Report for the Support of "Colloidal Quantum Dots/Nanocrystals for Biomedical Applications VI" in January 2011 in San Francisco, CA, USA

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1) Summary (up to 1 page)

Ongoing rapid progress in the synthesis of a variety of biofunctionalized colloidal nanocrystals with fascinating electronic, magnetic, and optical properties not associated with bulk materials symbolizes a fundamental breakthrough in physics and chemistry of condensed matter, which significantly extends our knowledge about the nature of materials and our abilities to manipulate their properties. Inorganic nanostructures that interface with biological systems are attracting an increasingly widespread interest in biology and medicine. Quantum dot intravascular probes can be used in a remarkable number of biomedical applications, such as highly specific markers for cellular microscopy, flow cytometry, DNA and protein chips, immunoassays for diagnostics, histology, cancer detection, in situ hybridization, PCR DNA detection, biochemical and cell-based drug screening, single molecule studies, and correlation spectroscopy. There are abundant opportunities for improved or completely novel probes and seemingly endless new applications. This conference will consider biomedical applications of colloidal nanocrystals, as well as recent advances in new materials and methods of synthesis, coating, and bioconjugation. Its objective is to provide a widely interdisciplinary forum for practicing clinicians, biomedical scientists, development engineers, physicists, and chemists specializing in different fields to benefit from each other's expert knowledge and to create trend-setting interdisciplinary links that will accelerate progress in this field. The conference will deal with biological applications of colloidal nanoparticles in general. Important classes of nanoparticles involve quantum dots for labeling, metallic nanoparticles for plasmonics, and magnetic nanoparticles. Emphasis will be given on application of these nanoparticles in the field of biology.

Several sessions have been exclusively related only to Au Nanoparticles and their application

2) Description of the scientific content of and discussion at the event

Previously unpublished experimental and theoretical papers are solicited on the following and related topics:

- synthesis of colloidal nanocrystals such as II-VI, I-VII, III-V, and group-IV semiconductor quantum dots; ternary compounds; core-shell nanocrystals; nano-onions; nanoshells; **metal nanocrystals**; magnetic nanocrystals; shape and size control; assembly of nanocrystals to bigger particles

- bioconjugation and biolabeling; bioconjugate chemistry; dendron ligands; thiol and oligonucleotide coatings; phospholipid micelles; biotin/avidin; sticky polymers; targeting peptides; target specificity

- measurement techniques; microscopy (AFM, SFM, STM, TEM, HRTEM, SNOM); XRD; spectroscopy (FTIR, EELS, ICP, DFS); spectroscopy of single quantum dots; multiphoton spectroscopy; frequency upconversion; magnetic sensing and imaging; plasmon spectroscopy

- physics and characterization of colloidal nanocrystals; electronic structure, band alignment; dielectric screening; optical, electronic, and magnetic properties; excitons and biexcitons; quantum efficiency; intraband transitions; spin dynamics; blinking mechanisms, surface-enhanced Raman spectroscopy; plasmons

- theoretical and experimental studies of interactions with surrounding ambient, including dynamics and electronic structures

- numerical modeling; multiscale modeling; density functional modeling; molecular dynamics; Brownian dynamics; quantum Monte Carlo simulations

- biomolecular sensing; FRET; molecular interactions

- biocompatibility; development of non-toxic nanocrystals; intracellular behavior; long-term effects

- biological applications of colloidal nanocrystals; in vitro and in vivo imaging; biology at molecular level; receptor-ligand interactions; protein folding/unfolding; DNA conjugation, sequencing, and assembly; cell motility; gene expression mutation, etc.

- medical applications of colloidal nanocrystals; immuno-fluorescent assays; applications in neuroscience; drug delivery and screening; cancer diagnostics and therapy; screening; cancer diagnostics and therapy; biomechanics; etc.

Several sessions have been exclusively related only to Au Nanoparticles and their application:

Session 5: Plasmonics I

Date: Saturday 22 January

Time: 4:35 PM - 5:45 PM

Session Chair: Stefan A. Maier, Imperial College London (United Kingdom)

Session 10: Plasmonics II

Date: Sunday 23 January

Time: 4:20 PM - 5:30 PM

Session Chair: Jochen Feldmann, Ludwig-Maximilians-Univ. München (Germany)

A more detailed view about the scientific presentations is given in the attached abstracts

3) Assessment of the results and impact of the event on the future direction of the field (up to 2 pages)

The European Science Foundation Reception was very helpful in bringing together people working on related topics and to stimulate cooperation. Prof. Dr. Stefan Maier introduced the ESP program in a short speech. His presentation as well as the one of Prof. Dr. Jochen Feldmann were the highlights of the plasmonics sessions. However, the meeting was also very important for researchers working on related fields. We had contributions of Dr. Martin Clift and Dr. Antonios Kanaras who were reporting about toxicity of gold nanoparticles. In this way people coming from different communities were brought together. The meeting resulted in planned cooperation. For example the group of Prof. Parak (the organizer) will start a cooperation with the group of Prof. Stefan Maier about plasmonic coupling between 2 Au nanoparticles. Both groups did not know each other personally before and in this way the European Science Foundation Reception helped to stimulate new research.

4) Final program of the meeting

The final program is attached. The announcement for the European Science Foundation Reception is given on page 2 of the program. In addition all scientific abstracts as presented on the meeting are attached.

Colloidal Quantum Dots/Nanocrystals for Biomedical Applications VI

Conference Chairs: **Wolfgang J. Parak,** Philipps-Univ. Marburg (Germany); **Kenji Yamamoto,** International Medical Ctr. of Japan (Japan); **Marek Osiński,** The Univ. of New Mexico

Program Committee: **Antigoni Alexandrou,** Ecole Polytechnique (France); **Moungi G. Bawendi,** Massachusetts Institute of Technology; **Maxime Dahan,** Lab. Kastler Brossel (France); **Jesus Martinez de la Fuente,** Univ. de Zaragoza (Spain); **Niko Hildebrandt,** Fraunhofer-Institut für Angewandte Polymerforschung (Germany); **Jennifer A. Hollingsworth,** Los Alamos National Lab.; **Thomas M. Jovin,** Max-Planck-Institut für biophysikalische Chemie (Germany); **Hedi Mattoussi,** The Florida State Univ.; **Paul Mulvaney,** The Univ. of Melbourne (Australia); Jay L. Nadeau, McGill Univ. (Canada); **Shuming Nie,** Emory Univ.; **Tania Q. Vu,** Oregon Health & Science Univ.; **Horst Weller,** Univ. Hamburg (Germany); **Michael S. Wong,** Rice Univ.

Saturday 22 January

Introduction

Room: 232 (Mezzanine). . . . . Sat. 8:25 to 8:30 am

Session Chair: **Wolfgang J. Parak,** Philipps-Univ. Marburg (Germany)

SESSION 1

Room: 232 (Mezzanine). . . . . Sat. 8:30 to 10:00 am

Properties of Quantum Dots

Session Chair: **Marek Osiński,** The Univ. of New Mexico

8:30 am: **Dithiocarbamates as capping ligands for water-soluble quantum dots** (Invited Paper), Aaron R. Clapp, Yanjie Zhang, Iowa State Univ. (USA) . . . . . [7909-01]

9:00 am: **Synthesis, properties, and applications of complex nanocrystal heterostructures,** Liberato Manna, Univ. del Salento (Italy) . . . . . [7909-02]

9:20 am: **Size determination of quantum dots with fluorescence correlation spectroscopy,** Diana Hill, Hans-Gerd Löhmannsröben, Univ. Potsdam (Germany); Ali Zulqurnain, Wolfgang J. Parak, Philipps-Univ. Marburg (Germany); Niko Hildebrandt, Cindy Ast, Fraunhofer-Institut für Angewandte Polymerforschung (Germany) . . . . . [7909-03]

9:40 am: **Engineered nanocrystals for imaging, sensing and therapeutics,** Ming-Yong Han, A*STAR Institute of Materials Research and Engineering (Singapore) . . . . . [7909-04]

DISCUSSION. . . . . Sat. 10:00 to 10:15 am

Coffee Break . . . . . 10:15 to 11:00 am

SESSION 2

Room: Room 232 (Mezzanine) . . . . . Sat. 11:00 to 11:40 am

NPs for Diagnosis and Treatment I

Session Chair: **María Valeria Grazú Bonavía,** Univ. de Zaragoza (Spain)

11:00 am: **Facile synthesis of FePt nanoparticles for CT/MRI dual-modal molecular targeting imaging contrast agents,** Chia-Chun Chen, National Taiwan Normal Univ. (Taiwan). . . . . [7909-07]

11:20 am: **Size and surface chemistry of Au nanoparticles determine doxorubicin cytotoxicity,** Jay L. Nadeau, Hicham Chibli, Xuan Zhang, McGill Univ. (Canada). . . . . [7909-51]

DISCUSSION. . . . . Sat. 11:40 to 11:55 am

Lunch/Exhibition Break . . . . . 11:55 am to 1:25 pm

SESSION 3

Room: 232 (Mezzanine). . . . . Sat. 1:25 to 2:35 pm

Toxicity of NPs

Session Chair: **Pilar Rivera Gil,** Philipps-Univ. Marburg (Germany)

1:25 pm: **State-of-the-art toxicological and microscopic assessment of biomedical nanocrystals on the lung in vitro** *(Invited Paper)*, Martin J. D. Clift, Peter Gehr, Barbara Rothen-Rutishauser, Univ. Bern (Switzerland). . . [7909-08]

1:55 pm: **Size- and structure-dependent toxicity of silica particulates,** Sanshiro Hanada, Kenichi Miyaoi, Akiyoshi Hoshino, Kenji Yamamoto M.D., International Medical Ctr. of Japan (Japan) . . . . . [7909-09]

2:05 pm: **Bridging the fields of nanoscience and toxicology: nanoparticle impact on biological models** *(Invited Paper),* Alfredo Ambrosone, Valentina Marchesano, Lucia Mattera, Angela Tino, Claudia Tortiglione, Istituto di Cibernetica Eduardo Caianiello (Italy) . . . . . [7909-10]

DISCUSSION. . . . . Sat. 2:35 to 2:40 pm

SESSION 4

Room: 232 (Mezzanine). . . . . Sat. 2:40 to 4:20 pm

Fluorescence, FRET, and Applications I

Session Chair: **Peter Reiss,**
Commissariat à l'Énergie Atomique (France)

2:40 pm: **Multiplexed solid-phase nucleic acid hybridization assays using semiconductor quantum dots as donors in fluorescence resonance energy transfer (FRET)** *(Invited Paper),* W. Russ Algar, Ulrich J. Krull, Univ. of Toronto Mississauga (Canada) . . . . . [7909-11]

3:10 pm: **Time-resolved and steady-state FRET spectroscopy on commercial biocompatible quantum dots,** David Wegner, Daniel Geissler, Hans-Gerd Löhmannsröben, Univ. Potsdam (Germany); Niko Hildebrandt, Fraunhofer-Institut für Angewandte Polymerforschung (Germany) . . . [7909-12]

Coffee Break . . . . . 3:30 to 4:00 pm

4:00 pm: **Time-correlated hyperspectral studies of biexciton characteristics in dimeric colloidal quantum dots under photo-oxidation,** Jeeseong Hwang, HyeongGon Kang, Matthew L. Clarke, National Institute of Standards and Technology (USA); Silvia H. DePaoli Lacaerda, U.S. Food and Drug Administration (USA); Leonard F. Pease III, The Univ. of Utah (USA). . [7909-13]

DISCUSSION. . . . . Sat. 4:20 to 4:35 pm

SESSION 5

Room: Room 232 (Mezzanine) . . . . . Sat. 4:35 to 5:55 pm

Plasmonics I

Session Chair: **Stefan A. Maier,**
Imperial College London (United Kingdom)

4:35 pm: **An optical nanoparticle gun** *(Invited Paper),* Jochen Feldmann, Ludwig-Maximilians-Univ. München (Germany) . . . . . [7909-14]

5:05 pm: **Localized surface plasmon properties of Au nanorings and their diffusion in biotissue,** Cheng-Kuang Lee, Shou-Yen Wu, Hung-Yu Tseng, Ting-Ta Chi, Kai-Min Yang, Jyh-Yang Wang, National Taiwan Univ. (Taiwan); Meng-Tsan Tsai, Chang Gung Univ. (Taiwan); Yean-Woei Kiang, Chih-Chung Yang, National Taiwan Univ. (Taiwan) . . . . . [7909-15]

5:25 pm: **Nanoscale plasmonic resonators with high Purcell factor: spontaneous and stimulated emission** *(Invited Paper),* Ewa M. Goldys, Macquarie Univ. (Australia) . . . . . [7909-16]

DISCUSSION . . . . . Sat. 5:55 to 6:10 pm

BiOS Hot Topics

Room: 134 (Exhibit Level) . . . . . Sat. 7:00 to 9:00 pm

Come hear 10-minute presentations by some of the brightest leaders in biophotonics.

See page 16 for details.

European Science Foundation Reception

Sat. 9:00 to 11:00 pm

Conference Reception Sponsored by

Open to attendees of Conferenece 7909. Location to be announced by chair.

The ESF network "New approaches to biochemical sensing with plasmonic nanobiophotonics" (PLASMON-BIONANOSENSE) is an open grouping of major European research groups in the areas of photonic and biomolecular nanoscience. The network is open for outside participation and funds both staff exchanges and conferences/workshops. More details can be found on **http://www.esf.org/plasmon**.

Sunday 23 January

SESSION 6

Room: 232 (Mezzanine) . . . . . Sun. 8:10 to 9:50 am

NPs for Diagnosis and Treatment II

Session Chair: **Kenji Yamamoto,**
Inetrnational Medical Ctr. of Japan (Japan)

8:10 am: **Magnetic supracolloidal assemblies for biophysical applications** *(Invited Paper),* J.-F. Berret, Univ. Paris 7-Denis Diderot (France) . . . . [7909-17]

8:40 am: **Gold nanoparticles in biomedical applications** *(Invited Paper),* Antonios G. Kanaras, Dorota Bartczak, Otto L. Muskens, Timothy M. Millar, Tilman Sanchez-Elsner, Univ. of Southampton (United Kingdom) . . . . [7909-18]

9:10 am: **Alloy metal nanoparticles for multicolor cancer diagnostics,** Pedro V. Baptista, Gonçalo Doria, João Conde, Univ. Nova de Lisboa (Portugal) . . . . . [7909-19]

9:30 am: **Locally increased mortality of gamma-irradiated cells in presence of lanthanide-halide nanoparticles,** Nathan J. Withers, John B. Plumley, Amber McBride, Brian A. Akins, Antonio C. Rivera, Nathaniel C. Cook, Gennady A. Smolyakov, Graham S. Timmins, Marek Osinski, The Univ. of New Mexico (USA) . . . . . [7909-20]

Coffee Break . . . . . 9:50 to 10:20 am

SESSION 7

Room: 232 (Mezzanine). . . . . Sun. 10:20 to 11:40 am

Imaging with NPs

Session Chair: **Walter H. Chang,** Chung Yuan Christian Univ. (Taiwan)

10:20 am: **Multifunctional fluorescent nanoparticles for biomedical applications** *(Invited Paper, Presentation Only),* Subramanian T. Selvan, A*STAR Institute of Materials Research and Engineering (Singapore) . [7909-21]

10:50 am: **Imaging heterostructured quantum dots in cultured cells with epifluorescence and transmission electron microscopy,** Erin M. Rivera, Casilda Trujillo Provencio, New Mexico State Univ. (USA); Andrea Steinbrueck, Pawan Rastogi, Allison M. Dennis, Jennifer A. Hollingsworth, Los Alamos National Lab. (USA) and Center for Integrated Nanotechnologies (USA); Elba Serrano, New Mexico State Univ. (USA) and Center for Integrated Nanotechnologies (USA) . . . . . [7909-22]

11:00 am: **In-vivo multiplexed optical imaging system with near-infrared emitting quantum dots and lanthanide-doped nanoparticles,** Sanghwa Jeong, Nayoun Won, Kangwook Kim, Joonhyuck Park, Sungjee Kim, Pohang Univ. of Science and Technology (Korea, Republic of). . . . . [7909-23]

11:10 am: **Synthesis of 'non-toxic' quantum dots and the in-vivo imaging applications thereof,** Youngrong Park, Jiwon Bang, Nayoun Won, Sanghwa Jeong, Kangwook Kim, Sungjee Kim, Pohang Univ. of Science and Technology (Korea, Republic of). . . . . [7909-24]

11:20 am: **Near-infrared quantum dots for in-vivo real-time multiplexed imaging applications,** Nayoun Won, Sanghwa Jeong, Kangwook Kim, Joonhyuck Park, Sungjee Kim, Pohang Univ. of Science and Technology (Korea, Republic of) . . . . . [7909-25]

DISCUSSION . . . . . Sun. 11:40 to 11:55 am

Lunch/Exhibition Break . . . . . 11:55 am to 1:20 pm

SESSION 8

Room: 232 (Mezzanine). . . . . Sun. 1:20 to 2:40 pm

Fluorescence, FRET, and Applications II

Session Chair: **Ulrich J. Krull,** Univ. of Toronto Mississauga (Canada)

1:20 pm: **Characterizing FRET in quantum dot-sensitized multivalent DNA photonic wires,** Kelly Boeneman, Duane E. Prasuhn, U.S. Naval Research Lab. (USA); Juan B. Blanco-Canosa, Philip E. Dawson, The Scripps Research Institute (USA); Joseph S. Melinger, Michael H. Stewart, Kimihiro Susumu, Alan L. Huston, Igor L. Medintz, U.S. Naval Research Lab. (USA) . . . . . [7909-26]

1:40 pm: **Quantum dots as FRET acceptors: multiplexing biosensors for in-vitro diagnostics and molecular ruler applications** *(Invited Paper),* Daniel Geißler, Univ. Potsdam (Germany); Frank Morgner, Fraunhofer-Institut für Angewandte Polymerforschung (Germany); Nathaniel G. Butlin, Lumiphore Inc. (USA); Hans-Gerd Löhmannsröben, Univ. Potsdam (Germany); Niko Hildebrandt, Fraunhofer-Institut für Angewandte Polymerforschung (Germany) . . . . . [7909-27]

2:10 pm: **Nanoprobes of fluorescent gold nanoclusters for cells labeling,** Walter H. Chang, Wan-Chun Yu, Cheng-An Lin, Wen-Hsiung Chan, Ji-Lin Shen, Chung Yuan Christian Univ. (Taiwan); Hung-I Yeh, Hsueh-Hsiao Wang, Mackay Memorial Hospital (Taiwan) . . . . . [7909-28]

2:20 pm: **Quantum dot-based time-resolved adhesion assay for cell co-cultures,** Pilar Rivera Gil, Wolfgang J. Parak, Fang Yang, Philipps-Univ. Marburg (Germany); Heidi Thomas, Andreas Terfort, Johann Wolfgang Goethe-Univ. Frankfurt am Main (Germany). . . . . [7909-29]

DISCUSSION . . . . . Sun. 2:40 to 2:55 pm

SESSION 9

Room: 232 (Mezzanine). . . . . Sun. 2:55 to 4:15 pm

Functionalization of NPs and Applications

Session Chair: **Subramanian Tamil Selvan,** A*STAR Institute of Materials Research and Engineering (Singapore)

2:55 pm: **Getting control in the antibody-nanoparticle stoichiometry,** María Valeria Grazú Bonavía, Ester Polo, Pilar Pina, Jesús Santamaría, Jesus M. de la Fuente, Univ. de Zaragoza (Spain) . . . . . [7909-31]

Coffee Break . . . . . 3:15 to 3:45 pm

3:45 pm: **Immobilized quantum dot bioprobes: microfluidics for the development of nucleic acid assays and bioconjugate assemblies** *(Invited Paper),* Ulrich J. Krull, Anthony J. Tavares, Lu Chen, W. Russ Algar, Univ. of Toronto Mississauga (Canada) . . . . . [7909-32]

DISCUSSION . . . . . Sun. 4:15 to 4:20 pm

SESSION 10

Room: 232 (Mezzanine). . . . . Sun. 4:20 to 5:40 pm

Plasmonics II

Session Chair: **Jochen Feldmann,** Ludwig-Maximilians-Univ. München (Germany)

4:20 pm: **Plasmonic nanostructures: new design methodologies and high-resolution mode imaging for applications in nanobiophotonics** *(Invited Paper),* Stefan A. Maier, Imperial College London (United Kingdom) . . . . . [7909-33]

4:50 pm: **Plasmonic Ag/SiO_2 composite nanoparticles doped with a europium chelate and their metal enhanced fluorescence,** Wei Deng, Krystyna Drozdowicz-Tomsia, Dayong Jin, Ewa M. Goldys, Macquarie Univ. (Australia); Jingli Yuan, Dalian Univ. of Technology (China) . . . . . [7909-34]

5:00 pm: **Ion sensing with colloidal nanoparticles,** Wolfgang J. Parak, Philipps-Univ. Marburg (Germany) . . . . . [7909-35]

5:10 pm: **Diagnosis and imaging with SERS encoded particles** *(Invited Paper),* Ramon A. Alvarez-Puebla, Univ. de Vigo (Spain) . . . . . [7909-36]

DISCUSSION . . . . . Sun. 5:40 to 5:55 pm

Monday 24 January

SESSION 11

Room: 232 (Mezzanine). . . . . Mon. 8:00 to 9:30 am

Delivery and Uptake of NPs

Session Chair: **Ming-Yong Han,** A*STAR Institute of Materials Research and Engineering (Singapore)

8:00 am: **Quantum dots and metal nanoparticle agents for manipulating cellular trafficking** *(Invited Paper),* Geoffrey F. Strouse, The Florida State Univ. (USA) . . . . . [7909-37]

8:30 am: **Distribution of quantum dots after intraperitoneal administration, with reference to area-specific distribution in the brain** *(Invited Paper),* Shinji Fushiki M.D., Kyoko Itoh M.D., Shingo Kato, Takeshi Yaoi, Masafumi Umekage, Takenori Tozawa, Kyoto Prefectural Univ. of Medicine (Japan); Yutaka Yoshikawa, Hiroyuki Yasui, Kyoto Pharmaceutical Univ. (Japan); Akiyoshi Hoshino, Noriyoshi Manabe, Kenji Yamamoto M.D., International Medical Ctr. of Japan (Japan) . . . . . [7909-38]

9:00 am: **Peptide-mediated cellular delivery and endosomal escape of quantum dots** *(Invited Paper),* Kelly Boeneman, James B. Delehanty III, Michael H. Stewart, Kimihiro Susumu, U.S. Naval Research Lab. (USA); Juan B. Blanco-Canosa, Philip E. Dawson, The Scripps Research Institute (USA); Igor L. Medintz, U.S. Naval Research Lab. (USA) . . . . . [7909-39]

SESSION 12

Room: 232 (Mezzanine). . . . . Mon. 9:30 to 11:50 am

Synthesis of NPs

Session Chair: **Horst Weller,** Univ. Hamburg (Germany)

9:30 am: **Carbon nanotubes/inorganic hybrid materials: synthetic approach and applications** *(Invited Paper),* Miguel A. Correa-Duarte, Univ. de Vigo (Spain) . . . . . [7909-40]

10:00 am: **Novel synthesis of gold asymmetric nanocrystals: molecular heaters** *(Invited Paper),* Pablo del Pino, Beatriz Pelaz, Jesus M. de la Fuente, Univ. de Zaragoza (Spain) . . . . . [7909-42]

Coffee Break . . . . . 10:30 to 11:00 am

11:00 am: **Synthesis of NaYF4:Yb^{3+}/Er^{3+} upconverting nanoparticles in a capillary based continuous-flow microfluidic reaction system,** Haichun Liu, Ola Jakobsson, Can T. Xu, Lund Univ. (Sweden); Haiyan Xie, Lund Univ. Hospital (Sweden); Thomas Laurell, Stefan Andersson-Engels, Lund Univ. (Sweden) . . . . . [7909-53]

11:20 am: **From inorganic nanocrystals towards their assembly in polymeric mesoscale structures designed for biological applications** *(Invited Paper),* Teresa Pellegrino, National Nanotechnology Lab. (Italy). . . . . [7909-54]

DISCUSSION . . . . . Mon. 11:50 am to 12:05 pm

Lunch Break . . . . . 12:05 to 1:10 pm

Ocean Optics Young Investigator Award

Mon. 1:10 to 1:20 pm

Ocean Optics Young Investigator Award will be given for the best paper presented by a leading author who is either a graduate student or has graduated within less than five years of the paper submission date. The award consists of a $1,000 cash prize to the Young Investigator and $1,000 Ocean Optics equipment credit to the laboratory where the work was performed.

Sponsored by

SESSION 13

Room: 232 (Mezzanine). . . . . Mon. 1:20 to 3:10 pm

Synthesis of Quantum Dots

Session Chair: **Liberato Manna,** Univ. del Salento (Italy)

1:20 pm: **Biocompatible nanoparticles for molecular imaging** *(Invited Paper),* Horst Weller, Univ. Hamburg (Germany) . . . . . [7909-52]

1:50 pm: **Indium phosphide-based core-shell quantum dots optimized for biological applications,** Allison M. Dennis, Andrea Steinbrueck, Jennifer A. Hollingsworth, Los Alamos National Lab. (USA) . . . . . [7909-41]

2:10 pm: **Compact and highly stable quantum dots through optimized aqueous phase transfer** *(Invited Paper),* Peter Reiss, Sudarsan Tamang, Gregory Beaune, Isabelle F. Texier-Nogues, Commissariat à l'Énergie Atomique (France) . . . . . [7909-44]

2:40 pm: **Microwaves and nanoparticles: from synthesis to imaging** *(Invited Paper),* Kenith E. Meissner, Texas A&M Univ. (USA); R. Majithiaa, Texas A&M Univ.; R. A. Brown, Swansea Univ.; Lihong V. Wang, Washington Univ. in St. Louis (USA); T. G. Maffeis, Swansea Univ. . . . . [7909-55]

DISCUSSION . . . . . Mon. 3:10 to 3:25 pm

POSTERS-Monday

Room: 103/104 (Exhibit Level) . . . . . Mon. 5:30 to 7:00 pm

Conference attendees are invited to attend the BiOS poster session on Monday evening. Come view the posters, enjoy light refreshments, ask questions, and network with colleagues in your field. Authors of poster papers will be present to answer questions concerning their papers. Attendees are required to wear their conference registration badges to the poster sessions. Poster authors, view poster presentation guidelines and set-up instructions on page 370.

Differential distribution of dopamine functionalized quantum rods in mouse, A. Guardascione, Istituto di Cibernetica CNR (Italy); A. Ragusa, National Nanotechnology Lab. CNR (Italy); M. Rimoli, R. Russo, Univ. Federico II (Italy); Claudia Tortiglione, Angela Tino, Istituto di Cibernetica CNR (Italy) . . . . . [7909-43]

Interactions between iron oxide nanoparticles and human lymphoblastoid cells studied by flow cytometry, M. Safi, Univ. Paris 7-Denis Diderot (France); V. Garnier-Thibaud, Univ. Pierre et Marie Curie (France); A. Galimard, M. Seigneuret, H. Conjeaud, J.-F. Berret, Univ. Paris 7-Denis Diderot (France) . . . . . [7909-50]

Tuesday 25 January

Nano/Biophotonics Program Track Plenary Session

Room: 306 (Esplande) . . . . . Tues. 1:30 to 3:00 pm

Optical biosensors and a perspective on the future
Dr. Frances S. Ligler, Center for Bio/Molecular Science & Engineering, Naval Research Lab.

Nanostructures for biological investigations
Prof. Harold G. Craighead, School of Applied & Engineering Physics, Cornell Univ.

See page 17 for details.

Conference 7909: Colloidal Quantum Dots/Nanocrystals for Biomedical Applications VI

Saturday-Monday 22-24 January 2011 • Part of Proceedings of SPIE Vol. 7909 Colloidal Quantum Dots/Nanocrystals for Biomedical Applications VI

7909-01, Session 1

Dithiocarbamates as capping ligands for water-soluble quantum dots

A. R. Clapp, Y. Zhang, Iowa State Univ. (United States)

We investigated the suitability of dithiocarbamate (DTC) species as capping ligands for colloidal quantum dots (QDs). DTC ligands are generated by reacting carbon disulfide (CS2) with primary or secondary amines on appropriate precursor molecules. A biphasic exchange procedure efficiently replaces the existing hydrophobic capping ligands on the QD surface with the newly formed DTCs. The reaction conversion is conveniently monitored by UV-vis absorption spectroscopy. Due to their inherent water solubility and variety of side chain functional groups, we used several amino acids as precursors in this reaction/exchange procedure. The performance of DTC-ligands, as evaluated by the preservation of luminescence and colloidal stability, varied widely among amino precursors. For the best DTC-ligand and QD combinations, the quantum yield of the water-soluble QDs rivaled that of the original hydrophobic-capped QDs dispersed in organic solvents. The mean density of DTC-ligands per nanocrystal was estimated through a mass balance calculation which suggested nearly complete coverage of the available nanocrystal surface. The accessibility of the QD surface was evaluated by self-assembly of His-tagged dye-labeled proteins and peptides using fluorescence resonance energy transfer. DTC-capped QDs were also exposed to cell cultures to evaluate their stability and potential use for biological applications. In general, DTC-capped QDs have many advantages over other water-soluble QD formulations and provide a flexible chemistry for controlling the QD surface functionalization.

7909-02, Session 1

Synthesis, properties, and applications of complex nanocrystal heterostructures

L. Manna, Univ. del Salento (Italy)

No abstract available

7909-03, Session 1

Size determination of quantum dots with fluorescence correlation spectroscopy

D. Hill, H. Löhmannsröben, Univ. Potsdam (Germany); A. Zulqurnain, W. J. Parak, Philipps-Univ. Marburg (Germany); N. Hildebrandt, C. Ast, Fraunhofer-Institut für Angewandte Polymerforschung (Germany)

Semiconductor quantum dots (QDs) are highly interesting fluorophores for all kinds of spectroscopic applications. Although their fluorescence properties are well investigated, accurate size determination of QDs is still a problem. TEM techniques can image the inorganic core/shell system of QDs, but size determination of polymer coated QDs is difficult. SEC (size exclusion chromatography) compares the QD size only with standard polymers and their sizes, and is therefore not easy to use on nanoparticles. As QDs are fluorescent, single molecule spectroscopy methods such as fluorescence correlation spectroscopy (FCS) can be used to determine QDs diffusion coefficients and hence their hydrodynamic radii. Moreover, this method for size determination requires only very low concentrations of quantum dots which is a mayor advantage compared to other techniques such as dynamic light scattering.

Within our contribution we present the size determination of commercially available and self-modified QDs and other fluorescent nanoparticles with FCS. The commercial QDs (QD525, QD565, QD605, QD655 and QD705 - purchased from Invitrogen Inc.) have a rather thick polymer shell and are functionalized with either streptavidin, biotin or carboxylic groups. The self-modified QDs consist of the same commercial core/shell QDs and are modified with a polymer shell and several bio-functionalization groups. Furthermore, FePt nanoparticles doped with fluorescent dyes are used for reference measurements.

For all nanoparticles the diffusion coefficients were measured by FCS and the hydrodynamic radii were calculated according to the Stokes-Einstein equation. The obtained results are in good agreement with the size information provided by Invitrogen Inc. which demonstrates that FCS is an important technique for QD size determination at very low concentrations.

7909-04, Session 1

Engineered nanocrystals for imaging, sensing and therapeutics

M. Han, A*STAR Institute of Materials Research and Engineering (Singapore)

Colloidal semiconductor nanocrystals have attracted great attention for their distinguished roles in fundamental studies and technical applications such as biological labeling and optoelectronic devices. In addition to the size-tunable binary or core-shell nanocrystals with different emission colors, great efforts have also been put to develop highly luminescent composition-tunable quantum dots across the whole visible spectrum. Surface-engineered nanocrystals have been used as multifunctional biological nanoprobes for imaging, sensing, diagnostics, controlled release, targeted delivery and therapeutic applications. For example, the photoluminescence of molecularly engineered non-fluorescent quantum dots with iron(III) dithiocarbamates was selectively switched on by nitric oxide from OFF to ON state through controlled energy-transfer process. Such a “turn on” rather than conventional “turn off” mechanism can be used for sensing nitric oxide, which has been found to be synthesized in mammalian cells and triggered an extraordinary impetus for scientific research in all the fields of biology and medicine.

7909-07, Session 2

Facile synthesis of FePt nanoparticles for CT/MRI dual-modal molecular targeting imaging contrast agents

C. Chen, National Taiwan Normal Univ. (Taiwan)

This research explored the potential for using FePt nanoparticles as dual contrast property in combined X-ray computed tomography (CT) and magnetic resonance imaging (MRI). We applied water-solvable FePt nanoparticles of 3, 6 and 12 nm in diameter (3 nm-, 6 nm- and

12 nm-FePt) as a dual modality contrast agent for CT/MRI molecular imaging. The cytotoxicity and hemolysis examinations revealed that FePt nanoparticles were excellent in the biocompatibility and hemocompatibility. The bio-distribution analysis showed the highest serum concentration and circulation half-life for 12 nm-FePt, followed by 6 nm-FePt then 3 nm-FePt. Thus, the 3 nm-FePt showed higher brain concentrations. Then, the amounts of FePt nanoparticles in major organs were very sparse after 168hr. Anti-Her2 antibody conjugated FePt nanoparticles demonstrated molecular expression dependent CT/MRI dual contrast effect in the MBT2 cells with high endogenous Her2 expression and its Her2/neu gene knock out counterpart. The CT/MRI contrast effect of 12 nm-FePt outperformed that of 3 nm-FePt. The selective contrast enhancement of Her2/neu overexpression cancer lesions in both CT and MRI was found in tumor bearing mice after tail vein injection of 12 nm-FePt conjugated with anti-Her2 antibody. With respects to the MR images before injection, a reduction of tumor lesion intensity to 51% was observed at 24 hr after injection. On the other hand, a 138% contrast enhancement of the tumor tissue 24 hr after targeting was observed in CT image analysis. The results indicated the potential of FePt nanoparticles to serve as novel multi-modal molecular imaging contrast agents in clinical settings.

7909-51, Session 2

Size and surface chemistry of Au nanoparticles determine doxorubicin cytotoxicity

J. L. Nadeau, H. Chibli, X. Zhang, McGill Univ. (Canada)

Several formulations of gold-doxorubicin conjugates (Au-Dox) have been reported. However, the effects of particle size, lability of the conjugating bond, and specific targeting have not been fully explored. In this work we compare the relative cytotoxicity of 5 nm vs. 2 nm Au-Dox, and explore the effects of polyethylene glycol (PEG) and specific cell-targeting sequences on toxicity in B16 melanoma cells and in mice. We find that Au-Dox does not show increased cytotoxicity over Dox alone unless the particles are small enough to enter the nucleus. Surprisingly, cleavable bonds do not increase effectiveness, with even stably-bonded Au-Dox showing maximum cytotoxicity in less than one hour. Preliminary studies on molecular mechanisms of action implicate reactive oxygen species formation leading to apoptosis as the primary cause of cell destruction, with Dox-resistant cancer cells showing reduced resistance to Au-Dox. These results have important implications for the development of Au nanoparticle-based anticancer agents.

7909-08, Session 3

State-of-the-art toxicological and microscopic assessment of biomedical nanocrystals on the lung in vitro

M. J. D. Clift, P. Gehr, B. Rothen-Rutishauser, Univ. Bern (Switzerland)

Due to the ever increasing production of nanosized materials for a variety of novel applications (e.g. biomedicine), increased research has focused upon understanding the potential toxicity of these nanomaterials. In order to determine the potential toxicity of nanoparticles (NPs), it is essential that, in parallel to biochemical and toxicological testing, their specific route of uptake (if any), as well as their possible and subsequent intracellular localisation is investigated. By using our novel 3D in vitro triple cell co-culture model of the human epithelial airway barrier (containing epithelial cells and macrophages (apical side) and dendritic cells (basolateral side) which has been shown to mimic the architecture of this structural arrangement in vivo, in combination with a novel air-liquid interface cell exposure system, it is possible to mimic the exposure of NPs to the lung in vitro. Using both conventional and state-of-the art toxicological tests, in addition to light, laser scanning and transmission electron microscopy methods, it has been possible to determine the interaction of both fluorescent (designed core-shell NPs with shell-embedded fluorophores) and electron dense NPs with the in vitro triple cell co-culture. It has been observed that the material of the engineered NPs has a significant influence upon their resultant toxicity, dependant upon the specific exposure method used, although no difference upon their intracellular localisation. The results of these studies show that despite different compositions, specific NPs intended for use in biomedical applications, when exposed realistically (exposure method/concentration/primary contact cells) cause minimal effects to the lung airway tissue in vitro.

7909-09, Session 3

Size- and structure-dependent toxicity of silica particulates

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Nano- and micro-particulates firmly attach with the surface of various biological systems, because their high-specific surface area might interact with surfaces of tissues or cells. In some chronic pulmonary disease such as asbestosis, pneumoconiosis and silicosis, causative particulates, which are accumulated in the lung, will induce chronic inflammatory disorder, followed by poor prognosis diseases such as fibrosis, lung cancer and mesothelioma.

Our group has been studying the biocompatibility of silicon nanoparticles. We assessed in vitro cytotoxicity of silicon nanoparticles and found that the silicon particles were not toxic in the low-concentration region. In this research, we assessed the cytotoxicity of the various kinds of silica particles, including amorphous silica (18 nm, 120 nm and 1400 nm) and crystal silica (1300 nm) in mouse alveolar macrophage cell line culture. Alveolar macrophages are phagocytic cells, which uptake inhaled particles and interact with other immune cells by attractants such as chemokines and cytokines.

Their median lethal concentrations (LC50) measured by WST assay depend on particle size and those were related with inflammation response, about which we measured MIP-2. By contrast, production of TGF-beta, which is a fibrosis maker, by addition of crystal silica was much higher than that of amorphous one in their low-concentrations.

We assume that TGF-beta production in the low-dose of crystal silica leads to future pulmonary fibrosis and that the difference between amorphous and crystal might be caused by particle shape, oxy-radical generation and low-solubility. We conclude that differences of silica particulate affect cytotoxicity and immune response.

7909-10, Session 3

Bridging the fields of nanoscience and toxicology: nanoparticle impact on biological models

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In the emerging area of nanotechnology a key issue is related to the potential impacts of the novel nanomaterials on the environment and human health so that this technology can be used with minimal risk. Specifically designed to combine on a single structure multipurpose tags and properties, smart nanomaterials need a comprehensive

characterization of both chemicophysical properties and adequate toxicological evaluation, which is a challenging endeavor: the in vitro toxicity assays that are often employed for nanotoxicity assessments do not accurately predict in vivo response. To overcome these limitations and gain a deeper understanding of nanoparticle-cell interactions, we have employed cnidarian models, and in particular the freshwater polyp Hydra vulgaris, not opposed to more complex and evolved systems, but to add valuable information, at an intermediate level between early metazoan and vertebrates, on both cytoxicity and on pollution affecting the environment. By testing nanocrystals of different sizes, core/shell composizion and surface coatings, in vivo, at whole animal level, we investigated the impact of their properties on uptake, accumulation, biodistribution, elicitation of behavioural responses. We assessed acute and sublethal toxicity by scoring for alteration of morphological traits, population growth rates, and influence on the regenerative capabilities of Hydra. Furthermore, we investigated the cellular and molecular mechanisms activated by nanoparticles internalization. Thus by using approaches spanning from animal biology to cell and molecular biology we provide an analysis on metal based and semiconductor NC , discussing the crucial role played by the synthesis route and chemical surface on the toxicity for living organisms.

7909-11, Session 4

Multiplexed solid-phase nucleic acid hybridization assays using semiconductor quantum dots as donors in fluorescence resonance energy transfer (FRET)

W. R. Algar, U. J. Krull, Univ. of Toronto Mississauga (Canada)

The use of quantum dots (QDs) as donors in fluorescence resonance energy transfer (FRET) provides new opportunities in bioanalysis. In our group, we have used mixed films of QDs and oligonucleotide probes immobilized on optical fibers to demonstrate the potential for novel spectroscopic detection platforms that capitalize on the unique optical properties of QDs and FRET. This presentation will highlight the use of different combinations of CdSe/ZnS QDs and fluorescent dyes as FRET pairs to achieve the two-plex, three-plex, and four-plex detection of target nucleic acid sequences. Multiplexed analyses are possible using a single excitation source and a single substrate, in the ensemble, and via ratiometric signals. Spatial registration or sorting methods, imaging or spatial scanning, and single molecule spectroscopy are not required. These strategies are competitive with established technologies, such as molecular beacons, with nanomolar (picomole) limits of detection, analysis times as short as one hour, and the absence of target labeling via a sandwich format. Spectroscopic and engineering approaches to signal optimization are identified, and a basic model to illustrate both the potential complexity, and potential control over multiplexed FRET interactions will be introduced. Important aspects of interfacial chemistry will also be described, and include: the methods and advantages associated with the solid-phase self-assembly of QD bioconjugates; the use of QD coatings and passivation for obtaining selectivity, including the discrimination of single nucleotide polymorphisms; and the potential for reusability and true biosensor development. This work is expected to lead to new biochip diagnostics in the future.

7909-12, Session 4

Time-resolved and steady-state FRET spectroscopy on commercial biocompatible quantum dots

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Semiconductor nanocrystals (quantum dots - QDs) possess unique photophysical properties making them highly interesting for many kinds of biochemical applications. Beside their use as common fluorophores in spectroscopy and microscopy, QDs are well suited for Förster resonance energy transfer (FRET). Their broad absorption cross-sections and size-tunable absorption and emission spectra offer several advantages for the use of QDs both as FRET donors and acceptors. Therefore, QD-based FRET pairs can be efficiently used as biological and chemical sensors for highly sensitive multiplexed detection. In this contribution we present the use of several commercial biocompatible QDs (Qdot® Nanocrystals - Invitrogen) as FRET donors in combination with commercial organic dyes as FRET acceptors. In order to investigate the FRET process within our donor-acceptor pairs, we used biotinylated QDs and streptavidin labeled with dyes. The well known biotin-streptavidin molecular recognition enables FRET from QDs to the dyes and provides defined distances between them. Steady-state and time-resolved fluorescence measurements were performed in order to investigate the QD-to-dye FRET. Despite the large size of the polymer coated biocompatible QDs our results demonstrate the efficient use of these QDs as efficient donors for steady-state and time-resolved FRET applications in nano-biotechnology.

7909-13, Session 4

Time-correlated hyperspectral studies of biexciton characteristics in dimeric colloidal quantum dots under photo-oxidation

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Optical properties of photooxidizing single and dimeric CdSe/ZnS core/shell colloidal quantum dots (QDs) are investigated. Single and clustered QDs of dimers, trimers, and tetramers are assembled and preferentially collected using electrospray differential mobility analysis with electrostatic deposition. A multimodal time-correlated hyperspectral confocal microscope capable of simultaneously measuring the time evolution of photoluminescence (PL) intensity fluctuation, PL lifetime, and emission spectra reveals the unique dynamic properties of interacting QDs in a dimer. Evidence of transition from coupled to decoupled states induced by photooxidation of one QD in the dimer is presented and described with a model involving multiexciton decay characteristics. Controlled assembly of a fixed number of QDs into clusters and quantitative optical analysis techniques will allow for measurements in understanding the excitonic charge transfer mechanism during the photooxidation of QDs.

7909-14, Session 5

An optical nanoparticle gun

J. Feldmann, Ludwig-Maximilians-Univ. München (Germany)

Gold nanoparticles combine several chemical, biological and optical advantages. During recent years some possibilities to manipulate gold nanoparticles with light have been investigated also for biological and medical applications. Here we show that light pressure can be used for “shooting individual gold nanoparticles” in aqueous solution. By balancing attracting and repulsive forces we can laser print single gold nanoparticles with an accuracy of several tens of nanometer.

7909-15, Session 5

Localized surface plasmon properties of Au nanorings and their diffusion in biotissue

C. Lee, S. Wu, H. Tseng, T. Chi, K. Yang, J. Wang, National Taiwan Univ. (Taiwan); M. Tsai, Chang Gung Univ. (Taiwan); Y. Kiang, C. Yang, National Taiwan Univ. (Taiwan)

At localized surface plasmon resonance (LSPR), coherent scattering and absorption of metal nanoparticles (NPs) are enhanced. Due to its interference (coherence) detection nature, optical coherence tomography (OCT) is a suitable approach for monitoring the LSPR of Au NPs. Hence, resonant Au NPs can be detected by OCT scanning with high sensitivity. Swept-source OCT systems based on sweeping-frequency lasers as the light sources around 1300 nm have been widely built for medical diagnosis. In this paper, aqueous solutions of Au nanorings (NRs) with different LSPR wavelengths are prepared. Their LSPR-induced extinction cross sections at 1310 nm are estimated with OCT scanning of solution droplets on coverslip. The results are reasonably consistent with the data at individual LSPR wavelengths obtained from transmission measurements of Au NR solutions and numerical simulations. Then, the resonant and non-resonant Au NRs are delivered into mouse liver samples for tracking Au NR diffusion in the samples through continual OCT scanning for one hour. With resonant Au NRs, the average A-mode scan profiles of OCT scanning at different delay times clearly demonstrate the extension of strong backscattering depth with time. The calculation of speckle variance among successive OCT scanning images, which can be used to represent the local transport speed of Au NRs, leads to the illustrations of downward propagation and spreading of major Au NR motion spot with time. In a homogeneous bio-tissue like mouse liver, the fabricated Au NRs can diffuse down to a depth of several hundred microns within 60 min.

7909-16, Session 5

Nanoscale plasmonic resonators with high Purcell factor: spontaneous and stimulated emission

E. M. Goldys, Macquarie Univ. (Australia)

Plasmonic nanoparticles with silver cores and silica shells containing Eu fluorophores near the surface produced by wet chemistry method exhibit reduced fluorescence lifetimes compared with the same fluorophores in free space conditions. These can be interpreted within the Purcell framework which highlights that the surface plasmon polariton modes of the nanoparticle behave as energy-storing resonators. Surprisingly, the structures show high Purcell factors of over 60, comparable with those observed in high quality semiconductor micropillar cavities. Such high Purcell factors result from very low mode volumes (~ 10 000 nm3 and comparatively high cavity Q factors (~ 100). Structures such as those are capable of lasing [ref Noginov], provided a gain medium is introduced into the shell. We present the method and predictions of the lasing wavelengths and lasing threshold. We also demonstrate a simple diagnostic method that can identify the proximity of a given nanoparticle to the lasing lasing threshold. Furthermore, we show that these structures can enhance the electric field by a factor of over 1500 (at 99.9% of threshold gain) and beyond. We discuss the implication of such enhancement for biosensing with these “smart dust” nanoparticles.

7909-17, Session 6

Magnetic supracolloidal assemblies for biophysical applications

J. Berret, Univ. Paris 7-Denis Diderot (France)

The possibility to use inorganic nanoparticles as building blocks for the fabrication of supracolloidal assemblies has attracted much attention during the last years. It is thought that these constructs could be made of different shapes and functionalities and could constitute the components of future nanodevices such as sensors, actuators or nanocircuits. In a first part, I report a protocol that allows us to fabricate supracolloidal assemblies in a controlled manner. The building blocks of the constructs are sub-10 nm iron oxide nanocrystals and polymers. I show that a fine control of the electrostatic interactions between the building blocks result in the formation of spherical or anisotropic aggregates at the micrometer length scale [1,2].

With lengths comprised between 1 and 100 µm, the anisotropic aggregates, also called nanorods were found to be very rigid (persistence length 10 cm) and to reorient themselves with an externally applied magnetic field. In a second part, I will review recent results on the toxicity and uptake of the nanomaterials and in particular those of the nanorods by murine fibroblasts and human lymphoblasts. Our studies revealed that the physico-chemical characteristics of engineered nanomaterials play an important role in the interactions with living cells. I will also show that the rods can be utilized for passive and active microrheology experiments of complex fluids inconfined environments. The mechanical responses of the intracellular medium will be presented and compared to that of model viscoelastic liquids.

1. Fresnais, J.; Berret, J.-F.; Frka-Petesic, B.; Sandre, O.; Perzynski, R., Adv. Mater. 2008, 20, (20), 3877-3881.

3. J. Fresnais, E. Ishow, O. Sandre and J.-F. Berret, Small 5 (22) 2533 - 2536 (2009).

7909-18, Session 6

Gold nanoparticles in biomedical applications

A. G. Kanaras, D. Bartczak, O. L. Muskens, T. M. Millar, T. Sanchez-Elsner, Univ. of Southampton (United Kingdom)

Realizing the interactions of complex biological systems with chemically produced colloidal nanocrystals is of great importance for the development of new diagnostic and therapy methods, drug delivery, and imaging, A key strategy towards this aim is to understand how different functionalities and types of colloidal nanoparticles affect specific cells and their functions.

In this presentation we demonstrate a new strategy to manipulate cell operations, which is based on the membrane-receptor specific interactions between colloidal peptide-capped gold nanoparticles and human umbilical vein endothelial cells. Colloidal gold nanoparticles of similar charge and size but capped with different sequences of peptides can deliberately trigger specific cell functions. On the other hand, we demonstrate the development of a mild type of hyperthermia, the nondestructive nanoparticle hyperthermia, which can be used to manipulate the viability and cellular functions of non-cancerous cells. Different types of colloids such as hollow gold, gold nanorods and silica-gold core-shell particles are employed as a toolbox for the nondestructive hyperthermia, in order to further tune the cellular manipulation.

The nanoparticles that we use in our experiments are coated with olygoethylene glycol-based ligands (OEG), in order to retain biological stability, and they are functionalized with peptides which target receptors allocated on the cellular membrane. Specificity and efficiency of the binding of gold/peptide conjugates are investigated and compared to the non-specific internalization of plain PEG-coated nanoparticles through the endocytosis pathway. Our findings open up new avenues towards the deliberate control of cellular functions using strategically designed nanoparticle and laser hyperthermia.

7909-19, Session 6

Alloy metal nanoparticles for multicolor cancer diagnostics

P. V. Baptista, G. Doria, J. Conde, Univ. Nova de Lisboa (Portugal)

Cancer is a multigenic complex disease where multiple gene loci contribute to the phonotype. The ability to simultaneously monitor differential expression originating from each locus results in a more accurate indicator of degree of cancerous activity than either locus alone. Metal nanoparticles have been thoroughly used as labels for in vitro identification and quantification of target sequences. We have synthesized nanoparticles with assorted noble metal compositions in an alloy format and functionalized them with thiol-modified ssDNA (nanoprobes). These nanoprobes were then used for the simultaneous specific identification of several mRNA targets involved in cancer development - one pot multicolor detection of cancer expression. The different metal composition in the alloy yield different “colors” that can be used as tags for identification of a given target. Following a non-cross-linking hybridization procedure previously developed in our group for gold nanoprobes, these multicolor nanoprobes were used for the molecular recognition of several different targets involved in chronic myeloid leukemia (e.g. BCR, ABL, BCR-ABL fusion product) as well as alternatively spliced variants of other relevant genes (e.g. p53, c-myc, BCRA1). Based on the spectral signature of mixtures, before and after induced aggregation of metal nanoparticles, the correct identification could be made. Further application to differentially quantify expression of each locus in relation to another will be presented. The differences in nanoparticle stability and labeling efficiency for each metal combination composing the colloids, as well as detection capability for each nanoprobe will be presented. Additional studies will be conducted towards allele specific expression studies.

7909-20, Session 6

Locally increased mortality of gamma-irradiated cells in presence of lanthanide-halide nanoparticles

N. J. Withers, J. B. Plumley, A. McBride, B. A. Akins, A. C. Rivera, N. C. Cook, G. A. Smolyakov, G. S. Timmins, M. Osinski, The Univ. of New Mexico (United States)

Cerium-doped lanthanum fluoride colloidal nanocrystals offer a way to improve radiation therapy through the enhanced absorption of high energy photons. 10% cerium-doped polyethylene-glycol-capped lanthanum fluoride nanocrystals were synthesized in water as platelets 2-4 nm in diameter and 1-3 nm thick and suspended in phosphate buffered saline. The nanocrystals were characterized by transmission electron microscopy, muffle furnace ashing, absorbance spectroscopy, dynamic light scattering, and photoluminescence spectroscopy. The lanthanum fluoride nanocrystals were used in radiation dose enhancement experiments that involved an incoming gamma flux from a Cs-137 source. Finally, increased cell mortality of radiation sensitive S. Cerevisiae, ATCC#208466, under gamma irradiation at varying concentrations of the PEG capped nanocrystals was explored using flow cytometry.

7909-21, Session 7

Multifunctional fluorescent nanoparticles for biomedical applications

S. T. Selvan, A*STAR Institute of Materials Research and Engineering (Singapore)

Hybrid multifunctional nanoparticles (NPs) are emerging as useful probes for magnetic based targeting, delivery, cell separation, magnetic resonance imaging (MRI), and fluorescence-based bio-labeling applications. Assessing from the literature, the development of multifunctional NPs for multimodality imaging is still in its infancy state. This talk would focus on our recent work on quantum dots (QDs), magnetic NPs and bi-functional NPs (composed of either QDs or rare-earth NPs, and magnetic NPs - iron oxide or gadolinium oxide) for multimodality imaging based biomedical applications. The combination of MRI and fluorescence would ally each other in improving the sensitivity and resolution, resulting in improved and early diagnosis of the disease.

The challenges in this area will be discussed.

Relevant Publications

1. S. T. Selvan*, T. T. Y. Tan, D. K. Yi and N.R. Jana, “Functional and Multifunctional Nanoparticles for Bioimaging and Biosensing”, Langmuir (2010) DOI: 10.1021/la903512m. Invited Feature Article.

2. G.K. Das, B.C. Heng, S-C. Ng, T. White, J.S.C. Loo, L. D’Silva, P. Padmanabhan, K. K. Bhakoo, S. T. Selvan*, T.T.Y Tan* Gadolinium oxide ultranarrow nanorods as multimodal contrast agents for optical and magnetic resonance imaging. Langmuir 2010, 26, 8959-8965.

3. C. Y. Ang, L. Giam, Z. M. Chan, A. W. H. Lin, H. Gu, E. Devlin, G. C. Papaefthymiou, S. T. Selvan*, and J. Y. Ying*, “Facile Synthesis of Fe2O3 Nanocrystals without Fe(CO)5 Precursor and One-Pot Synthesis of Highly Fluorescent Fe2O3-CdSe Nanocomposites”, Advanced Materials 2009, 21, 869-873.

4. S. T. Selvan, P. K. Patra, C. Y. Ang and J. Y. Ying*, “Synthesis and Live-Cell Imaging with Semiconductor and Magnetic Quantum Dots,” Angewandte Chemie Int. Ed. 2007, 46, 2448-2452.

7909-22, Session 7

Imaging heterostructured quantum dots in cultured cells with epifluorescence and transmission electron microscopy

E. M. Rivera, C. Trujillo Provencio, New Mexico State Univ. (United States); A. Steinbrueck, P. Rastogi, A. M. Dennis, J. A. Hollingsworth, Los Alamos National Lab. (United States) and Center for Integrated Nanotechnologies (United States); E. Serrano, New Mexico State Univ. (United States) and Center for Integrated Nanotechnologies (United States)

Quantum dots (QDs) are semiconductor nanocrystals with extensive imaging and diagnostic capabilities, including the potential for single molecule tracking. Commercially available QDs offer distinct advantages over organic fluorophores, such as increased photostability and tunable emission spectra, but their cadmium selenide (CdSe) core raises toxicity concerns. For this reason, replacements for CdSe-based QDs have been sought that can offer equivalent optical properties. The spectral range, brightness and stability of InP QDs may comprise such a solution. To this end, LANL/CINT personnel fabricated moderately thick-shell novel InP QDs that retain brightness and emission over time in an aqueous environment. We are interested in evaluating how the composition and surface properties of these novel QDs affect their entry and sequestration within the cell. Here we use epifluorescence and transmission electron microscopy (TEM) to evaluate the structural properties of cultured Xenopus kidney cells (A6; ATCC) that were exposed either to commercially available CdSe QDs (Qtracker® 565, Invitrogen) or to heterostructured InP QDs (LANL). Epifluorescence imaging permitted assessment of the general morphology of cells labeled with fluorescent molecular probes (Alexa Fluor® phalloidin; Hoechst 33342), and the prevalence of QD association with cells. In contrast, TEM offered unique advantages for viewing electron dense QDs at higher resolution with regard to subcellular sequestration and compartmentalization. Preliminary results show that in the absence of targeting moieties InP QDs can passively enter cells and sequester nonspecifically in cytosolic regions whereas, commercially available targeted QDs principally associate with membranous structures within the cell. Supported by: NIH 5R01GM084702.

7909-23, Session 7

In-vivo multiplexed optical imaging system with near-infrared emitting quantum dots and lanthanide-doped nanoparticles

S. Jeong, N. Won, K. Kim, J. Park, S. Kim, Pohang Univ. of Science and Technology (Korea, Republic of)

Quantum dots (QDs) have the potential for bioimaging contrast agents by bright luminescence, resistance against photobleaching, and tunable emission wavelengths. Lanthanide-doped nanoparticles (LNs) can have advantages in bioimaging applications due to their narrow emission bandwidth, nonblinking, and relatively low toxicity. Both QD and LN can emit at near-infrared (NIR) wavelengths which can provide maximal tissue penetrations from the minimal interferences by water and biomolecules and from the reduced auto-fluorescence. Multiplexed imaging technique provides the opportunity to investigate the complex biological phenomena governed by multiple biomolecules. QDs with different emission wavelengths can be multiplexed by single excitation light. Multiplexing between QDs and LNs can be obtained by switching the excitation sources while they emit at same wavelength domain. NIR emitting QDs and LNs were synthesized with judicious emission wavelength control by pyrolysis method to expand the multiplexing capability in 700 to 900 nm. Surface chemistry of QDs and LNs will be addressed including the biocompatibility. Using small animal models, in vivo real-time multiplexed imaging will be demonstrated with QDs and LNs exploited simultaneously and complimentarily for the contrast agents. Following issues will be also discussed such as the penetration depth, signal-to-noise ratio, and the limit of multiplexing.

7909-24, Session 7

Synthesis of 'non-toxic' quantum dots and the in-vivo imaging applications thereof

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Quantum dots (QDs) can be a promising fluorescent marker in biological imaging applications due to the unique optical properties such as high extinction coefficient, high quantum yield, broad absorption, and narrow and symmetric emission profiles. Another advantage of QDs is the emission wavelength tunability from the visible to infrared regions by varying their sizes, compositions and morphologies. Near-infrared (NIR) wavelengths can provide maximal tissue penetrations and reduced auto-fluorescence by the minimal interferences from water and biomolecules. Typical NIR emitting QDs may contain toxic elements such as Cd, Pb, Hg, or As. This inherently limits QDs from potentially being widely used for medical or biological applications. High quality 'non-toxic' QDs were synthesized that include InP and CuInS2 QDs. The solvent and QD precursors were judiciously chosen to obtain highly bright and stable QDs with reproducible manner. Their photoluminescence spectra were tuned down to far-red and NIR regions for bio-imaging applications. For example, high quality InP QDs were obtained by means of a simple one-pot synthesis in the presence of polyethylene glycol (PEG). PEG is cost-effective and is proven almost non-toxic in human physiology. The PEG is also recyclable; can be easily recovered after synthesis by simple physical separation. Various precursors were tested for InP and CuInS2 QD syntheses. Using small animal models, real-time multiplexed in vivo imaging was demonstrated with the 'non-toxic' NIR emitting QDs. Furthermore, we will discuss penetration depths of the QD imaging along with the contrast to noise ratios and the image sharpness.

7909-25, Session 7

Near-infrared quantum dots for in-vivo real-time multiplexed imaging applications

N. Won, S. Jeong, K. Kim, J. Park, S. Kim, Pohang Univ. of Science and Technology (Korea, Republic of)

Near-infrared (NIR) quantum dots (QDs) promise a new modality for in vivo bio-imaging and future medical imaging applications. QDs have proven the potential for imaging contrast agents by the bright luminescence, the resistance against photobleaching, and the multiplexing capability. NIR wavelengths can provide maximal tissue penetrations by the minimal interferences from water and biomolecules and the reduced auto-fluorescence. We developed an in vivo real-time multiplexed NIR QD imaging system that has a Si CCD and an InGaAs CCD which in combination cover the NIR wavelength range from 700 to 1700 nm. Each CCD has a filter wheel with emission filters which enable the real-time multiplexed imaging of relatively slow events. To verify the capability of our home-built imaging system for the surgical imaging applications, the penetration depth of the QD imaging was simulated using biological tissues such as bovine liver and porcine skin samples. CdTeSe, PbS, or PbSe QDs were synthesized for the imaging experiments. We investigated into the imaging parameters that affect contrast to noise ratios (CNRs) and sharpness. The CNRs of QD emissions measured at the tissue surface showed exponential decreases as increases of the tissue thickness, the slops of which depend on the excitation and emission wavelengths. In liver tissues, longer excitation and emission wavelengths showed slower CNR decrease. In skin tissues, longer wavelengths provided less blurred images but showed little effect on the CNRs. The dependencies on QD imaging qualities will be discussed regarding the fluence rate, incidence angles, and polarizations.

7909-26, Session 8

Characterizing FRET in quantum dot-sensitized multivalent DNA photonic wires

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The use of semiconductor quantum dots (QDs) as optimized Förster resonance energy transfer (FRET) donors in a variety of sensing and imaging configurations with fluorescent dye acceptors has become well-established. Here we examine the ability of QDs to transfer energy through a DNA photonic wire. In these types of assemblies, the QD acts as both a central nanoscaffold and FRET donor to a series of dyes sequentially placed along an attached DNA sequence. The DNA, attached to the QD via a hexahistidine peptide linker, provides a rigid and controllable template for the dye attachment with complementary labeled DNA sequences. The dyes are arranged in a manner that allows consecutive FRET interactions along the photonic wire. The effects on overall energy transfer of modifying dye placement on the DNA sequence, homo-FRET interactions among identical dyes and the use of a DNA intercalating dye in these hybrid assemblies were also examined. Results suggest that energy transfer is limited by dye re-emission properties and by energy loss through non-FRET pathways. Optimization in choice of acceptor dyes used and their placement along the DNA strand are expected to improve energy flow and allow for efficient photonic wire assemblies with widespread potential in nanotechnology.

7909-27, Session 8

Quantum dots as FRET acceptors: multiplexing biosensors for in-vitro diagnostics and molecular ruler applications

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FRET applications play an important role for the determination of concentrations and distances within nanometer-scale systems in vitro and in vivo in many fields of biotechnology. Semiconductor quantum dots (QDs) possess ideal properties for their application as FRET acceptors when the donors have long excited state lifetimes and when direct excitation of QDs can be efficiently suppressed. Therefore, luminescent terbium complexes (LTCs) with excited state lifetimes up to milliseconds are ideal FRET-donor candidates for QD-acceptors. Here we present the application of LTC-QD FRET pairs for multiplexed ultra-sensitive diagnostics and nanometer-resolution molecular distance measurements by time-resolved luminescence analysis. A time- and spectrally-resolved simultaneous measurement of five FRET-sensitized Invitrogen QdotsTM using one commercial LTC (www.lumiphore.com) as FRET-donor within a biotin-streptavidin bioassay is demonstrated. Our color-coded, nearly background-free multiplexed homogeneous assay yields sub-picomolar detection limits for all five QDs in one single sample, making the quantum dot-based FRET probes ideal candidates for highly specific and sensitive companion diagnostics. Different donor-acceptor distances are determined by decay-time analysis, demonstrating the application as multiplexed nanometer scale spectroscopic ruler over very large molecular distances (> 10 nm). Further investigation of the pre-exponentials of the multi-exponential donor and acceptor luminescence decay functions show that the FRET-nanoprobes are suitable for size and shape determination of QDs under physiological conditions and potentially suited for high-resolution multiplexed conformational and functional studies in cell imaging. The results also provide insight into the energy transfer mechanism from LTCs to QDs showing a FRET type (r^-6) distance dependence.

7909-28, Session 8

Nanoprobes of fluorescent gold nanoclusters for cells labeling

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Semiconductor quantum dots are attracted by its stability and tunable wavelengths, but containing toxic ions such as Cd2+, Pb2+ is a concerned issue for broad clinical application. To face on this problem, researchers have focused on developing new biocompatible materials with fluorescent properties. Fluorescent gold nanoclusters are becoming the alternative nanomaterials for nontoxic cellular labeling. Gold nanoclusters, consisting of several atoms, exhibit discrete electronic states and fluorescent properties. As a biocompatible materials, gold nanoclusters show a good candidate of novel fluorophore with many advantages, such as chemical stability, and general surface chemistry. In this study, synthesis of ultrafine fluorescent gold nanoclusters is included in this report. We focus on the issue how to efficiently label cells using specific carrier. we study the cell labeling efficiency of fluorescent gold nanoclusters using different forces (electric, megnetic). The nanoprobes design of fluorescent gold nanoclusters are also included. Specific staining of cells and nonspecific uptake by living cells are studied.

7909-29, Session 8

Quantum dot-based time-resolved adhesion assay for cell co-cultures

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Colloidal inorganic semi-conductor nanocrystals - commonly known as Quantum dots (QDs) - are prepared as fluorescent probes in biological staining. Compared with conventional fluorophores, QDs have a narrow, tunable (depending on the size), symetric emission spectrum and are photochemically stable [1]. The bright fluorescence allows for sensitive detection, the reduced photo-bleaching [2] permit measurements over long periods of time, and enable live cell imaging. Due to their narrow emission peaks they are suitable for multiplexing, in which multiple colors can be obtained in parallel from single excitation sources. Furthermore, QDs are spontaneously ingested by living cells [3], are confined in the cell and are only transferred to daughter cells upon cellular division. According to the advantageous characteristic of QDs, one of the main applications in cell biology is the use of QDs as marker for cell lineage. In this work, a QD label-based time resolved adhesion assay for co-cultures is presented. This is a novel technique, which allows for quantifying the adhesion properties of cell co-cultures on one substrate. Two different cell lineages were labeled with fluorescent QDs of two different colors and were grown within a co-culture onto different substrates. Due to the high contrast and the low brightness variations of the background, a software was developed to count the cells automatically. The adhesion of one against the other cell type was quantified by the ratio of the different colors. With this technique, the effect of different nano- and micro-structured surfaces on the adhesion behavior within co-cultures can be quantified.

7909-31, Session 9

Getting control in the antibody-nanoparticle stoichiometry

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Gold nanoparticles (GNPs) have attracted huge attention recently for both biosensor and biomedical applications. This interest is based mostly owing to their unique optical and catalytic properties, excellent colloidal stability, and relative ease of preparation. Up to now, a large number of different approaches to conjugate different biomolecules to GNPs had been reported. However, controlling the number of functional ligands and biomolecules conjugated to NPs still remains as a significant challenge. Controlled nanoparticle valency would open new perspectives in bottom up nanotechnology for controlling nanomaterial orientation and new properties generation. Besides, it will be also advantageous for biological applications such us single-molecule imaging in cells, as a tool for imaging protein dynamics at the single-molecule level, to improve nanoparticle amplification methods for biodetection (mass enhancers), etc.

In this sense, only a few limited approaches have been developed for making NPs with a discrete number of chemical functional groups: by solid phase synthesis methodology, using polymers with single functional groups at their ends, taking advantage of higher reactivity of surface gold atoms at certain areas of NPs, etc. Besides, the papers that report the union of only one molecule of antibody per NP are even less. Here, we present an easy strategy that allows both to control the binding orientation and the number of molecules of antibodies attached on the GNPs surface. Different techniques were used to demonstrate this monovalent antibody functionalization (TEM, ELISA assays, UV-VIS adsorption spectra, etc).

7909-32, Session 9

Immobilized quantum dot bioprobes: microfluidics for the development of nucleic acid assays and bioconjugate assemblies

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Quantum Dots (QDs) have been used as donors in fluorescence resonance energy transfer (FRET) for the multiplexed detection of fluorescence from DNA targets in a single assay. This presentation will explore the use of QD-bioprobes that are immobilized within microfluidic channels as a multiplexed assay platform, and the use of microfluidics to bioconjugate probe oligonucleotides and peptides for the assembly of QD-bioprobes.

The typical challenges associated with assembly of unique QD-bioprobe systems on a surface include: non-specific adsorption, slow kinetics of hybridization, and sample manipulation. Our work has considered immobilization of mixtures of different QD-bioprobes onto glass-PDMS microfluidic chips using various chemistries. The ability to dynamically control stringency by adjustment of the potential in an electroosmotic-based microfluidics experiment is advantageous. QD-bioprobes can be covalently anchored, or can be immobilized using a labile tethering system for removal and replacement. As a specific example of the latter, bi-conjugated QDs can be used where one oligonucleotide sequence on the QD is available for immobilization by hybridization with complementary oligonucleotide on a glass surface, and a different oligonucleotide sequence on the QD serves as a probe to transduce hybridization with target in a sample solution.

We are also exploring microfluidic-based solid phase synthesis for QD-bioprobe assembly, purification, and recovery. The process involves multi-step assembly on a layer of QDs that are immobilized in a microfluidic channel. Initial work has considered click chemistry for activation, and then further conjugation with the desired biomolecules for QD-bioprobe assembly.

7909-33, Session 10

Plasmonic nanostructures: new design methodologies and high-resolution mode imaging for applications in nanobiophotonics

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We present new design principles for plasmonic nanostructures based on transformation optics and plasmon hybridization theory. This allows us to create structures optimized for electromagnetic field enhancement, a strong or suppressed scattering response, and indeed broadband light absorption. We further present correlative mode imaging of such nanostructures using electron and optical spectroscopies. We show that particularly electron energy loss spectroscopy is well suited for the investigation of electromagnetic hot spots, and present results obtained both for colloidal systems as well for cavities fabricated using electron beam lithography on ultrathin silicon nitride membranes. Applications in the nanobiosciences will be outlined. We will further discuss a new methodology for bioassays exploiting metal nanoclusters with Raman-active reporter molecules as linking units.

7909-34, Session 10

Plasmonic Ag/SiO2 composite nanoparticles doped with a europium chelate and their metal enhanced fluorescence

W. Deng, K. Drozdowicz-Tomsia, D. Jin, E. M. Goldys, Macquarie Univ. (Australia); J. Yuan, Dalian Univ. of Technology (China)

We report silver nanostructure-enhanced fluorescence of a europium (Eu) chelate, BHHCT-Eu-DPBT, which was covalently bound in Ag/SiO2 nanocomposites. The fluorescence enhancement was examined as a function of core and shell size and optimum thicknesses of 52 ± 10 nm and 25 ± 2 nm were found, in agreement with theoretical predictions. An increase in the fluorescence intensity by a factor of ~10.4 and decrease in the lifetime by a factor of ~3.5 were observed. Single nanocomposite particles were bright enough to be observed in fluorescence microscopy under 365 nm LED excitation. The increased brightness and reduced lifetime of such fluorescent core-shell nanocomposites will enhance their applicability for ultrasensitive bioassays and bioimaging, especially with time-gating.

7909-35, Session 10

Ion sensing with colloidal nanoparticles

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Colloidal nanoparticles composed out of an inorganic core and a polymer shell have been synthesized. Both, the core and the polymer shell are either fluorescence, magnetic, or radioactive, so that they can be imaged with fluorescence, magnetic resonance, or radioactivity, respectively. By combining different cores with different polymer shells nine different types of particles for dual imaging have been obtained, as for example fluorescent cores with radioactive polymer shells. In this way a toolkit of nine types of nanoparticles has been created out of which each can be imaged with two different modes. Due to the topography of the polymer shell all nine different types of particles possess very similar surface chemistry and thus have virtually the same interface for consecutive conjugation with ligands.

7909-36, Session 10

Diagnosis and imaging with SERS encoded particles

R. A. Alvarez-Puebla, Univ. de Vigo (Spain)

SERS encoded particles have been establish as a solid and reliable analytical technique for the detection in extremely low amounts of a wide variety of bioanalytes. SERS encoded particles for indirect detection and labeling can be implemented on chip or even inside living cells, tissues or a variety of microorganisms.

However, there are still open challenges, mainly related to the reproducibility of the methods for substrate fabrication, in particular when dealing with the formation of hot spots, which are responsible for the highest enhancement factors, but their efficiency is extremely sensitive toward small geometrical details within the nanostructure. Additionally, although portable Raman spectrometers are available, most of the published reports are based on very sophisticated instruments that will not find a place in routine analysis labs or hospitals. Thus, the field of SERS codification, in particular toward biomedical applications has a great potential, as demonstrated by many examples, but is open to new developments that will undoubtedly continue amazing us in the near future.

7909-37, Session 11

Quantum dots and metal nanoparticle agents for manipulating cellular traficking

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Nanometals and Quantum Dots are finding wide ranging applications as phosphors, energy transfer agents, and cargo delivery vehicles in cellular applications. Whether the end goal is a drug delivery agent, a phosphor, or a molecular beacon understanding the potential of these materials in biological applications is crucial. In this presentation we will explore the transport of nanomaterials across skin (in-vivo), the fate and transport of QDs modified by cell penetrating peptides for delivery of genetic information in-vitro, and simple molecular beacon applications to measure cellular metabolite levels.

7909-38, Session 11

Distribution of quantum dots after intraperitoneal administration, with reference to area-specific distribution in the brain

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Quantum dots (QDs) are well-known for their potential application in biosensing, ex vivo live-cell imaging and in vivo animal targeting. The brain is a challenging organ for drug delivery, because the blood brain barrier (BBB) functions as a gatekeeper guarding the body from exogenous substances. Here, we evaluated the distribution of bioconjugated QDs, i.e., captopril-conjugated QDs (QDs-cap) following intraperitoneal injection into male ICR mice as a model system for determining the tissue localization of QDs, employing ICP-MS and confocal microscopy coupled with spectrometric analysis. We have demonstrated that intraperitoneally administered QDs-cap were delivered via systemic blood circulation into liver, spleen, kidney and brain at 6 hours after injection. Although QDs-cap were located predominantly inside the blood vessels in liver, kidney and brain, but a few were distributed in the parenchyma, especially noteworthy in the brain. In addition, we have studied the effects of chronic exposure to QDs-cap in the brain, and demonstrated a significant increase of the oxidative stress-mediated products in the brain, especially in the hippocampus. Further studies on acute as well as chronic toxicity of QDs in the brain are required prior to clinical application to humans.

7909-39, Session 11

Peptide-mediated cellular delivery and endosomal escape of quantum dots

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Currently there is considerable interest in using bioconjugated nanoparticles for in vivo imaging and sensing applications along with theranostics. Luminescent CdSe/ZnS core shell semiconductor quantum dots (QDs) have unique optical properties and bioconjugation capabilities that make them ideal prototypes for these purposes. We have previously described the metal-affinity association between the imidazole groups of terminal hexahistidine residues of peptides and proteins and the ZnS shell of quantum dots as a useful bioconjugation technique [1]. We have also demonstrated that QDs labeled with an oligohistidine tagged cell penetrating peptide (CPP) derived from the HIV TAT-protein could undergo specific endocytosis-mediated cellular uptake in both HEK293T/17 and COS-1 cells [2]. However, the QDs were predominantly sequestered in the endosomes. This remains a significant hindrance to future potential cellular imaging applications which require the QDs to access other subcellular organelles. Here we describe the design, synthesis and cellular application of a hexahistidine-labeled modular peptide containing various functionalities including a palmitylate group that is capable of both cellular uptake and endosomal escape in multiple cell lines without concomitant toxicity [3]. Optimal cellular uptake and endosomal escape of QDs bearing these peptides takes approximately 48 hours. We have also tested various modifications of this peptide to identify the attributes required for both its cellular uptake and its endosomal escape capabilities. A model of how the various functionalities within the peptide contribute to its activity will be presented.

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7909-40, Session 12

Carbon nanotubes/inorganic hybrid materials: synthetic approach and applications

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Carbon nanotubes (CNT) can be considered as ideal templates for the formation of one dimensional nanoparticle assemblies by means of Wet-Chemistry methods. Despite their relative chemical inertness, several strategies have been devised for the preparation of CNT-nanoparticle composites, either through in situ nanoparticle synthesis or by the assembly of pre-formed nanoparticles. In both cases surface modification of the CNT is required, sometimes implying the chemical development of defect-sites and subsequent covalent functionalization or non-covalent adsorption of macromolecules on their side walls.

Herein, we report on the fabrication of one dimensional nanomaterials based on the non-covalent functionalization of CNT by means of a combination of polymer wrapping and layer-by-layer assembly through the deposition of nanoparticles of different morphology and nature (magnetic, metallic or semiconductor) and the description of the properties of the resulting hybrid materials.[1-5] This approach allows producing CNT/inorganic hybrid nanocomposites with two main requisites, desired in many of their applications; produce well dispersed inorganic nanostructures onto the carbon support, at time that gives a precise control over the morphology, structure, composition and nature of the deposited nanostructures. Additionally, the usefulness of the designed heterostructures in applications ranging from biosensing to catalysis will be briefly exposed.

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7909-42, Session 12

Novel synthesis of gold asymmetric nanocrystals: molecular heaters

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In the last years, gold nanoparticles have found a great deal of interest in the area of bioscience. This is due to the interesting physicochemical properties that these materials bear including biocompatibility, localized surface plasmons or ease of biofunctionalization by means of molecules bearing thiol groups. More recently, asymmetric gold nanoparticles (NPs) such as nanorods, triangular nanoprisms or core-shell dielectric-gold NPs have achieved an increasing popularity; this trend is mainly originated from the absorption band that they present in the NIR range of the electromagnetic spectrum. Upon excitation with NIR radiation, these asymmetric materials can release heat to their most immediate vicinity. Here we describe a novel synthesis route to produce gold triangular nanoprisms. These asymmetric tabular single-crystalline NPs exhibit a characteristic absorption band in the near infrared (NIR) range which can be tuned by varying the aspect ratio (edge to thickness) of the nNs. The aspect ratio is ultimately controlled by the synthesis conditions. Photothermal conversion of NIR radiation can be exploited for nanomedicine applications such as remote drug release or photothermal therapy.

7909-53, Session 12

Synthesis of NaYF4:Yb3+/Er3+ upconverting nanoparticles in a capillary based continuous-flow microfluidic reaction system

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Upconverting nanoparticles doped with lanthanide ions have drawn much attention due to their potential as optical imaging probes in biomedical applications[1,2]. Among upconverting nanomaterials, lanthanide-ions-doped NaYF4 nanoparticles have been shown to be the most efficient. Currently, NaYF4 nanoparticles are synthesized in batch-control modes in small volumes[3,4]. Although great achievements have been made, batch syntheses tend to suffer from irreproducibility of nanoparticles quality from batch to batch and difficulty to implement fast screening. Microfluidic reaction systems offer a solution to these challenges and have an increasingly important role in synthesis of nanoparticles as highly controlled thermal and stoichiometric microenvironments can be obtained in the synthesis process. [5].

In this paper, we report continuous flow based synthesis of NaYF4 nanoparticles in a capillary-based system with sequential temperature zones [6]. In a typical synthesis, first lanthanide (0.01 M) and NaF (0.03 M) ethylene glycol (EG) solutions were prepared by dissolving stoichiometric amounts of Ln(NO3)3 6H2O (Ln= Y, Yb, Er) and NaF in EG, respectively. Two solutions were subsequently aspirated in two syringes respectively and injected into a coaxial mixing system by syringe pumps. The coaxial mixture was injected in a polytetrafluoroethylene microcapillary with an inner diameter of 800 um and heated in a 180 oil bath for 5 s, and subsequently heated in a 110 oil bath for 60 s. Finally, the samples were collected from the outlet of the capillary. The nanoparticles were separated by diluting the obtained suspension using acetone followed by centrifugation for several times.

The nanoparticles show good water-dispersibility.and emit visible light when excited at 980 nm. In depth characterizations of the obtained nanoparticles are ongoing and will be included in future manuscript.

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7909-54, Session 12

From inorganic nanocrystals towards their assembly in polymeric mesoscale structures designed for biological applications

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In the fast advancing scenario of nanotechnology, the development of multifunctional nano-tools, able to carry out at the same time different tasks, is a subject under exploration and it will provide opportunities for the diagnosis and the cure of diseases. The bricks of such nanostructures are inorganic nanocrystals of different materials (such as metals, semiconductors, magnetic oxides) that at the nanoscale present new and unexpected properties.

Assembling them together, in a controlled manner into still nano/meso structures, characterizing their performances and exploiting them in biomedical applications is the subject of this talk.

As an example, the preparation, the characterization and the application of nanostructures which display at the same time fluorescence and magnetic properties will be discussed. Such nanostructures are interesting biomedical platforms and can find applications as in vivo dual modal imaging probes based on optical and magnetic resonance imaging (MRI), or for in vitro bio-separation, as for example the simultaneous magnetic separation and multiplexing optical detection of tumour cells from a pool of different cell populations. A proof of concept for such application will be shown in this work.1

Additionally, surface functionalization of such magnetic or magnetic/fluorescent mesoscale structures with intelligent coatings able to sense stimuli deriving from the internal cellular environment (as for instance, the pH of different cellular compartments, the reducing environment of tumor cells) or from the external surroundings (such as for instance a physical stimulus like a magnetic field applied) will be also discussed. These nanostructures might find application as carriers for the controlled delivery of drugs under defined stimuli.

1. “Fluorescent-magnetic hybrid nanostructures: preparation, properties and applications in biology” A Quarta, R. Di Corato, L. Manna, A. Ragusa and T. Pellegrino, (Transaction on NanoBioscience, 2007, 6, 298-308) topical review

2. “Magnetic-Fluorescent Colloidal Nano-Beads: Preparation and Exploitation in Cell Sorting Experiments” R. Di Corato, P. Piacenza, M. Musarò, R. Buonsanti, P. D. Cozzoli, M. Zambianchi, G. Barbarella, R. Cingolani, L. Manna and T. Pellegrino (Macromolecular Bioscience, 2009, 9, (952-958)

3. “Multifuctional Nanostructures Based on Inorganic Nanoparticles and Oligothiophenes and their Exploitation for Cellular Studies” A. Quarta, R. Di Corato, L. Manna, S. Argentiere, R Cingolani, G. Barbarella and T. Pellegrino, (Journal of the American Chemical Society, 2008,130,10545-10555)

7909-41, Session 13

Indium phosphide-based core-shell quantum dots optimized for biological applications

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Diverse arrays of biological sensors and imaging tools have been developed using semiconductor nanocrystal quantum dots (NQDs) (1).

Concerns linger, however, regarding the toxicity of traditional cadmium-containing nanomaterials (2). Indium phosphide (InP) offers a "green" alternative to the traditional cadmium-based NQDs, but suffers from an extreme susceptibility to oxidation. Coating InP cores with more stable shell materials has been shown to significantly improve nanocrystal resistance to oxidation and photostability (3), although higher quantum yields of InP core-shell NQDs in an aqueous milieu are needed to rival the more common CdSe/ZnS preparations.

We have developed synthetic methods for producing bright and tunable InP-based core-shell QDs suitable for transfer into water. Our one-pot synthesis technique minimizes oxidation of the InP cores while maintaining control of the shelling process to produce well-defined core-shell structures. Thicker shells enhance photostability while affording potential for suppressing blinking, improving on current InP core-shell preparations. NQDs made water-soluble using suitable ligands (e.g. mercaptoundecanoic acid) were analyzed for their quantum yield and stability. Thicker shells were shown to enable better retention of the quantum yield in aqueous milieu. Several shelling materials, including zinc sulfide and zinc selenide have been utilized, and the different photophysical effects elicited on the InP by the various shell materials have been investigated. Using shell materials of various bandgaps can yield type I or quasi-type II semiconductor materials, allowing the InP core-shell material properties to be tuned not only in emission wavelength, but also in electronic properties, to best suit the biological application.

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7909-44, Session 13

Compact and highly stable quantum dots through optimized aqueous phase transfer

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In recent years a large number of different approaches for the aqueous phase transfer of quantum dots, synthesized in organic solvent, has been proposed. Among those, surface ligand exchange with small hydrophilic thiols has been shown to yield the lowest hydrodynamic diameter, on the order of 5-15 nm. Compact quantum dots are required for specific imaging applications (e.g. sentinel lymphnode detection, study of synaptic signaling) and for maximizing renal excretion in in-vivo studies. Thiol-containing amino acids such as L-cysteine are of particular interest as capping ligands for hydrosoluble quantum dots as they exhibit low non-specific binding to serum proteins due to their zwitterionic character. However, cysteine is prone to dimer formation, yielding cistine, which limits the colloidal stability of the quantum dots.

We will demonstrate that the precise control of the pH value during aqueous phase transfer dramatically increases the colloidal stability of InP/ZnS quantum dots. While precipitation typically occurs within one day, DLS measurements show that no aggregation takes place even after several weeks in case of the correct choice of the pH during the phase transfer. Cysteine and various other bifunctional thiols have been tested. The pH has to be adjusted according to the pKa value of the thiol function as only the thiolate ion exhibits strong binding to the quantum dot surface. The formation of disulfides has been prevented through addition of reducing agents, e.g. TCEP. Disulfides significantly diminish the fluorescence quantum yield (QY). To the contrary, in our procedure up to 90% of the initial QY is maintained. The obtained InP/ZnS quantum dots emit at 650-720 nm with a QY of 10% at pH 7.4 and their hydrodynamic diameter is 9.5-15 nm. The described procedure can equally be used for a large number of other types of nanoparticles.

Finally we will present the in vitro and in vivo behavior of the hydrosoluble quantum dots after surface functionalization with the cell-penetrating peptide maurocalcine.

7909-52, Session 13

Biocompatible nanoparticles for molecular imaging

H. Weller, Univ. Hamburg (Germany)

The talk describes recent advances in the synthesis of highly luminescent and magnetic nanoparticles. It is shown that preparing the particles under continuous flow conditions allows reproducibility far beyond the limits of batch synthesis.

Special emphasis is put on the development of a protocol for ligand exchange against substituted polyethylene-oxide containing ligands. It is shown that small changes in the composition result in tremendous differences in stability against serum and buffer solutions and fluorescence quantum efficiencies in the biological environment. We present various types of ligands allowing reproducible and stable fluorescence properties of quantum dot and quantum rod systems.

We further present in-vitro and in-vivo data on molecular imaging with such modified quantum dots and superparamagnetic iron oxide nanoparticles for T1 and T2 contrast imaging. Examples for in vivo tumor targeting are given.

7909-55, Session 13

Microwaves and nanoparticles: from synthesis to imaging

K. E. Meissner, Texas A&M Univ. (United States); R. Majithiaa, Texas A&M Univ. (USA); R. A. Brown, Swansea Univ. (USA); L. V. Wang, Washington Univ. in St. Louis (United States); T. G. Maffeis, Swansea Univ. (USA)

No abstract available

7909-43, Poster Session

Differential distribution of dopamine functionalized quantum rods in mouse

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The conjugation of bioactive molecules to water soluble fluorescent semiconductors nanocrystals, opens new perspectives to the studies of drug distribution in target tissues and organs. The neurotransmitter dopamine (DA) is involved in a variety of signaling pathways and its altered levels have been found in different pathological conditions, such as Parkinson's disease and attention deficit hyperactivity disorder (ADHD). The possibility to modulate brain DA levels might hold great promise for therapeutic purposes. As free DA is not able to cross the blood-brain barrier DA based produg, such as galactosylated DA, GalDA, already proved to mediate DA diffusion across the BBB. With the aim to investigate the extent of their release/accumulation into target cells, we have recently produced fluorescent nanocrystals (Quantum Rods) conjugated to GalDA. Here, we characterize the pharmacodistribution of the functional abduct (GalDA-QRs) administered intravenously in mice. We present the selective distribution of GalDA-QRs one hour after injection and the relative amount detected ex vivo in different organs is discussed in the general frame of cell- and tissue specific interactions with nanoparticles, opening new perspectives in the design and feasibility to use inorganic nanoparticles for diagnosis and therapeutic purposes.

7909-50, Poster Session

Interactions between iron oxide nanoparticles and human lymphoblastoid cells studied by flow cytometry

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We report here the effect of the coating and aggregation state of engineered nanoparticles on their interactions with human lymphoblastoïd cells. The particles put under scrutiny were magnetic iron oxide sub-10 nm nanocrystals, which are used in several biomedical applications (MRI, hyperthermia). Coating strategies comprise low-molecular weight ligands such as citric acid and polymers such as poly(acrylic acid). Electrostatically adsorbed on the surfaces, the organic moieties form an adlayer around the particles and provide a negatively charged coating in physiological conditions. Flux cytometry performed in side- and forward-scattering configurations at 4° and 37°C reveals that cell/nanoparticle interactions depend on the coating, on the dose ([Fe] = 0.01 - 30 mM) and on the incubation time (0 - 24 h). One important result is the strong increase of the side-scattered intensity with increasing dose of citrate-coated particles. These later particles are found to precipitate in the cell culture medium [1], resulting in submicronic aggregates which adsorb at the surface of the cells in large amount, around 100 pg of iron per cell. This adsorption causes the increase of the flux cytometry signal. In contrast, the polymer-coated particles are taken up at much lower levels, 10 pg of iron per cell [2]. These results were confirmed by transmission electron microscopy (TEM). TEM reveals the existence of 200 - 500 nm layers of densely packed citrate-coated particles at the cell surface, as well as large clusters inside endosome-like structures. In contrast, polymer-coated particle are barely detectable at the cellular membranes and accumulate only in endosomes. The kinetics of adsorption and uptake for both particles are also presented. In this study, we demonstrate that the uptake of nanomaterials by living cells depends on the coating of the particles and on the ability of the coating to preserve the colloidal nature of the dispersions.

References:

[1] B. Chanteau, J. Fresnais and J.-F. Berret, Langmuir 25, 9064-9070 (2009)

[2] M. Safi et al. Nanotechnology 21, 145103 (2010)