Contributors to the Emerging Investigators issue

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This is the first time that *Lab on a Chip* has put together an issue that features the younger members of the community that are potential rising stars. We often hear the opinions of supervisors and leaders in the field, but rarely do we hear the voices of students, post-docs or young researchers. Therefore we decided to elicit the opinions of these emerging investigators on issues of current concern, such as the killer application, bottlenecks and issues as well as the future for this field. Their responses to the questions listed below are included at the end of each biography and we hope they give an idea of what problems young researchers face and their outlook and aspirations.

(1) *What is your view of the "killer application"?*

(2) *What are the main difficulties you face working in this area of research?*

(3) *What do you think the future holds for this field and these technologies?*

Amar Basu

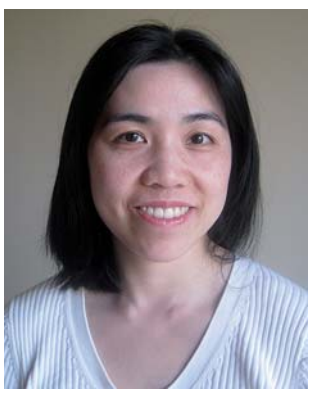
Amar Basu was born in Rochester, Michigan in 1978. He received BSE and MSE degrees in electrical engineering in 2001 and 2003, an MS degree in biomedical engineering in 2005, and a Ph.D. in electrical engineering in 2008, all with honors from the University of Michigan. Amar has worked for Intel's Advanced Technology group, General Motors, Silicon Graphics, and served as an adjunct faculty member at the University of Michigan from 2007–2008. Currently, Amar is assistant professor of electrical engineering and biomedical engineering at Wayne State University. His research interests are in developing multiphase fluidic and electronic technologies for high throughput screening in systems biology. Amar was a recipient of the Whitaker Foundation Biomedical Engineering Fellowship, and was voted IEEE Professor of the Year by students 2009. His work as a consultant with Mobius Microsystems and Picocal has resulted in a several US patents.

(1) *I think the killer app. will be high throughput screening for systems biology. The US National Research Council (NRC) emphasizes that next generation solutions to societal challenges in health, energy, food, and environment will be driven by a more comprehensive understanding of complex pathways and interactions in biological organisms. Accordingly, biological research is evolving from reductionist studies of single proteins and genes to system-wide 'omics' studies involving thousands of genes, proteins, and environmental conditions. This new model of research clearly requires instrumentation which can perform large-scale screens at a reasonable cost. Microfluidics, particularly droplet-based fluidics, is well positioned to make HTS affordable to researchers by dramatically reducing reagent consumption (the most significant cost of HTS) and capital costs of laboratory automation. Equally important, the ultra-high throughput capability of droplet-based fluidics is leading to promising new screening protocols, such as directed evolution.*

(2) *Interfaces and methods which convert screening libraries between the macro and micro domains are particularly challenging in droplet systems due to the precise volumes and high throughputs needed, as well as the large number of compounds in typical screening libraries. Other challenges include detection in small volumes, interdroplet diffusion, and the difficulty in performing complex fluidic handling (such as washing steps) required for immunological and other heterogeneous assays. Being able to integrate and automate high speed fluidic operations in a user friendly package is another engineering challenge which needs to be addressed. Generally speaking, the highly interdisciplinary nature of this research (involving fluidic phenomena, electronic detection/control, chemistry/biochemistry, and biology) makes it enjoyable but also challenging. Finding collaborators willing to invest time in high-risk technologies, and training new students in multiple skill-sets requires patience and earnest effort.*

(3) *I think that there is considerable promise in high throughput screening and droplet-based screening in particular. Although there are many practical issues which need to be addressed, the ability to perform screening in pL and fL volumes at unprecedented throughputs has the potential to transform biology in a profound way. For example, we are already starting to see screens in the range of millions which can be used for optimizing and evolving new enzymes, as well as new biological studies at ultra-low volumes. Given the rapid pace of technology development and its growing need in systems biology, I believe that multiphase fluidics will play a central role in the future of lab-on-a-chip technologies.*

Karen C. Cheung



Karen C. Cheung received her Ph.D. degree in bioengineering from the University of California, Berkeley, in 2002. From 2002–2005, she was a postdoctoral researcher at the Ecole Polytechnique Fédérale de Lausanne, Lausanne, Switzerland. She is now an Assistant Professor

at the University of British Columbia, Vancouver, BC, Canada. Her research interests include lab-on-a-chip systems for cell culture and characterization, inkjet printing for tissue engineering, and micro- and nanoscale implantable neural interfaces.

(1) *The killer app. might be successful replacement of entire animal studies using engineered constructs for drug testing.*

(2) *Students working in this area are very open-minded and they welcome the challenges in learning and understanding concepts in these interdisciplinary projects. We need to be able to find more collaborators in medicine and biology who have the time and are willing to work with us in order to really develop the technology for real applications.*

(3) *Although these technologies will bring a lot of benefit to our laboratory diagnostics, a larger impact may be seen in underdeveloped and poor communities. There, lab on a chip can be used to address global health issues. In developed nations, lab on a chip may bring incremental (some) improvement to healthcare. In the rest of the world, cheap, disposable, and rapid lab on a chip analysis could bring much more dramatic improvement to quality of life.*

David T. Eddington

David T. Eddington received a B.S. degree in materials science and engineering from the University of Illinois at Urbana-Champaign and Ph.D. degree in biomedical engineering from the University of Wisconsin-Madison. He joined the Department of Bioengineering at the University of Illinois at Chicago in 2006 after a postdoc in the HST program at Harvard/MIT. His research interests include developing novel solutions to current unmet experimental and clinical needs through applying simple microfabricated devices.

(1) *For academic research, this would be a device that tests new hypothesis or enables new experimental possibilities that would not be possible with currently available and standardized methods. For a commercial product, this would be a device that someone would want to buy. There are several useful LOC devices currently available that started in academic labs and turned into products such as chemotaxis assays, protein crystallization platforms, and high throughput PCR. The commercial successes of these will enable more to follow. However, even if there is no killer application bringing LOC devices to every biomedical research lab, they will remain as powerful tools enabling new possibilities.*

(2) *The main difficulty is identifying interesting new device designs that are also useful tools that others would benefit from and have not been previously demonstrated. I have many interesting ideas, but only a limited set would be useful.*

(3) *I think LOC devices will continue to offer new solutions for unmet experimental and clinical needs. The field is beginning to transition from proof of concept demonstrations to using these devices to learn something new. Even if few of these become commercial realities, they will continue to offer exciting possibilities for the research community.*

Axel Günther

Axel Günther is an Assistant Professor in the Department of Mechanical and Industrial Engineering with cross-appointment to the Institute of Biomaterials and Biomedical Engineering at the University of Toronto. He obtained his Ph.D. from the Swiss Federal Institute of Technology (ETH) in Zurich and conducted postdoctoral research at MIT. He has published >25 papers, patented 3 inventions (patent families) and has received the ETH medal (2002), Ontario Early Researcher Award (2009) and I.W. Smith Award of the Canadian Society for Mechanical Engineering (2010). Dr Günther is the Scientific Director of a new Centre for Microfluidic Systems in Chemistry and Biology in Toronto.

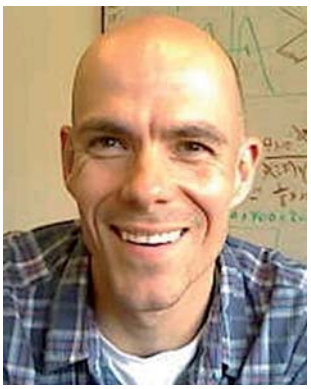
(1) *Ultimately successful applications of a technology are often found in quite unexpected and less obvious areas. In the area of biology, I see great opportunities in the comprehensive in vitro investigation of engineered tissues, small intact organs and organisms. In our contribution to this Special Issue, we demonstrate to our knowledge the first scalable approach allowing the structure and function of intact cardiovascular tissues to be assessed in health and disease (e.g., heart failure, diabetes, vasculopathies, tumor biology, and toxicology). The ability to routinely probe small artery function is expected to have wide implications in cardiovascular drug development and, ultimately, personalized medicine. I expect lab-on-a-chip systems to continue in providing new technological solutions that potentially translate to a number of disciplines, including the by now obvious candidates: analytical chemistry, molecular and cell biology, organic chemical synthesis. To complement the creation of new technologies, the scientific community has often to do a better job of translating microfluidic devices into commercially viable solutions. Only that way, microfluidic systems have a chance to become broadly available, mass-produced commodities. This translational aspect is not yet sufficiently addressed, partly because a true translation of the technology and not a mere mass-production of a chip are required. Robust and seamless fluidic world-to-chip interconnects and also hybrid concepts that allow us to combine existing (analytical) technology and lab-on-a-chip systems are of the essence.*

(2) *I thoroughly enjoy working in this field and don't face too many difficulties. I actually think that researchers in our field are quite fortunate, given the diverse*

range of opportunities. A challenge that is common to everyone conducting interdisciplinary science is the necessity of researchers with very different training attacking all (or most) aspects of a problem, not just the aspects closest to their traditional scientific training and experience. A microfluidics researcher working on a cardiovascular question for instance, will need to ultimately think about basic questions in vascular biology, and vice versa. Only such a multifaceted approach will lead to the detailed scientific discussions, sometimes controversial ones, necessary to answer relevant questions, not just device a "new toy". To reflect this need and comprehensively train future graduate students across disciplines involving nano/microfabrication, cell and vascular biology, analytical and materials chemistry, fluid mechanics and transport phenomena, approximately ten colleagues and I at the University of Toronto and its associated Teaching Hospitals and York University in Canada, Corning, Inc. (Corning, N. Y.) and CMC Microsystems (Kingston, ON) have recently launched the six year graduate training program in Microfluidic Applications and Training in Cardiovascular Health (MATCH).

(3) *The future of this field is exceptionally promising, for university researchers as well as for companies. The fact that commercial "killer applications" have yet to be demonstrated currently gives university researchers an edge in securing intellectual property. Companies on the other hand can adapt microfluidic technologies to their existing markets and expertise to serve real commercial needs with new technological solutions. Here are a few bolder options. Soon, we will likely see distributed, iPhone or iPad operated integrated microfluidic platforms that are portable, automated and will allow challenging chemical reactions that are otherwise confined to fume hoods or glove boxes to be routinely carried out. Low cost analytical devices will be widely used to screen water samples for pathogens and to comprehensively assess the interaction between carbon dioxide and sea water to gain an improved understanding of the carbon balance in the world's oceans. With respect to biological applications, tissue culture and life-cell imaging will be combined and broadly available in intuitive, portable devices as well as integrated with powerful high-content screening platforms.*

Carl Hansen



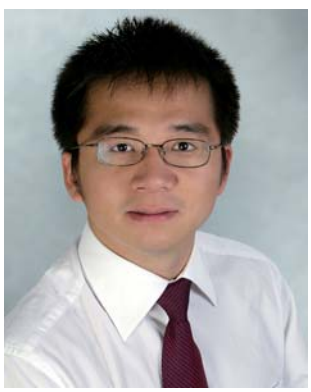
Carl Hansen is a an Assistant Professor in the Department of Physics and Astronomy at the University of British Columbia and the recently established UBC Center for High Throughput Biology. Dr Hansen holds a BASc in Engineering Physics and a PhD in Applied Physics from the California Institute of Technology. He is a Michael Smith Scholar in Biomedical Research, a Canadian Institute for Health Research New Investigator, and holds an affiliate faculty membership at the Institute for Systems Biology in Seattle. The Hansen lab works on the development and application of microfluidic systems for applied and fundamental research in genomics and cell biology. This interdisciplinary work uses methods ranging from microengineering, to single molecule detection, to live-cell microscopy. Specific research questions are focused around the themes of single cell analysis and genomic diagnostics with applications in the fields of stem cell science, cancer biology, microbiology, small RNA, and immunology.

(1) *I wouldn't say there is one obvious "Killer application" in microfluidics. Handling fluids is fundamental and microfluidics will likely have impact in research areas ranging from genetics, to diagnostics, to drug discovery. Ultimately the best applications are the ones that not only benefit both from economy of scale, but also are fundamentally improved in microfluidic implementations. In our work we have identified genomics and cell biology as important areas for development and these are well-suited to the specific technology platform we use. Other important areas include point of care diagnostics, chemical screening, chemical synthesis, protein engineering, and environmental monitoring. I expect that each of these applications will demand its own flavor of microfluidics.*

(2) *In our work we have been fortunate to interface with excellent collaborators from the biological sciences. This interaction is critical to working effectively in the field of microfluidics and also sets a high bar for new technologies. I would say that in our research the plumbing is now a solved problem. The main challenges are (i) finding innovative ways to outperform existing methods, (ii) getting control over the biology and the chemistry, and (iii) engineering a system to be reliable and robust.*

(3) *Microfluidics research will continue to thrive as a field with the emphasis increasingly turned towards applications. Although accelerated adoption of new technologies will be driven by commercialization, the range of applications will likely grow more slowly than demand. This means that customized technologies will be increasingly important and this will require more labs that can work effectively across disciplines. Moving forward I expect that the leaders in the field will be primarily concerned with answering biological questions, using microfluidics as one of several key experimental approaches.*

Tony Jun Huang



Tony Jun Huang is an Associate Professor in the Department of Engineering Science and Mechanics at The Pennsylvania State University. He received his Ph.D. degree in Mechanical Engineering from the University of California, Los Angeles (UCLA) in 2005, and

his B.S. and M.S. degrees in Energy and Power Engineering from Xi'an Jiaotong University, China, in 1996 and 1999, respectively. His research is focused on (1) multi-physics of active nanostructures, and (2) multi-physics of microfluidics and lab-on-a-chip systems, including acoustic microfluidics and optofluidics. He has authored or coauthored over 100 technical publications in these fields. His work on lab-on-a-chip has been highlighted in *National Science Foundation* and many public media such as *US News and World Report*, *Yahoo News*, *Live Science*, *Medical News Today*, *Science Daily*, *Wired Science*, *Popular Mechanics*, *Highlights in Chemical Technology*, *Nanotechnology Now*, and *R&D Magazine*. More information about him and his research group can be found at www.esm.psu.edu/huang/.

(1) *There are many important fields* (*e.g.*, *rapid point-of-care diagnostics*) *in which lab-on-a-chip systems can be quite useful. Many on-chip technologies developed in recent years have shown superior performance and have great potential to lead to "killer applications". However, I believe the key is whether we can provide simple and robust techniques that work well outside research labs. Fancy techniques that are not reliable or are difficult to employ in the real world just won't cut it. I have heard many complaints from the industry and colleagues that many devices currently developed are actually "Chips-in-a-Lab", rather than "Labs-on-a-Chip".*

(2) *In my opinion, one of the main difficulties in our field is that there is little to no incentive for university laboratories to invest limited research funds to address current challenges in applying our lab-on-a-chip devices to real-world applications. The pressure* (*especially for funding purposes*) *is always to come up with "novel" concepts and "novel" designs. Getting funding support to perfect our existing devices* (*so that it will actually do their job in real-world applications*) *is difficult.*

(3) *I believe that as researchers, although it is vital to constantly push the envelope of technology and innovation, we need to spend a little bit more time thinking about how to convert some of existing technologies into marketable products. I believe that there are many technological challenges that need to be overcome so as to ensure technologies that work well in the labs will also work well in the real world. Many of these challenges have been "conveniently" overlooked in the past; however, this situation has to change before the field of microfluidics and lab-on-a-chip lives up to its potential. Although challenges remain, I am optimistic that with so many talented people working in this field, the lab-on-a-chip community will be able to deliver many useful tools to support applications, innovations, and discoveries and have significant impact in the fields of biology, chemistry, and engineering.*

David Juncker

David Juncker was born in Switzerland, in 1973. He studied electronics-physics at the University of Neuchâtel in Switzerland, and spent one year at the National Institute of Metrology in Japan in 1998. He was at the IBM Zurich Research Laboratory under the supervision of Emmanuel Delamarche between 1999 and 2004 and received his PhD in 2002 from the University of Neuchâtel. After spending one year as a Post-doc at the ETH Zurich, he joined the Biomedical Engineering Department of McGill University in Montreal as an assistant professor in 2005. He currently holds a Canada Research Chair and directs the Micro and Nanobioengineering lab. His current research interests are capillary-force based microfluidics (including yarn-based devices) for diagnostics, antibody microarrays for biomarker discovery, nanocontact printing and microfluidic probes for microenvironment control of neurons, and lab on a chip systems for cell culture, cell filtering, and model organism manipulation.

(1) *The question of the killer application is one that I have heard repeatedly, and I think it's already there, we just haven't realized it. The LOC killer application existed before the concept of LOC was formulated, namely in the form of lateral flow diagnostic systems such as pregnancy tests that abide to the "sample in – answer out" vision of a lab on a chip applied to diagnostics. The question to me is "what can LOC contribute to science and society?" LOC devices will benefit science as an enabler for new research, and society directly by means of better diagnostics; there are already several devices in use for emergency care and they will likely expand from there.*

(2) *The interdisciplinary nature of our work, ranging from the development of novel microfabrication processes for making LOC, to yeast cell analysis and to multiplex biomarker validation in breast cancer patients sometimes leaves my brain fuming. But by working together as a team with my students and collaborators, we are able to tackle such complex questions while expanding our knowledge and having a lot of fun at the same time!*

(3) *The range of applications of LOC is staggering as it ranges from basic studies of fluid physics, to the manipulation of live organisms, and so is the range of applications. LOC will be used increasingly as a research tool, although they will probably be more an enabler rather than the end product, as for example in next generation sequencers that all integrate some microfluidic aspects, but are not particularly advertising it. The greatest opportunity for LOC lies in new applications where there is no precedent or alternative. I thus think that personalized medicine, which will require the repeated analyses of multiple molecular markers to monitor disease progression and response to treatment, will be one of the many areas that will drive the emergence of novel LOC-based systems.*

Hirokazu Kaji

Hirokazu Kaji is an Assistant Professor at Department of Bioengineering and

Robotics at the Graduate School of Engineering, Tohoku University, Japan. He received his Ph.D. (2005) in Bioengineering, M.Eng. (2003) in Biomolecular Engineering, and B.Eng. (2001) in Molecular Chemistry and Engineering from Tohoku University. His current interests include surface chemistry, microfluidics, biomaterials, and the application of micro- and nanotechnologies in the fields of cell and tissue engineering.

(1) *The "killer application" for lab on a chip technology has yet to be found from the point of view of biological applications. More research is required to find suitable applications that yield biologically meaningful outcomes in a simple manner. Also, assessment of the value of such applications by biologists will be important.*

(2) *This area is multidisciplinary and has many researchers from various fields. Although communicating with researchers from other fields may be difficult in a short period of time, collaboration with such researchers based on mutual understanding is very exciting.*

(3) *Micro- and nanoscale technologies have provided some insight into fundamental cell biology as well as cell and tissue engineering. This knowledge will be used to direct cell fates as a cell source or to be incorporated into newly designed biomaterials capable of controlling cell behavior. The continued challenges in this area will enable the creation of more physiologically relevant models suitable for fabricating tissues and make drug development and toxicology screening more reliable while decreasing the need for animal testing.*

Ali Khademhosseini

Ali Khademhosseini is a faculty member at Harvard-MIT's Division of HST, Brigham and Women's Hospital and Harvard University. He has edited 3 books and authored over 100 journal papers, 30 chapters and 17 patent applications. His research efforts have earned him the TR35 Award, the ALA Innovation Award, the early career awards from AIChE, NSF, ONR, EMBS, IAMBE and BMW, as well as the ACS's LaMer and the Unilever awards.

(1) *In my view the "killer application" of lab on a chip devices is still eluding the field. Clearly there have been some commercial successes in various diagnostics and analytical areas, however, there has always been a greater commercial potential than what has been realized so far. If history from other scientific areas, such as tissue engineering, may indicate, the killer applications often arrive with increased maturity of the field. Personally I feel that the killer applications may involve the use of BioMEMs systems for therapeutic applications as biological tissue substitutes or miniaturized implants.*

(2) *The major challenge of the application of the microdevices in tissue engineering has been the inherent limitation of the microfabrication technologies as a two-dimensional platform. We and others have developed a number of approaches to bridge the gap between the 2D microfabrication techniques and 3D microenvironments that are experienced by the cells in the body. However, despite much progress this remains a challenge in the field.*

(3) *The future looks bright for lab on a chip technologies. In particular diagnostic devices and high-throughput screening systems may revolutionize medicine and drug discovery processes. Also, microengineering approaches look highly promising for generating 3D engineered tissues for regenerative medicine and in vitro tissue models.*

Saif A. Khan

Saif A. Khan was born in Mumbai, India, in 1979. He received his Ph.D. in chemical engineering from the Massachusetts Institute of Technology in 2006, where he was an R. T. Haslam Presidential Fellow. In 2006 he joined the National University of Singapore (NUS) as Assistant Professor in chemical and biomolecular engineering. He was appointed Fellow of the Singapore-MIT Alliance (SMA) in chemical and pharmaceutical engineering in 2007. His current research interests include microfluidics, soft condensed matter physics, colloid science, plasmonic nanomaterials and chemical reaction engineering. His research group at NUS focuses on various aspects of microscale fluid physics and phenomena, with the aim of developing new experimental methods for chemistry and biology that complement or extend existing macroscopic methods.

(1) *We envision rapid, online, sequential separations from minuscule volumes of complex biological mixtures, containing large macromolecules (DNA, RNA, proteins, polysaccharides, etc.), smaller oligomeric molecules (such as micro-RNA) and other components such as salts. This is currently an extremely challenging time and resource intensive task.*

(2) *The most exciting aspect of this area of research, which can also be the most daunting, is its inter-disciplinary nature. Therefore, one of the key challenges is maintaining a constant and vigorous dialogue between experts from different scientific disciplines, and also between us, the 'method developers', and potential end-users.*

(3) *The field of 'compartmentalized' microfluidics with droplets and bubbles has rapidly expanded in the past few years. Droplet-based chemical and biological assays, essentially minaturized versions of macroscale experimental protocols, have been well demonstrated and have led to commercial ventures. The near future will see microfluidic methods that go beyond simply miniaturizing established macroscale protocols, offering fundamentally new capabilities that leverage physical and chemical phenomena specific to confined micro- and nanoscale fluid spaces.*

Michelle Khine

Michelle Khine is an Assistant Professor of Biomedical Engineering at UC Irvine and scientific founder of Shrink Nanotechnologies (Nasdaq:INKN). She was an Assistant & Founding Professor at UC Merced. Michelle received her PhD under Luke Lee in Bioengineering ('05) from UC Berkeley and UCSF. She co-founded Fluxion Biosciences in graduate school. Michelle was the recipient of the TR35 Award in 2009.

(1) *This technology enables the prototyping of custom and complete microfluidic devices in minutes. This would allow researchers to design on the fly with minimal costs and no infrastructure. Because we can also robustly integrate metallic nanostructures directly in the microfluidic channels for enhanced signal to noise ratio, this technology is particularly applicable for the development of low cost point of care diagnostics.*

(2) *I think whenever you try to do something radically different it is first met with skepticism. So the main challenge has been to prove how effective this technology is.*

(3) *Hopefully adoption by many labs! I sincerely believe that if we make it easier and faster to prototype innovative microfluidic designs, we will help catalyze the translation from research to real-world solutions for point of care diagnostics.*

Catherine Klapperich

Catherine Klapperich joined the faculty of the Boston University College of Engineering in 2003. She was promoted to Associate Professor in 2010. She is the director of the Biomedical Microdevices Laboratory in the Departments of Biomedical and Mechanical Engineering. She is also a member of the Center for Nanoscience and Nanotechnology at BU. Before coming to Boston, Dr Klapperich was a Visiting Postdoctoral Fellow at Lawrence Berkeley Laboratory in the lab of Dr Carolyn Bertozzi, and was a Senior Research Scientist at Aclara Biosciences in Mountain View, CA. She earned her Ph.D. in Mechanical Engineering in 2000 from the University of California, Berkeley; her M.S. in Engineering Sciences from Harvard University and her B.S. in Materials Science and Engineering at Northwestern.

(1) *I believe that the "killer app" in next generation microfluidics will be in the area of systems biology both as discovery tools and in patient care. The ability to look at large ensembles of single cells that are not synchronized will enable previously unimaginable discoveries in biology. As these technologies mature and new biomarkers for disease are validated, running large numbers of tests on a single patient will become feasible. In the best case scenario, faster and more precise diagnoses and treatments will lower the cost of care.*

(2) *Currently our major challenges lie in the areas of raw materials and standardization. It is very difficult to source quality controlled materials for small scale devices in which one is performing surface sensitive reactions. Standardization of device design (inlets, outlets, materials, etc.) is critical to the future of microfluidic device design.*

(3) *I think there is a lot of critical rethinking of lab on a chip technologies going on around the world right now in both industry and academia. People are really thinking about what is necessary to scale up these technologies to production levels. I've also had a significant increase in my interactions with non-engineers interested in deploying these technologies as research tools, so I'm quite hopeful about the future.*

J. Christopher Love

J. Christopher Love is an assistant professor in chemical engineering at MIT, an associate member at the Eli and Edythe L. Broad Institute, an associate faculty member at the Ragon Institute of MGH, MIT, and Harvard, and a member of the Koch Institute for Integrative Cancer Research. Dr Love received his Ph.D. in 2004 in physical chemistry at Harvard University. He extended his research into immunology at Harvard Medical School from 2004–2005, and at the Immune Disease Institute from 2005–2007. His research uses microsystems to characterize heterogeneity among single cells. Dr Love was named a Dana Scholar for Human Immunology and a Keck Distinguished Young Scholar in Medical Research in 2009.

(1) *Lab-on-a-chip technologies are beginning to mature commercially for miniaturized bioanalytical assays that replicate large-scale systems and for microscale synthetic chemistry. Validation of these classes of technologies will result from the deliberate demonstration of their usefulness in generating new fundamental discoveries in biology or chemistry that could not be made with existing tools.*

(2) *One difficulty is recruiting personnel with sufficient interdisciplinary training to work fluidly at the boundaries of chemistry, materials science, engineering, and biomedical research. New educational mechanisms that increase knowledge and practical awareness at these interfaces are essential for this developing area of research.*

(3) *There are many opportunities for lab-on-a-chip technologies, particularly those for single-cell analysis, in the fields of clinical immunology, disease pathogenesis, and vaccinology. New tools to characterize phenotypic and functional attributes of heterogeneous sets of primary human cells with correlated, dynamic measures are critical for those areas of biomedical research, especially when the volumes of samples of interest are very limited–for example, tissue biopsies. For lab-on-a-chip solutions to best facilitate the study of clinical samples, there is a need to develop and practice methods that conserve the samples available for analysis and collect multiple classes of data from the same cells. Shifting from unidimensional to integrated, multidimensional analytical processes is one of the current challenges facing the field of single-cell analysis.*

Matthew Munson

Matthew Munson received his PhD in bioengineering from the University of Washington in 2004, and completed one post-doctoral year at University of Chicago prior to being awarded a National Research Council post-doctoral fellowship at the National Institute of Standards and Technology, where he now holds the position of Research Bioengineer. His research has focused on exploiting the fundamental physical properties at the microscale to enable development and optimization of analytical tools for the quantification of proteins and the controlled perturbation of protein reaction networks, in both research and clinical applications. This work has spanned several distinct sub-disciplines such as continuous laminar flow, multiphase flow, and electrokinetic separations, as well as many different device platforms such as silicon, thermopolymer laminates, multilayer PDMS, and hybrid material devices. The views expressed here are his own, and do not reflect the views or policies of NIST or the US government.

(1) *As a scientist, I am interested in any technology or application that can be employed to enable the measurements necessary to test a hypothesis under investigation. As a developer of technology, however, the best technologies are the ones that can be used in the investigation of many different hypotheses. I believe that technology development in the non-commercial setting should lie at the intersection of these philosophies. As such, the killer application in this environment varies between hypotheses and is the tool that most clearly addresses the measurement needs at hand. I have found that microfluidics in general offers an ideal platform for the development of these applications because of the scalability, the deterministic nature of the underlying physics, and the potential for automation.*

(2) *The primary challenge I have faced in this area has been the selection of appropriate problems. The microfluidics community has a great depth of knowledge and understanding of physical phenomena at the microscale. As such, once relevant problems are identified, we have an extensive toolkit that can be applied to their solution. The great opportunity of this challenge is to make connections with scientists in other disciplines who have well defined measurement needs that cannot be addressed by other means. When these connections are made, great science emerges that furthers both the technology developer and basic scientist.*

(3) *I think the future will be dedicated to thoughtful application of the technologies developed within this field to the solution of real research and commercial problems. As we begin to embrace the entirety of the microfluidic toolkit, and abandon the narrow focus that comes with specialization we will be able to solve increasingly complex and increasingly interesting scientific problems. In turn, the application of all available tools to interesting problems will highlight areas where the current toolkit is lacking and will inspire development of new tools that are complementary to the existing ones.*

Shashi Murthy

Shashi Murthy is an Assistant Professor in the Department of Chemical Engineering at Northeastern University in Boston, USA. Prof. Murthy established his laboratory at Northeastern in 2005 following postdoctoral work at the Harvard Medical School and Massachusetts General Hospital under Prof. Mehmet Toner where he designed microfluidic devices to isolate lymphocyte subpopulations from blood. The major thrust areas in his laboratory currently include microfluidic isolation of stem/progenitor cells for regenerative medicine, ocular diagnostics, new materials for adhesion-based cell capture, and understanding cell-level phenomena in the context of microfluidic flow. Prof. Murthy is the recipient of U.S. National Science Foundation's CAREER Award (2008), the agency's most prestigious award for junior faculty members, and the Søren Buus Award for Outstanding Research in Engineering at Northeastern University (2009). He has authored over 30 publications in the areas of microfluidic cell separation and biomaterials. He earned his Ph.D. in Materials Science & Engineering at MIT in 2003 and his B.S. in Chemical Engineering at Johns Hopkins University in 1999.

(1) *I don't think that there will be a distinct "killer application." Rather, I think that the potential is significant for a single product and/or brand based on microfluidic technology to stand out among similar products that may or may not use microfluidic technology. The best analogy that I can think of is the iPod, which already stood out when it was first released many years ago and continues to do so,*

despite the existence of numerous other products with similar capabilities.

(2) *The two main challenges that I face working in this area are skepticism ("why do you need a microfluidic device to do this?") and high expectations ("when will this device be available in clinics worldwide?"). These challenges may seem contradictory but they can be better understood considering that the former challenge mainly comes from fellow researchers and funding agencies whereas the latter comes from the general public and the media. The first challenge is an extremely important element in our work in this field; simply put, if miniaturization has no clear advantages over conventional approaches, it is simply not worth the effort from an applications perspective. Dealing with high expectations however, particularly in medical applications, is not quite as clear-cut. It is important for us as members of this research community to sustain excitement in the minds of the general public for the potential of this field but at the same time, expectations need to be balanced with the realization that microfluidics is not all that different from other areas in terms of the lag time between discovery and market availability.*

(3) *I think that this is a very exciting time to be a researcher in this field. The potential for microtechnologies in a wide range of areas has been proven, key scientific and engineering principles have been recognized and formalized, and a healthy level of skepticism exists in evaluating research findings and commercial prospects. All of these factors will contribute to a bright and exciting future for the field. Based on my own expertise, I envision major contributions to the fields of clinical medicine, biology (cell and molecular), and chemistry (synthetic and analytical).*

Aydogan Ozcan

Dr Aydogan Ozcan received his Ph.D. degree at Stanford University Electrical Engineering Department. He is currently an Assistant Professor at UCLA, leading the Bio- and Nano-Photonics Laboratory (http://innovate.ee.ucla.edu/) at the Electrical Engineering Department. Dr Ozcan holds 17 issued patents and another 8 pending patent applications; and is the author of one book and the co-author of more than 110 peer-reviewed research articles in major scientific journals and conferences. Dr Ozcan received several awards including NSF CAREER Award, NIH Director's New Innovator Award, ONR Young Investigator Award, IEEE Photonics Society Young Investigator Award and MIT's TR35 Award for his seminal contributions to near-field & on-chip imaging, and telemedicine based diagnostics. Dr Ozcan is also the recipient of the National Geographic Emerging Explorer Award, Gates Foundation Grand Challenges Award, Netexplorateur Award, the Wireless Innovation Award given by the Vodafone Americas Foundation, as well as the Okawa Foundation Award.

(1) *One of the most important signs of a killer application is that you should be able to explain it to your grandparents in an elevator within less than a minute, and still deeply excite them with the prospects of your work. If this combines with solid research and development validating those prospects, this would indeed be a successful killer application of an idea.*

(2) *Addressing global health challenges, especially in third-world settings, requires a different mindset. You cannot readily assume that most of the well established technologies that shaped our thinking for decades would be available or would even be functioning in such resource poor settings. As a result, we need to detach ourselves from conventional designs, and rethink the solution for these challenges. This often requires an interdisciplinary effort, which needs both depth and breadth in various fields to provide a well engineered solution.*

(3) *One of the most impactful things that the consumer electronics market brought to our lives is the cellphone. Benefiting from this revolutionary platform, telemedicine will surely help us to address several global health challenges that we face today; and in this regard we will see new telemedicine based technologies that aim to make the most out of this digital platform. Hopefully, the end result will make life simpler for everyone, helping to close the gaps between the developed and the developing nations.*

Adrian Ozinsky

Adrian Ozinsky is a medical doctor who received a Ph.D. in biochemistry from the University of Cape Town in 1996. After a postdoc in immunology at the University of Washington, he joined the Institute for Systems Biology in 2000, where he became a Faculty member in 2005. His current research focuses on developing tools that can isolate selected cells from patients, and can resolve the behavior of relevant cells from the complex population typically present within each sample. The need to discern responses at the level of individual cells underlies many key challenges in shaping immunity against infections and developing effective vaccine responses, and in probing the steps underlying cancer metastasis. The ISB provides a unique collaborative and interdisciplinary environment to develop new tools, to use the technology to probe immunity and cancer biology, and to collaborate with superb groups at other institutions.

(1) *One view is that success should be claimed when microfluidic devices are the default tool that are used on a daily basis, such as how mRNA quality now routinely is assessed with the Agilent bioanalyzer. The vision that inspires me is to aim for a landmark accomplishment, such as a medically-relevant discovery that could not easily have been achieved by other*

means. This type of application likely would exploit several of the key advantages of the microfluidics approach, and should combine elements of miniaturization, integration, scaling/parallelization, and automation. We are trying to bring these themes together with a device that is able to measure multiple proteins from each cell of a population of mammalian cells. We anticipate that great insight will follow from measurements that reveal the manner in which individual cells are regulated, and bypass the roadblocks to interpretation imposed by averaged data.

(2) *A personal difficulty has been undertaking device development research in a laboratory that previously was focused on biology, and did not have researchers with physical science/engineering training. I was surprised by the relative lack of support by biologist colleagues who preferred to leave device development to others, and advanced their careers by focusing on applying the current generation of available analytical tools rather than developing next-generation tools. I believe that at each moment, science faces critical challenges, and one current challenge lies with purifying relevant cells for analysis and analyzing them directly, while rigorously excluding irrelevant cells. Another challenge within the academic setting is to go beyond the development of a proof-of-concept device, and to be able to develop a device to the point that it readily can be applied by a biologist. Furthermore, academic biologists seem reluctant to credit the incremental successes along the path of development, and express interest only when the final device is fully-operational and has been validated.*

(3) *While the reality is that few biologists currently utilize microfluidics devices, I think one should be inspired and motivated to develop solutions to critical biological challenges that face researchers and that are not solved with current-generation tools. With the clear recognition of the central role that the cell plays in our conception and understanding of biology, it is not outrageous to anticipate the extraordinary benefits that will result from the widespread application of analytical tools that will provide measurements with single-cell resolution. It is not hard to envision the benefits of moving beyond a dependence on averaged data that suggests what cells might be doing, and towards single cell data that provides insight into what cells actually are doing.*

James M. Spotts

James M. Spotts began his career as a chemist, first at Dartmouth College and then at the California Institute of Technology where earned a doctorate in chemistry in 1998 for laser spectroscopic studies of gas phase metal solvent clusters. He then shifted his research focus to biology, pursuing postdoctoral research in molecular and cellular neuroscience at Children's Hospital Boston and Harvard Medical School. In 2005, he joined to the Institute for Systems Biology as a Senior Research Scientist, where he has focused his efforts on developing microfluidic platforms to perform quantitative measurements from single mammalian cells. Current research projects include the development of devices to perform highly multiplexed protein expression measurements from single cells, to capture and culture single mammalian cells within isolated assay chambers, and to measure single cell transcriptomic profiles.

(1) *Biological and biomedical research is entering a phase where a detailed understanding of cellular processes at the single cell level is paramount. A first order "killer application" would directly perform quantitative, highly multiplexed measurements of one cellular variable, either mRNA or microRNA expression, protein expression, or protein post-translational modifications, from each of hundreds to thousands of isolated single cells. Molecular-level snapshots such as these would enable the first direct comparisons of cellular processes between individual cells, and could reveal correlations in behavior that shed new insight into biological function and responsiveness – information that is inaccessible using standard population-based measurements of cells. A higher order and more distant "killer application" would combine two or more of these single cell measurement capabilities within a single experimental measurement platform. By defining the state of a cell along two or more dimensions, unprecedented detail would be gained about how molecular information is processed and integrated by different molecular agents working in concert within an isolated cellular network.*

(2) *There are two key challenges that we continuously confront as device developers on one hand, and as research biologists who want to perform routine measurements using these devices on the other. The first challenge is how to bridge the gulf between the often limited functionality of a proof-of-concept device to a scale and format compatible with the routine workflow of the average bench biologist. Merging devices to a standard 96- or 384-well assay format remains inaccessible given the resources of an average academic laboratory, although commercial entities such as Fluidigm have achieved elegant solutions to his challenge. The commercial availability of a standardized assay plate with flexible, defined format onto which custom microfluidic devices could be adapted would be invaluable. The second challenge that we encounter is how to best merge different measurement applications that are often best suited to different materials and formats. The available choices can impose compromises in order to achieve some level of functionality at the expense of performance, or require the adoption of more complicated fabrication procedures and designs that, in turn, impose greater demands on the end user to operate the device.*

(3) *There is little value to this ongoing background debate whether microfluidic technologies have or have not had a significant impact to date. The bottom line is that the scale, sensitivity, sample numbers, and degree of measurement multiplexing necessary for biomedical researchers to explore new frontiers of biological and biomedical inquiry will require micro/nanofluidic technologies. As agents who can guide this transition, we need to*

maintain focus not only on developing devices that directly address the key roadblocks to these groundbreaking applications, but also on how to best translate these proof-of-principle technologies into commercial products that will encourage broad adoption by the biomedical community. Achieving this, impact will invariably follow.

Todd Squires

Todd Squires earned a B.S. in Physics and B.A. in Russian literature at UCLA, then spent a year as a Churchill Scholar at Cambridge University. He earned his Ph.D. in physics at Harvard University, focusing on problems in colloidal hydrodynamics and electrokinetics. He then spent three years as a Lee A. Dubridge Prize Postdoctoral Fellow and National Science Foundation Mathematical Sciences Postdoctoral Fellow at the California Institute of Technology, where he continued theoretical work in electrokinetics and microfluidics, and initiated new studies of nonlinear microrheology. Squires has been on the chemical engineering faculty at the University of California Santa Barbara since 2005. He continues to investigate a range of topics in micro-scale fluid mechanics and transport, both experimentally and theoretically. Honors include the NSF CAREER Award, the Beckman Young Investigator, the Camille and Henry Dreyfus Teacher-Scholar award, the 2009 Francois Frenkiel Award, the 2010 Allan P. Colburn Memorial Lecturer, and the 2010 Pierre-Gilles de Gennes Prize.

(1) *For me as a scientist, the "killer application" is truly the lab on a chip itself. The clean room can serve as an exquisite "machine shop" to construct experimental laboratories that can probe fundamental scientific questions in a way that would be otherwise impossible. More broadly, I feel there are many "killer apps" for microfluidics, ranging from cheap, fast, disposable medical diagnostic chips (enabled by the small sample volumes and favorable physics/chemistry) to micro-reactor/fabrication chips for the synthesis of designer materials. Our lab has been investigating electrokinetic effects, largely to develop intuitively clear (but quantitatively accurate) pictures to understand the core physico-chemical effects that arise in these systems. At the same time, however, we are pursuing strategies that would employ induced-charge electrokinetic effects to establish high fluid pressures with low, AC voltages – with the ultimate goal of enabling small electrokinetic pumps that could drive fluids in arbitrarily complex chips in a way that would be portable or even implantable.*

(2) *The difficulties we face are many – electrokinetic effects are, at their core, interfacial effects. As such, they depend sensitively on the chemical equilibria established between the surface and the electrolyte. One's ignorance of the precise state of the surface can limit one's ability to predict – and thus rationally design – electrokinetic devices. The work described here makes quantitative predictions for the induced-charge electrokinetic flows over a precisely-defined surface, and finds quantitative agreement with experiments. Using "controllably contaminated" surfaces, however, gives flows that are 10–100 times slower than one would expect over "clean" metal surfaces. Understanding why these flows are slow does not change the fact that they are. With what we've learned here, we're now working to explore and design material systems that will maximize ICEK flows, with the hope of developing surfaces that will give robust, strong flows in a range of conditions.*

(3) *As for the future, several outstanding questions remain concerning electrokinetics, where existing theories make predictions that are wrong on even a qualitative level. Such discrepancies reflect gaps in our core understanding, which I suspect will be resolved within the next decade. Again, microfabrication allows one to precisely define systems to probe key questions in a way unthinkable decades ago. More broadly, I've been fascinated by the growing level of sophistication the community has shown in manipulating ion transport – whether for ICEK, concentration polarization and preconcentration, water desalination, directed self-assembly of colloids and nanoparticles, and electric double-layer capacitors ('super-capacitors') for energy storage. It seems that interesting, fundamental scientific questions as well as compelling applications, will persist for the near future.*

Shoji Takeuchi

Shoji Takeuchi received the B.E, M.E., and Dr Eng. degrees in mechanical engineering from the University of Tokyo, Tokyo, Japan, in 1995, 1997, and 2000, respectively. He is currently an Associate Professor in the Center for International Research on Micronano Mechatronics (CIRMM), Institute of Industrial Science (IIS), University of Tokyo. His current interests include membrane protein chips, bottom-up tissue engineering and bio-hybrid MEMS. He received several awards including the award for Advanced Research from the Japan Society of Medical Electronics and Biological Engineering in 2001, Young Scientists' Prize, the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology in 2008, and the JSPS prize from the Japan Society for the Promotion of Science in 2010.

(1) *Our group has proposed a meander-shaped dynamic microarray that can transport, immobilize and make an array of samples efficiently with a small amount of sample volume since all of the introduced*

beads can be trapped at each site sequentially. We believe our device presented here as paired sample array can be applied to observe molecular diffusion and analyze cell–cell interactions between the two samples; these analyses are very important in the pharmacokinetics studies and tissue engineering and so on.

(2) *We had some trouble trapping small samples (smaller than 2 μm), and elastic samples such as single cells, liposomes or micro droplets; they tend to pass through the narrow channels after trapping. I think that, as the next challenge, we need to add some mechanisms in the fluidic channels to overcome the above problems such as micro pillars, valves and electrodes and so on.*

(3) *In the near future, we will try to improve the dynamic microarray by adding new functions such as: (i) to make an ordered array of heterogeneous samples, (ii) to release all samples at once for reuse, (iii) to increase the density of sample array by modifying the design of the channels, and (iv) to trap a variety of samples such as single cells, protein-coated microbeads, liposomes and spheroids.*

Wei Wang

Wei Wang received his Ph.D. degree at the Aerospace School, Tsinghua University, China, majoring in Thermal Engineering, in 2005. After that, he joined the MEMS research center in Peking University (China) as a postdoctoral researcher. From 2007, Dr Wei Wang started his research group on micro/nanofluidics in Peking University (http://ime.pku.edu.cn/~microfluidics/). Presently, Dr Wei Wang is an associate professor in Institute of Microelectronics, Peking University and the vice director of MEMS research center in Peking University. Dr Wei Wang's research interests include polymer micro/nanofabrication and micro/nanofluidics. So far, Dr Wei Wang has published more than 20 peer-reviewed journal articles on related topics.

(1) *For me, it's hard to say there are any killer apps in micro/nanofluidics, as we are still on the way to succeed in real commercial applications. But, I would love to take what Prof. G. Whitesides did on the PDMS based soft-lithography and what Prof. A. Manz did on the continuously-flow (bio) reactor as killer applications in the micro/nanofluidics society, as they really changed our minds on how to do micro/nanofluidics and what micro/nanofluidics can do.*

(2) *As a researcher with a fluid mechanics and microelectromechanical system (MEMS) background, I'm facing difficulties in communication with researchers in the fields of biology or medicine, not the problem of personal communication ability, but the difficulties in establishing 'bridges', rethinking disciplinary borders, and discovering modes of collaboration among people whose 'meanings' and 'processes' are very different, as said by Ronald Schleifer in Stanford Humanities Review, 1995, 4(1).*

(3) *No doubt, micro/nanofluidics holds a bright future, especially when people pay more and more attention to their health, and the micro/nanofluidics technologies have been widely acknowledged as worthy potential solutions for points of care, local health monitoring, disease diagnosis, or even clinical treatments. In my opinion, the main issue which may affect the future of micro/nanofluidics in the above fields is the price/performance ratio of the product. We do need to find out a way to make micro/nanofluidics devices with a reasonable price/performance ratio. To achieve this target, I really think we should learn more from the existing successful technologies, such as integrated circuit (IC), and some microelectromechanical systems (MEMS) applications.*

Justin Williams

Justin Williams is an Associate Professor of Biomedical Engineering at the University of Wisconsin-Madison. He obtained his Masters and PhD in Bioengineering from Arizona State University in 2001. He followed with postdoctoral fellowships in Neurosurgery at the University of Wisconsin and in Neuroengineering at the University of Michigan. He joined the faculty at the University of Wisconsin in 2003 as an Assistant Professor. His research program is centered around the development of implantable microtechnology for treating neurological disease and microfluidic platforms for studying basic neurobiology.

(1) *I think an area where LOC applications are poised to make significant progress is in the field of basic biology. An application that could simultaneously explore a myriad of factors, and their interactions, that influence a cell's microenvironment, growth and development would be especially powerful to the biological community. Ideally, this technology would also be robust, scalable and amenable to automation, which are some of the reasons why it remains an illusive challenge to the LOC community.*

(2) *One of the difficulties we face is in trying to get researchers in other fields to adopt new technologies. There are a number of issues we face in this regard, but in particular, validation of new microtechnologies against existing more standardized techniques can be challenging. For example, there are many different reasons why cells may grow differently in microfluidic environments; some are insightful, others may just be artifacts. It can often be difficult to tease out these differences, and can be a particular stumbling block for new investigators in this field.*

(3) *The field continues to expand at a rate that can make it difficult to keep up with at times. As fast as it is expanding though, there is clearly still room for continued growth. In the future I hope that microtechnology is going to become ubiquitous in many current fields and will start to emerge into areas that haven't even been considered yet.*