielectrophoretic microfluidics with 3D electrodes

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Keywords: Microfluidics, dielectrophoresis

Introduction: Bioparticle manipulation is required in wide variety of biomedical applications such as drug screening, disease detection and single cell analysis. Dielectrophoresis (DEP) is suitable method for bioparticles manipulation at micro scale. DEP is the movement of particles in a non-linear electrical field due to the interaction of the particle's dipole and spatial gradient of the electrical field. DEP can be utilized to discriminate and identify bioparticles from other particles or to detect and isolate diseased or damaged bioparticles without any need for labeling of bioparticles [1]. DEP have been successfully implement-ed for many biomedical applications like cells separation, trapping and lysis [1-3]. In order to use DEP for bioparticle separating microfluidics device with asymmetric pair of electrodes should be considered.

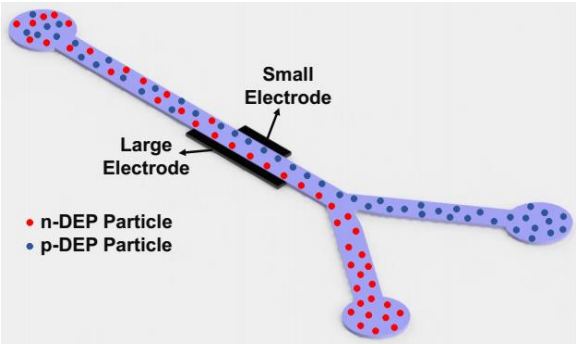

Fig. 1. Schematic of DEP based separation

Fig. 1 shows schematic of DEP device for biological applications. One major issue about the DEP-based microfluidic devices is the throughput. One way to increase the performance of the DEP-based separation and the impedance-based counting is to use 3D electrodes at the sidewalls which eliminates the fringe-like structure of the electric field lines.

DEP is the motion of particles within a non-uniform electric field due to interaction of the electrical field gradient with the dipole moment of the particle. Depending on the dielectric properties of the medium and the particle, DEP can be either in the direction of higher electric field gradient (positive-DEP, pDEP) or lower electrical field gradient (negative-DEP, nDEP).

In this study, to demonstrate effect of the 3D side wall electrodes, the particle trajectories of the particles are simulated by using COMSOL Multiphysics software for a DEP application with planar and 3D side-wall electrodes. In the simulation, the particle trajectory within a microchannel can be modeled by using point particle approach. In this approach, particle is

assumed to be a point-particle and the effect of the particle presence on the flow and electric field is ignored. To model the particle trajectory within the microchannel the flow filed and the electric field needs to be determined. In the simulations, is utilized. For the flow field, Navier-Stokes equations together with no-slip boundary condition at the channel wall, predefined flow rate at the channel inlet and zero pressure at the channel exit. For electric field, Laplace equation is solved together with insulated boundary condition at the channel wall, zero voltage at the small electrode and the predefined voltage at the larger electrode. Once the electric and flow field is obtained, the particle trajectories are obtained by using the streamline function of COMSOL by using COMSOL-MATLAB interface. To simulate the random distribution of the particle flow at the device inlet, the initial locations of the particles at the channel inlet are assigned randomly by using normal distribution function of MATLAB. 100 pDEP and 100 nDEP particles are released, and the number of particles collected in different outlet reservoirs is determined.

For the fabrication of the 3D side-wall electrodes, a hybrid approach which integrates the CNC-based mechanical machining with the lithography based technique is implemented. With this approach, 3D side-wall electrodes are fabricated in a robust and highly repeatable manner. Some preliminary experimental results regarding the manipulation of nDEP particles are also demonstrated. With such a robust fabrication technique, 3D side-wall electrodes have the potential to find more electrokinetic based applications with a better performance.

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Immobilization of β-glucosidase in silica sol-gel matrix

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Keywords: β-glucosidase, immobilization, sol-gel

Introduction: Immobilization techniques have long been used to improve enzyme activity and stability under some conditions such as high temperature, pH changes and organic solvents. Immobilization enzymes create important advantages such as providing opportunity for reusing and easy handling of enzymes. Silica based sol-gel technique is an efficient and versatile one that provides successful enzyme immobilization while preventing leaching of entrapped enzyme with a rigid polymer structure and allowing for high yields of immobilization and efficient diffusion with mesoporous structure and high pore volume [1]. In this study, immobilization of β-glucosidase in silica based sol-gel matrix was achieved and activity of the immobilized enzyme was investigated in comparison to the free enzyme.

Methods: Two step sol-gel process was achieved according to the procedure which was described by Ferrer et al., 2002. Sols were prepared by mixing vigorously 5.8 ml of tetraethoxysilane (TEOS), 1.9 ml of ultrapure water and 1 ml of HCl (0.1 M) at room temperature for one hour [2]. Following this step, buffered enzyme solution prepared at different pH values (4.5, 5.5, 6.5, and 7.5) and the sols were mixed at a ratio of 1:1. The effect of different pH values on gelation time was investigated. β-glucosidase activity assay [3] was applied to determine the activity of β-glucosidase in TEOS-based mesoporous gel.

Results: It was determined that pH of the buffer solution decreased gelation time drastically. Duration of gelation varied 2 days, 3 hours, 30 minutes and 3 minutes when pH values were adjusted as 4.5, 5.5, 6.5 and 7.5 respectively. β-glucosidase activity was expressed as unit where one unit was defined as the amount of enzyme releasing 1 mg of reducing sugar in one minute. Activity of immobilized enzyme was determined as **0.125 units** while free enzyme activity was **0.166 units**, so the residual activity of sol-gel immobilized enzyme was found as **75 %.**

Discussion & Conclusion: As a conclusion, immobilization of enzyme in pores of silica sol-gel matrix is accepted as a good strategy in order to protect catalytic activity and stability of enzymes. In this study, it was shown that immobilized β-glucosidase could be used in bio catalytic reactions for different applications [4]. This study constitutes the first step in developing enzymatic microreactors including immobilized enzymes in microchannels conduct biocatalytic reactions.

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