Report on Nano-Electronics, -Photonics, and –Magnetics: Acquiring

Prepared by: Steve Blair, Leon Chua, Anupam Madhukar, Gail Brown, Paul Evans, Charles Paulson, Axel Scherer, Scott Meller

1. Vision

[**LC**] The "rods" in human retina can sense a single photon of light and the human eardrum can detect ultraweak sound waves at nearly the level of Brownian motion. Both senses exploit an array architecture and lateral inhibition to achieve the ultimate in smart sensing. The rod achieves over 10 decades of dynamic range by adapting ambient brightness of neighboring cells. The eardrum achieves frequency coding via an array of spectrum analyzers. Nature has also evolved unique mechanisms for efficient recognition of molecules, such as complementary pairings of DNA and antibody-antigen matching, for example.

[**LC**] One "Grand Challenge" for acquisition is to leverage nano-electronics, -photonics, and –mangetics with nature's organizing principles to design smart, adaptive, and multi-modal sensors with high sensitivity, selectivity, and dynamic range. Smart nanosensors can emulate nature's optimized sensors through a locally-interacting cellular architecture, such as the cellular nonlinear network (CNN), using point-wise local adaptation and lateral inhibition to significantly enhance sensitivity and dynamic range by several orders of magnitude over "raw" signals. [**SB**] These principles serve as the enabling tools for a diverse range of acquisition problems, including the identification of individual molecules, real-time nanoscale imaging, the exploitation and augmentation of biological sensory systems, and the acquisition of multi-spectral signatures from the terahertz to the ultraviolet. [**AM**] Smart acquisition and processing applied to *in-vivo* environments for neural prosthetics that restore or augment damaged vision or memory are visionary examples of Grand Challenges in human health.

2. Current State-of-the-Art

2.1. Nanoantennae (Receivers, Transmitters, Tranceivers)

[**SB**] Nanoantennae and nanometric light sources are essential elements of nanophotonics, with the former serving as efficient couplers between nanoscale devices and microscale light and the latter as near-field excitation sources. Nanoantennae thus provide the means for information transport across the nano–micro interface from the UV-visible to the IR.

[**SB**] Semiconductor quantum dots (QD) can be used as nanoantennae and nanometric light sources. Semiconductor QD's are important because their electro-magnetic properties can be tuned via quantum size effects. [**AM**] In recent years two independent classes of semiconductor quantum dots have emerged with considerable potential for advancing nanotechnologies relevant to information sensing, processing, communication, and computing. These are the semiconductor epitaxial island quantum dots on a

crystalline substrate such as InAs/GaAs, Ge/Si, etc. [1,2] dubbed self-assembled quantum dots (SAQDs), and the colloidal semiconductor nanocrystal quantum dots (NCQDs) such as CdS, CdSe, core-shell CdSe/ZnS, InAs/ZnSe, etc. in solution [3,4]. The SAQDs have led to advanced devices such as ultra low threshold and high speed lasers [5] and long wavelength infrared detectors [6] that are already competitive with their counter part, the established quantum well based devices, and hold promise for significantly higher performance. By contrast, the strength and use of the colloidal nanocrystal quantum dots is as improved luminescent labels for biological molecules and cells in solution and adhered to surfaces [7-9]. [**SB**] Recent developments have enabled semiconductor NCQD's with transition energies in the near-infrared spectral regime. In particular, InAs/ZnSe based and lead-salt semiconductors (PbS, PbSe, PbTe) [1] have strongly size-quantized optical transitions in the near-infrared. Synthesis problems have been solved with the demonstration of monodisperse colloidal synthesis [2]. [**AM**] The added unique and novel quantum nanostructures that the integration of the strengths of these two disparate classes of semiconductor quantum dots can provide in hybrid structures for information sensing and processing in ambient and solution environments are being investigated and hold considerable promise of opening new paradigms of information sensing, transduction, and amplification in one integrated step [10].

[**SB**] Plasmonic nanostructures can serve as efficient optical nanoantennae and enable efficient coupling with visible and IR light. Over the past few years, quantitative and predictive methods have been developed for controlling the plasmonic spectral response of metallic nanostructures for their deployment as optical nanoantennae [3]. For example, core-shell dielectric metal geometries, or plasmonic nanoshells, have been shown to have high quality factor in their tunable plasmon resonance [3], and can be used as optical nanoantennae for efficient coupling to light at any frequency in the visible and IR.

[**SB**] Plasmonic nano-antennae can be designed to focus micrometer-scale light into nanoscale volumes with high spatial and spectral control of the concentrated energy. Bow-tie nanoantennae can efficiently concentrate light into 10nm gaps between the two wings, with local field enhancement up to 10^4. [4] C-shaped metallic apertures have been shown to possess similar properties [5]. Other nanoantennae structures can concentrate light incident over a large area into a small nanometer-scale aperture in metal film. Bulls-eye structures consist of concentric grooves with a single sub-wavelength aperture at the center. The annular grooves have radii that differ by the design wavelength. Optical transmission measurements demonstrate that the bulls-eye structures allow for 125x greater transmission than an equivalent bare aperture with no surrounding nanostructure. [6] The wavelength of peak optical transmission is directly related to the groove periodicity and the effective refractive index of the surface plasmon wave that mediates the enhanced transmission. At the resonance wavelength, the surrounding surface corrugation creates a region of high electric field strength near the entrance of the aperture. A portion of the concentrated field evanescently couples through the aperture and radiates into the far-field. The geometry of the corrugation on the back-side of the

structure greatly affects the near- and far-field field radiation patterns.

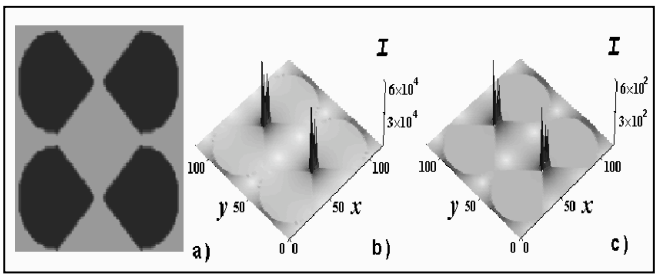

Fig. 4. Bow-tie nanoantennae and enhanced local fields calculated for λ=0.5 and 0.8μm. Shalaev, Purdue Univ.

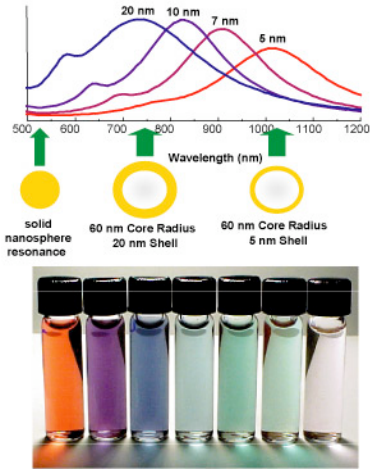

Fig. 5. Upper: silica core-gold shell nanoshell resonances as a function of their core-shell ratio. Lower: gold nanospheres (left) and gold nanoshells, with resonances that span the corresponding wavelength range indicated above. Halas, Rice Univ.

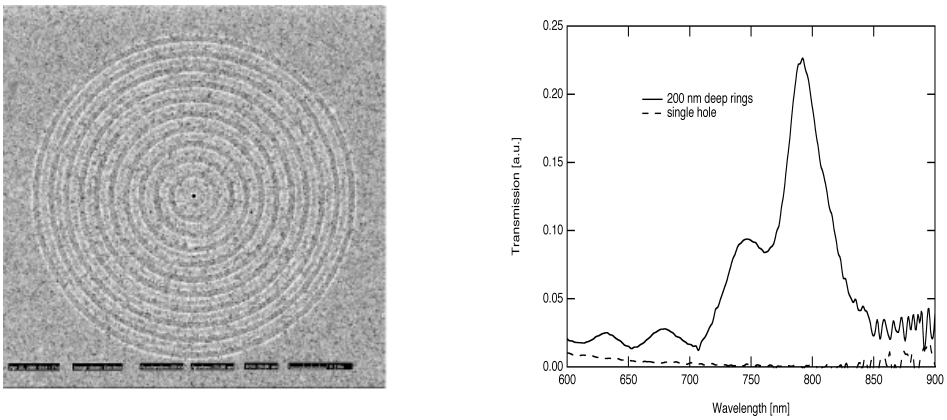

Fig. 6. (a) Electron micrograph of a single sub-wavelength aperture with surrounding periodic surface corrugation. The pattern was formed by milling a bullseye pattern into a sapphire substrate and subsequently overcoating the substrate with 300 nm of silver. As a final step, a 200 nm diameter aperture was fabricated at the center. (b) Zero order transmission for the bullseye structure and an equivalent bare aperture with no surrounding surface corrugation with normal incidence optical illumination. The traces correspond to measurements obtained using a white light source. Nahata, Univ. of Utah.

2.2. Molecular Detection

[**PE**] The development of sensors with single-molecule sensitivity and high selectivity hinges on the integration of biological molecules such as nucleic acids, antibodies/antigens, and other receptors, and simpler organic materials for chemical passivation or activation. The interface of inorganic and organic systems includes problems at a range of length scales extending from single atoms to the conformation of large macromolecules. The potential of this integration has already been demonstrated: sensors for specific antibodies, oligonucleotide sequences, and specific molecules. Traditionally, these devices have been formed as bulk systems but the nanoscale analogs of these systems have been shown to have high sensitivity and the possibility of design-in functionality using well-defined interfaces. The electrical and optical properties of molecules are at the heart of sensors, but are understood only in limited circumstances. The interfaces of relatively simple molecules with surfaces are within the realm of simple extensions of present theoretical and characterization techniques. Biological molecules are orders of magnitude larger and will require unique new tools, but promise a vast new class of sensors and integrated materials.

[**PE**] The formation of biological-inorganic interfaces has steadily progressed. The thiol-based attachment of large molecules to gold surfaces has been one of the enabling technologies for sensor modalities based direct electrical measurement or the resonant enhancement of spectroscopic and non-linear signatures of molecules. Chemical functionalization of electronic materials including silicon, carbon, and II-VI nanostructures is rapidly progressing, notably with the introduction of intermediate molecular terminations of attached molecules that can be the basis for more general functionalization.

[**SB**] Nanoantennae have been used extensively in molecular detection applications by attaching metallic nanoparticles and semiconductor quantum dots to molecules for use as mass labels [7], fluorescence labels [8], and light scattering labels [9, 10], for example. Nanostructured metallic surfaces have also been studied extensively for surface-enhanced fluorescence [11] and Raman scattering (SERS) [12], where single-molecule detection can be obtained [13]. One of the major drawbacks of these surface-enhanced techniques is that if the nanostructure is random (or possesses fractal order), the fluorescence or Raman enhancement factors are spatially-varying as evidenced by random “hot-spots” on the surface [14]. The hot-spot effect makes these techniques unsuitable for quantitative detection, especially in an array format, as the average enhancement over a defined sensing zone may not be very high, and the enhancement from zone to zone may vary. As a result, there have also been efforts in which molecules are attached to lithographically-defined arrays of metallic nanoparticles [15, 16]. With these architectures, uniformity in nanoparticle size, shape, and spacing result in well-defined enhancement in terms of magnitude and spatial location. One of the benefits that can be obtained via proximity of a fluorescing molecule to a metal surface is that of increased quantum yield, which is a strong function of the separation from the metal surface, and reaches its maximum enhancement in the 3 to 10nm range [11, 17]. However, these techniques do not provide complete isolation from background produced by unbound species as uniform

illumination can excite fluorescence from molecules located between nanoparticles, which emits in the same direction as the fluorescence from bound target molecules. For higher-order (i.e. nonlinear) processes, such as SERS or multi-photon fluorescence, these techniques can have strong isolation. In both regular and random nanoparticles arrangements, many of the drawbacks can be solved by using a scanning confocal arrangement in which both excitation light and fluorescence are delivered through a high numerical aperture objective.

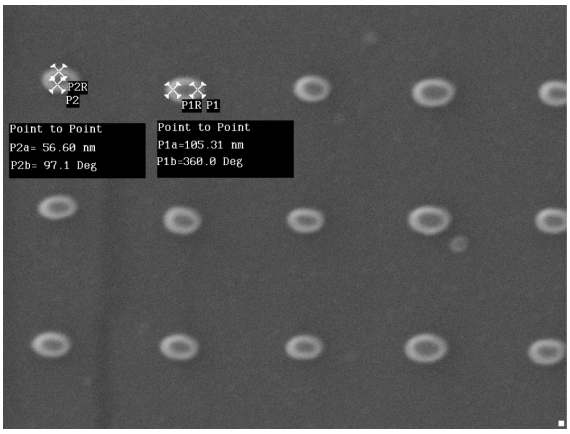

Fig. 7. Periodic array of elliptical gold nanodots, which are roughly 57nm by 105 nm. Blair, Univ. of Utah.

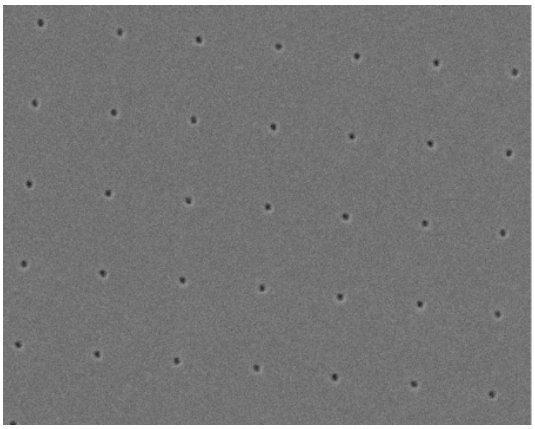

Fig. 8. Periodic array of metallic nanoapertures in gold. The lattice spacing is 1 μm. Blair, Univ. of Utah.

[**SB**] Another regular array architecture is that of periodic arrangements of nanoapertures in metal films, which are known to exhibit enhanced light transmission properties [18]. Under the condition of light transmission, which corresponds to the excitation of surface-plasmon modes, incident light is enhanced within the nanoapertures. Molecules located within the nanoapertures therefore experience enhanced optical excitation [19], but also experience enhanced fluorescence and their fluorescence signal is strongly isolated from that produced by molecular species that lie outside the nanoapertures [20].

[**SB**] Natural and artificial nanopores and nanotubes are additional enabling technologies for nanoscale acquisition. Nanopores and nanotubes can be used for a variety of nanofluidic, biosensor, and molecular-electronics devices. Self-assembled alumina nanopores, for example, can be used directly in many of these applications, or serve as templates for nanotubes constructed from metallic, semiconducting, and dielectric media [37]. Lithographically-defined nanopores have been used in measuring the electrical conduction properties of single molecules [38]. Nanopores integrated with silicon MOSFET technology may allow the real-time electrical identification of molecules passing through the nanopore [39].

2.3. Nanoscale Imaging

[**SB**] A variety of nanoantennae have been employed for a number of imaging modalities, enabling effective resolutions beyond that predicted through the classical Rayleigh criterion. In biological media, for example, semiconductor nanocrystals have been employed as nanoscopic light sources via fluorescence imaging [24]. Metallic nanoanteannae don't suffer from photobleaching or "blinking" and have been used to provide nanoscale contrast in scanning electron microscopy [25], single and multi-photon optical imaging methods [26,27], surface-enhanced Raman scattering [28], and magnetic resonance imaging [29]. These nanoantennae can be functionalized to recognize a specific target to enable intra-cellular imaging of specific proteins [30] and targeted phototherapy [31], both of which rely on the strong optical absorption and subsequent change in temperature about a nanoscale volume. Photothermal microscopy of metallic nanoantennae can be used to achieve spatial resolutions beyond the Rayleigh limit [30,32].

[**CP**] Several different forms of near-field probes with nanoantenna have been developed over the last decade. The diffraction-limit to optical microscopy has been overcome with the tapered and metal-coated NSOM probe [1]. Also, apertureless techniques involving localized dipole scattering of laser light from a sample have been developed, exhibiting high spatial resolution (<30nm) and chemically specific dielectric responses for inhomogeneous materials [2]. Apertureless near-field techniques offer easier tip fabrication than aperture-based NSOM. A hybrid probe, having a metallic antenna extending from the aperture of conventional NSOM probe, has also been demonstrated. This probe enhances the throughput of conventional aperture probes, and produces a sharper tip [3].

[**CP**] Apertured probes have also been developed for the microwave regime in the form of metal-coated silicon probes [4]. Magnetic dipoles on cantilever beams have demonstrated high sensitivity in the GHz regime [5]. Ultra-floppy magnetic cantilevers with unprecedented force sensitivity have been developed which are capable of sensing the drag induced by small numbers of magnetic nuclei in Magnetic Resonance Force Microscopy [6]. These probes offer the chemical specificity associated with MR techniques. High frequency mechanical probes to 100MHz and beyond have been demonstrated [7]. With all of these electromagnetic-specific probes, we also have seen the development of so-called protein pulling techniques, where the protein forces on a cantilever are monitored as the protein is pulled apart. This makes the scanned probe a sort of force-nanoantenna. The binding of the protein is non-specific in the particular case cited, but chemical modification can also be done, thus exhibiting certain advantages.

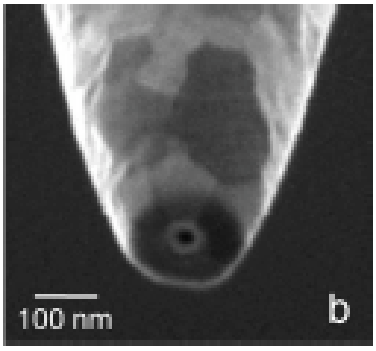

Fig. 1. Apertured NSOM probe tip. Veerman, Univ. of Twenty [1].

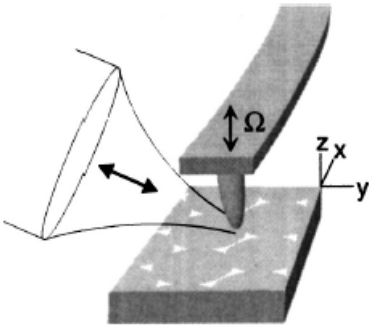

Fig. 2. Apertureless NSOM probe. Keilmann, Max-Plank Institut fur Biochemie [2].

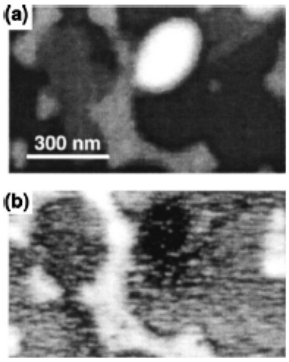

Fig. 3. Topography of Au patterned on Si and the corresponding optical image at 633nm, Keilmann [2].

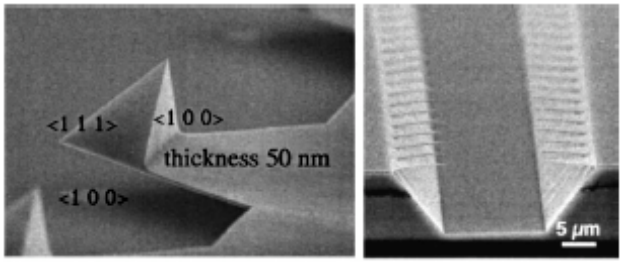

Fig. 4. Single-crystal cantilevers. Kawakatsu, Univ. of Tokyo [7].

[**SB**] Left-handed materials simultaneously possess negative dielectric permittivity and permeability, such that the refractive index is negative [33]. This implies that electromagnetic waves propagate with phase velocity in the opposite direction of energy flow. Proof-of-principle experiments on negative refraction have been performed in the microwave regime [34]. Left-handed materials can result in so-called "perfect-lensing" [35] in which focusing and imaging can be achieved well beyond the Rayleigh limit with a simple slab of material. Efforts to extend this phenomenon to the optical regime have been undertaken, with the theoretical prediction that plasmonic nanostructures consisting of closely-spaced pairs of nanowires [36] can act as an artificial left-handed material that enables the focusing of light at resolutions in the tens of nanometers.

2.4. Acquisition of Multi-Spectral Signatures

[**GB**] Quantum dot infrared photodetectors have recently shown improved performance with long wavelength detectivities $>3x10^{11}$ $cmHz^{1/2}/W$ at 77K. One of the advantages of these photodetectors is the sensitivity in a narrow spectral band. This selectivity property combined with the great design flexibility to shift this spectral band, shows potential for creating hyperspectral detectors. Superlattice materials have been used to create infrared photodiodes that can be tailored to detect wavelengths anywhere between 2 and 30 microns. Carbon nanotubes on silicon have also recently demonstrated an infrared photoresponse in a relatively crude prototype device. A crystallized biological molecule has been reported that shows high sensitivity in the ultraviolet portion of the spectrum. Theoretical modeling and large-scale computer simulations over multi-length and multi-

time scales on massively parallel platforms using O(N) algorithms are coming of age and are poised to realistically undertake studies of multi-million atom nanostructures designed for multi-spectral acquisition.

[**SB**] The optical properties of metallic nanoparticle nanoantennae can be strongly controlled by their three-dimensional shape, leading to wavelength-selective and multi-wavelength behaviors accessible within a diffraction-limited spot. One example is the recent demonstration of plasmonic nanoparticle data storage [23], in which multiple nanoparticle arrangements were used to spectrally-encode multiple data bits within a single, optically-addressable, spot. The ultimate limits to this technique in terms of spectral selectivity and applicability to more general acquisition problems remains an open issue.

2.5. Sensitivity, Selectivity, and Adaptation

[**LC**] To enhance *sensitivity*, nature has evolved over eons a CNN architecture [Chua, 2002] capable of lateral inhibition and supporting simultaneous propagation of excitatory and inhibitory nonlinear waves. For example, the compound eyes of the *horseshoe-crab* (limulus), a direct descendant of the trilobite who roamed the earth 600 million years ago, is made of several thousand locally-interacting light sensors called ommatidium [Rtlif, 1965]. Lateral inhibition in the horseshoe crab has resulted in a greatly enhanced sensitivity to discontinuities in space (edges) and time (motion), thereby endowing the horseshoe crab with superior edge and motion detectors. Neuroscientists have come to realize that lateral inhibition is present in all visual systems, and most other sensing systems as well,

[**LC**] Similarly, *Brittlestars* have evolved a highly selective microlens array where each microlens is optically anisotropic with different refractive indices for light polarized in different directions. CNN interactions among neighboring cells via bundles of nerve fibers have greatly enhanced *selectivity*. The high-tech microlens arrays invented only a few years ago and now used extensively in directional displays and in micro-optics (as signal routing connectors) is in fact an imitation of the Brittlestar's ingenious design [Aizenberg, 2001].

[**LC**] More recently CNN layers of human ganglion retina cells have been discovered to process images via nonlinear dynamical interactions between an excitatory wave, and an inhibitory wave [Roska, 2001], called the *twin-wave computing principles*, thereby achieving much grater selectivity.

[**LC**] All man-made and biological sensors have limited dynamic ranges, as manifested by darkened camera images resulting from sharply contrasting black and white area. Such "blooming" phenomenon is due to the fixed and uniform pixel response of the camera sensor array. Nature has, however, evolved smart retinas by *tuning each pixel individually*, as in situations when one steps suddenly from a brightly lighted lobby into a

jetblack movie theater. Current CNN technology can mimic this pixel-by-pixel adaptation in human retinas [Balya, 2002], [Wagner, 2004], thereby suppressing the undesirable blooming artifact [Wagner, 2004].

[**LC**] It may be possible to enhance the sensitivity, selectivity, and performance measures of nanosensors by several orders of magnitude by exploiting the enabling CNN technology to endow the sensors with low-level intelligence and adaptability.

3. Hard Problems

[**SM**] Nano-electronic, -photonic, and -magnetic based acquisition systems will provide several key advantages over current technology:

- Interaction with the environment on the molecular level – this will provide new sensing schemes that have improved sensitivity and specificity.
- Extremely small transducers – this will allow arrays of sensors to fit in a small area. Sensor arrays can then be used to monitor multiple parameters with improved sensitivity, resolution, and accuracy via statistical sampling instead of single point sampling and integration with adaptive processing.
- Low power operation – this will allow long life operation via batteries or conceivably operation via energy scavenging devices, requiring no batteries.

[**AM**] Sensing of a single "molecule" is of paramount significance to at least two classes of important problems: (a) fighting bio/chemical hazards, and (b) designing molecular level intervention therapies for diseases such as cancers through the study of the intra-cellular spatio-temporal dynamics and function of individual biomolecules. A fundamentally critical aspect of this goal, which lies at the heart of molecular medicine, is to uncover the behavior of individual molecules. This goal remains largely inaccessible in current measurements, which are primarily based upon ensemble averages. Indeed, beyond merely sensing, the real-time "probing" and "tracking" of single molecules in live cells to examine their function, relative to *in-vitro* studies, is the ultimate goal with untold applications in medical intervention at the molecular/genetic level.

[**AM**] Restoring lost bodily functions, particularly those that result from damage to the central nervous system (such as loss of vision due to degeneration of the retinal cells or loss of memory due to damage to hippocampal cells) is a goal worthy of the promise of nanoscience and nanotechnology. Considerable recovery of lost function is possible through implanted adaptive nanoelectronic systems requiring minimal power consumption and dissipation in physiological environment. [**SB**] Related to this is the augmentation of normal bodily functions and the transferrance of these augmented functions to autonomous systems, which may provide unsurpassed sensitivity and selectivity in critical and/or harsh environments.

3.1. Nanoantennae

[**AM**] Colloidal nanocrystal QDs offer great potential for flexible classes of advanced electronic, photonic, and magnetic devices if they can be incorporated in solid matrices while providing competitive functionalities. Progress towards their incorporation in polymeric solid matrices while providing potentially useful functionality such as stimulated emission is being made. Epitaxially-grown solid phase incorporated QDs conform to the basic architectural paradigm that underlies the success of the electronic and optoelectronic systems based upon hierarchical length scales of component organization. Combining the flexibility of the nanocrystal QDs with the power of the epitaxial QDs through hybrid integration will present unprecedented opportunities for break-through concepts in the creation of truly novel acquisition, transduction, and amplification devices. At the same time, such integration is a hard problem in the science and technology of structure- and function- preserving materials integration between disparate materials and their natural environments.

[**AM**] The innovative use of nanocrystals to enable and enhance spectroscopies is a very promising approach to nanoscale probing. Examples of topics include Raman scattering, fluorescence resonant energy transfer (FRET), nanocrystal induced electron transfer, surface plasmon enhanced fluorescence and nonlinear optical effects, nanocrystal conjugation of molecules for dynamic and structural studies, nanocrystal modifications of single molecule spectroscopies, and the use of nanostructures as near-field probe tips for enhanced nanoscopic resolution.

[**AM**] The identification and synthesis of non-toxic (i.e. compatible with intracellular conditions) probes with improved luminescent characteristics is one approach to the objective of examining intracellular dynamics. Compared to the currently used techniques such as confocal microscopy and near-field scanning optical microscopy (NSOM), instrumentation with much higher spatial and temporal resolution must be developed, such as higher resolution (~20nm) and simultaneous sub-picosecond time-resolved detection in NSOM; multiphoton spectroscopy in the 50 nm range; and flow chambers designed for a few-microsecond measurements.

[**SB**] Computational modeling of nanoantennae has progressed rapidly such that the electromagnetic field is coupled with first-principles calculation of the electrical and optical properties [21]. Building upon this modeling capability, there are multiple directions to pursue for nanoscale acquisition systems. One direction is to develop inverse design methods for nanoantennae structures that perform a desired multi-functional mapping between the macroscale and the nanoscale, including the properties of space-variance, state of polarization, and spectral content. Another direction is to utilize tomographic reconstruction techniques to perform multi-spectral nanoscale imaging with assemblies of nanoantennae, where each nanoantenna may be functionalized to recognize a specific molecular or chemical target. A related technique has been developed for biological imaging using the modification of molecular fluorescence lifetime via direct energy transfer among a collection of fluors [22], and can be extended to include structural imaging due to near-field interaction among a collection of nanoantennae.

[**SM**] In many nanoscale acquisition problems, transducing will occur on the nanoscale, where the signal must be converted to the macro-scale and be rendered readable on a typical analog or digital signal protocol. Review of the history of the MEMs industry reveals that although sensor designs were successfully demonstrated early in the lab, the main roadblock to volume manufacturing was efficient and effective packaging of the device. Interfacing and packaging of nano-acquisition systems to the "bulk" world needs attention and should be pursued in parallel with system designs.

3.2. Improving sensitivity while maintaining selectivity

[**AM**] To find effective means of prevention as well as after-the-fact treatment of chemical, biochemical, and biological threats, detection and identification of molecules at levels better than parts per billion (ppb) is required. Nanostructures in the form of nanowires, quantum dots, and other nanoantennae (owing to their enormously-enhanced surface-to-volume ratio) provide the modalities through which this objective can be realized. Such exquisite detection sensitivity, however, is accompanied by an enormous burden on the specificity of the sensor to the molecule to be detected in the environment in which detection is needed. Inability to achieve such specificity results in false positives, thus rendering the sensor ineffective. While approaches to specificity are known (such as antibody-antigen reactions, or the hybridization of single-stranded DNA to form a duplex, etc), the quantitative effectiveness of these, particularly in real-life environments (as opposed to idealized laboratory conditions), is usually limited by the thermodynamically defined affinity kinetics of the competing molecules. Finding ways of creating highly-localized differential affinities between the species of interest and all others that are consistent with the exquisitely high sensitivities achieved is a hard and challenging problem. To address the underlying fundamental and critical issues, considerable investment is needed in advancing nanoscale techniques that provide quantitative information on the appropriate (chemical, optical, electrical) signatures of the chemical/biological species involved. The identification and synthesis of non-toxic (i.e. compatible with intracellular conditions) probes with improved luminescent characteristics is one approach to such an objective.

[more info here, perhaps Raman, multi-spectral, electrical conductance DC to RF, novel scanning probes]

3.3. Integration of nanoscale array transduction with adaptive processing

[**GB**] Developing adaptive nanoscale acquisition arrays that can perform such functions as adjusting dynamic range or wavelength band autonomously to match time-dependent environmental conditions is a challenging problem. One approach is through the interfacing of nanoscale sensor outputs with CMOS-based cellular architectures in order to exploit nature's proven sensitivity enhancement principles (e.g. lateral inhibition) as well as to significantly increase the dynamic range via pixel-wise adaptation. Another approach is to design materials with inherent multi-functional capabilities, such as multiple spectral bands or polarization diversity. This necessitates the exploration of the materials, processes, models, and prototype devices for combining more than one

nanoscale material or function into a compact element, which requires addressing a wide variety of issues from selective deposition of different materials in a controlled area, to the integration of disparate materials, to interconnections between these different functions, and the readout and/or fusion of these different signals. The locally-interacting cellular architecture should be combined with the local activity principle (from nonlinear electronics) to develop ultra-smart and adaptive non-CMOS single-chip sensors with orders of magnitude improvements in sensitivity, selectivity, dynamic range, and minimized false positive/negatives.

[**SB**] Several possible avenues can be identified for the integration of adaptive processing with nanoscale acquisition. [**LC**] Current CMOS-based CNN technology allows the integration onto each pixel of up to 25 nanoantennae, spanning a spectrum from the infrared to visible light. In addition to nanoscale sensing, *on-chip* CNN processing via recently developed excitatory-inhibitory twin wave computing principles can be applied to enhance the sensitivity and selectivity by orders of magnitude. Locally-active bio-materials such as bacteriorhodopsin can be used to provide pixel-by-pixel local memory, thereby enabling smart processing in real time [Jortner, 1997].

[**PE**] The degree to which noise and fluctuations can influence the output of nanoacquisition systems is a key parameter in the design of devices. The scaling of noise (1/f, shot noise, chemical attachment and detachment) across large numbers of devices and throughout sensor systems will be a critical issue. An extension of the statistical methods that evolved in chemical descriptions of interfaces must be extended to the few-molecule limit and exploited in sensor design.

3.4. Multi-modality over compact area

[**GB**] Selectively combining different quantum engineered materials to create multi-functional capabilities within an imaging array is a challenging, but important enterprise. The development of quantum dot photodetectors needs to continue. This involves: continued studies in growth improvements, improved models of quantum states and electron transport mechanisms at this scale, refined control of quantum dot size, and developing models for device design. This may also involve combining nanophotonics to enhance optical absorption in thin or small volume devices. There is a need to explore a wide variety of wide band gap nanodots and nanowires to select the most promising materials for ultraviolet detection. Similarly, exploring quantum structures for efficient terahertz detection is a fruitful area for in-depth exploration. Control of quantum dot size and location, to develop a means to do spectroscopy on an imaging array is essential. Similar issues should be addressed for semiconductor nanorods or quantum wires. Models for predicting the optical and electrical properties of complex quantum dot or quantum wire heterostructures need to be developed, such that the optimum dot/wire size are known, as well as the optimum combination of materials for highest performance at a given wavelength.

[**AM**] Virtually all advanced nano-electronics, -photonics, and –magnetics devices providing the desired function involve interfaces between different materials, often

belonging to different classes operationally (such as semiconductor, insulators, conductors, magnetic, etc) and chemically (such as inorganic, organic, biochemical). The hard problem of realizing arrays of smart, multi-modal information acquisition devices for the wide variety of sensing applications ranging from detection of physical phenomena (e.g. E&M, stress/strain dist., etc.), chemicals (such as toxins, explosives, etc), and biochemical and biological pathogens (such as anthrax, viruses), demands use of a variety of combinations of two or more classes of materials. The frameworks for understanding the structure and electronic states of some of these interfaces are quite well understood (such as compound semiconductor-semiconductor or silicon-silicon dioxide), some reasonably (semiconductor-metal), others not so well (semiconductor-organic), and yet others hardly at all (inorganic-biochemical).

[**AS**] Nanobiotechnology is the convergence of state-of-the-art device engineering, which has emerged over the past two decades, with the molecular and cellular machinery of living systems, which has evolved over eons. This unusual union is now poised to engender powerful new applications in science and technology, ranging from single-cell and single–molecule biology, to disease diagnosis, pathogen detection, high throughput biomolecular identification, and pharmaceutical screening. Within interdisciplinary teams, it will be possible to emphasize two critical themes: the development of integrated nanobiotech systems, and early deployment of these devices in the pursuit of frontier biological investigations. These endeavors are both cross-disciplinary in the fullest sense of the word. The national nanoscience and engineering initiative offers the prospect of providing critical and timely nurturing of these nascent efforts, to enhance them and accelerate the rate of their development. The combination of nanotechnology, biotechnology, and microfluidics, makes possible new engineering pathways that can take advantage of the best of both the biologically- and human-engineered worlds. It seems clear today that this hybrid technology will enable many opportunities such as the merging of living cells with "chips". Specifically, various elements of micro- and nanotechnology should together enable the culturing of arrays of living cells on chips – in such a way that each individual entity within the array can be monitored by separate banks of detectors while its interactions with the "network" are completely controlled. Such interacting, chip-based cell networks might be used to realize an artificial "immune system", which could serve as an ultrasensitive laboratory for rapid detection of biological pathogens, and for identifying and testing pharmaceutical responses to those pathogens (e.g. inducing and monitoring infections on a chip-based networks). This is but one example of a broad class of new opportunities that are conceivable and that, in our opinion, are certain to emerge with the advent of hybrid nanobiotechnological sensing systems. One of the goals of the national nano-science and engineering initiative should be to explore the opportunities of combining these sensing techniques onto common platforms, to determine the limits of sensor miniaturization, and to define the ultimate sensitivities of such microfabricated sensors.

3.5. Nanotransducer design and characterization

[**PE**] The theoretical description of the adsorption of molecules at inorganic surfaces have traditionally been based either on fully quantum-mechanical models using techniques including density functional theories or phenomenological descriptions such as molecular dynamics calculations. The quantum mechanical descriptions are highly computationally intensive and are at present limited to the order of hundreds of electrons. The successes of this approach are limited to systems of small molecules (i.e. the reactivity of chemically important metal surfaces) [1] but produce highly quantitative results. At larger scales, structural techniques such as molecular dynamics can scale to several million atoms using pseudo-potential interactions rather than quantum mechanics – and have shown great promise in self-assembled monolayer systems [2] and polymer nanonstructures [3] Multiscale approaches can bridge these length scales in certain circumstances and need to be extended from their present uses to describe dynamics of bulk structural defects to the larger-scale problems of large molecules at surfaces.

[**PE**] At present, a set of characterization techniques based on the traditional tools of biology and chemistry have had limited success in probing these interfaces. The development of designer interfaces has been based on scanning microscopy [4] area-integrated spectroscopic and electronic probes [5] and structural scattering probes. These tools have provided a framework for understanding the nanoscale properties of interfaces. The extension of these probes to higher spatial resolution, new spectral regions will have some impact. But new strategies are required to meet the challenge of materials integration over large areas, in appropriate ambient environments, and at potentially heterogeneous interfaces.

[**PE**] The integration of molecular functions with electrical and optical systems depends on the chemical functionalization of inorganic surfaces. Chemical selectivity and electronic and optical response of the sensor depend on the nanoscale design and production of systems that include materials whose integration presently remains difficult.

[**PE**] The interface of biological and chemical functions with solid materials is an area where new chemical and physical techniques are required in the formation of interfaces. For example: How can proteins at the scale of tens of nanometers be chemically (or otherwise) attached to surfaces in well-defined situations? Multiscale techniques must be developed to describe the properties of interfaces including large molecules, an area of the surface and the surrounding environment. Such technique may be based on extensions of present approaches, or on new paradigms for scaling computing to large systems.

[**AM**] The environment in which the sensors are to be employed poses an interface, the least examined being the abiotic-biotic interface faced in in-vivo applications,such as implant chips for augmented or replacing damaged/lost body function. This interface, at the core of human health issues, provokes the body's inflammatory response to the foreign body, and thus necessitates rendering the foreign body "bio-compatible." A fundamental approach to this very hard problem is to find biomimetic surface coatings that make the foreign body appear biologically to the immune system. Biomimetic

coatings demand dealing with the still poorly understood inorganic-polymer coatings and the virtually unexamined inorganic-polypeptide/peptide polymer coatings.

[**AM**] Identifying the nature of the fundamental issues, and defining the corresponding solutions through appropriate design, synthesis, and testing of these polymeric and peptide coatings with nano-scale uniformity, and in many cases with incorporated features for drug release, is a hard problem. It also requires development of techniques for nanoscale characterization in physiological environment and defining figures of merit/performance metrics.

4. Implementation Strategies

[**GB**] Continue to fund basic research at university and government laboratories. A wide variety of potential approaches should be explored initially. Provide opportunities for small businesses to further develop promising materials and devices, and assess their performance.

[**SM**] In the short term, focus on developing nanomaterial based acquisition schemes that do not require physical connection to the macro world, utilize "stand-off" interrogation of the sensor arrays via optical or electro-magnetic means, and focus on developing sensing methodologies that are quantum leaps over what is available today. In the long term, focus on effective manufacturing approaches that fit with new interconnection schemes that need to be developed, develop statistical approaches that will utilize the full benefit of a multi-parameter sensing platform to make intelligent decisions based on the measurands, and utilize high sensor counts to reduce cross-sensitivities and false positives

5. Scientific and Technological Infrastructure Needs

[**AM**] A very large part of the challenges faced involve the integration of biotic and abiotic materials, requiring knowledge of process protocols of multiple disciplines as well as co-located process and characterization equipment. There is a critical need for the wide-spread establishment of institutionally-centralized user fee-based facilities in educational and research environments.

[**SM**] In order for new acquisition schemes to become a reality, several challenges in the industry must be overcome. Lack of nanotechnology manufacturing and analysis equipment is one roadblock to innovation. New tools must be developed to analyze the interactions that occur in the nano-regime. In addition to analysis tools, modeling at the nano-scale needs to be developed. Having accurate and proven models of material interactions will allow researchers to progress at a fast pace, predicting sensor behavior before major investment is made in building the device.

[**AS**] To date, biological and chemical sensing and imaging tools have been developed to offer unprecedented analytical capabilities. However, such tools have resulted in relatively large individual instruments optimized for specific tasks. We have only recently begun to embark on the opportunities of miniaturization and integration of analytical instruments into compact systems. Such miniaturization may lead to the faster analysis of smaller volumes with greater sensitivity. In the National Nano-science and engineering Initiative, it should be encouraged to apply nanotechnology for the integration of nano-scale sensors with the purpose of measuring and manipulating picoliter sample volumes, and intend to focus on four major research thrusts:

- (A). Integrated hand-held disease diagnostic systems for the rapid detection of biological pathogens and for testing pharmaceutical responses to those pathogens.
- (B) Integration of chip-based electrical, optical, magnetic and mechanical sensors with silicon CMOS "intelligence" for the rapid identification of chemicals with a single device.
- (C) Single molecule detection systems testing the performance limits of nanofabricated sensors
- (D) Manipulation and imaging of structures within fluid channels for intra-cellular nanomanipulation and measurement.

From these research thrusts, it becomes readily apparent that the proposed integrated sensor systems are realizable only through innovative, cross-disciplinary approaches. For each of these research thrusts, the nanoscale subcomponents serve critical functions or provide enabling characteristics attainable only through miniaturization.

[**LC**] New experimental tools must be developed to uncover complex processing pathways in the nervous systems, including the visual pathways. One promising tool currently being developed at Harvard university combines transgenic and virus assisted techniques for *in vivo* tracing of the visual pathways.

6. Priorities and Conclusions

[**AM**] As nanoscale acquisition demands nanoscale probes, support for synthesis and characterization of quantum nanostructures (quantum dots, rods, and wires) of semiconductors, metals, ceramics, and polymers in novel architectures motivated by acquisition functionality must be given the highest priority. If you can't make it, you can't study it!

[**AM**] As a large part of the use of nano- electronic, -magnetic, and –photonic systems increasingly needs to be in the context of "hostile" environments, much greater emphasis and priority needs to be placed on support of research focused upon "use environment compatibility", particularly biotic/abiotic.

[**AM**] The critical need for university educational laboratory infrastructure for multi-disciplinary activity between the physical and life sciences must be addressed at an accelerated pace through funds ear-marked for the establishment of co-located process and characterization equipment. This is not to be confused with the Major National

facilities that house highly specialized, sophisticated, and expensive equipments accessible only to a handful of experts.

7. Recommendations

8. References

[AM]

1. V. Shchukin, N. N. Ledentsov, and D. Bimberg, "Epitaxy of Nanostructures", Springer Verlag, Berlin (2003)
2. A. Madhukar, Ch.2 in "Nano-Optoelectronics", Ed. M. Grundmann, Springer-Verlag, Berlin, (2002)
3. U. Woggon, "Optical Properties of Semiconductor Quantum Dots", Springer-Verlag, Berlin, (1997)
4. A. P. Alivisatos, MRS Bulletin, 23, 18 (1998)
5. NanoOptoelectronics, Ed. M. Grundmann, Springer-Verlag, berlin (2000)
6. E. Kim, A. Madhukar, Z. M. Ye, and J. C. Campbell, App. Phys. Lett. (submitted) and references therein.
7. M. P. Bruchez, M. Moronne, P. Gin, S. Weiss, and A. P. Alivisatos, Science, 281, 2013 (1998)
8. W. C. W. Chan and S. Nie, Science, 281, 2016 (1998)
9. B. Dubertret, P. Paris, D. J. Norris, V. Noireaux, A. H. Brivanlou, A. Libchaber, Science 298, 1759 (2002)
10. A. Madhukar, Siyuan Lu, and A. P. Alivisatos (unpublished results).

[SB]

1. F. W. Wise, "Lead-salt quantum dots: the limit of strong quantum confinement," Acc. Chem. Res. 33, 773 (2000).
2. C.B. Murray, S. Sun, W. Gaschler, H. Doyle, T. Betley, and C. Kagan, "Colloidal synthesis of nanocrystals and nanocrystal superlattices," IBM J. Res. Dev. 45, 47 (2001)
3. E. Prodan, C. Radloff, N.J. Halas, and P. Nordlander, "A hybridization model for the plasmon response of complex nanostructures," Science 302, 419 (2003)
4. V. Shalaev, Purdue University
5. X. Shi, L. Hesselink, and R. L. Thornton, "Ultrahigh light transmission through a C-shaped nanoaperture," Optics Letters 28, 1320 (2003)
6. A. Nahata, R.A. Linke, T. Ishi, K. Ohashi, "Enhanced nonlinear optical conversion from a periodically nanostructured metal film," Opt. Lett. 28, 423 (2003)
7. S. Kubitschko, J. Spinke, T. Bruckner, S. Pohl, and N. Oranth "Sensitivity enhancement of optical immunosensors with nanoparticles," Analytical Biochemistry 253, 112–122 (1997)

8. J. Yguerabide and E. E. Yguerabide “Light-scattering submicroscopic particles as highly fluorescent analogs and their use as tracer labels in clinical and biological applications,” Analytical Biochemistry 262, 157–176 (1998)
9. T. A. Taton, C. A. Mirkin, and R. L. Letsinger “Scanometric DNA array detection with nanoparticle probes,” Science 289, 1757–1760 (2000)
10. L. R. Hirsch, J. B. Jackson, A. Lee, N. J. Halas, and J. L. West “A while blood immunoassay using gold nanoshells,” Analytical Chemistry 75, 2377 (2003)
11. A. Wokaun, H.-P. Lutz, A. P. King, U. P. Wild, and R. R. Ernst “Energy transfer in surface enhanced luninescence,” Journal of Chemical Physics 79, 509–514 (1983)
12. K. Kneipp, H. Kneipp, R. Manoharan, E. B. Hanlon, I. Itzkan, R. R. Dasari, and M. S. Feld “Extremely large enhancement factors in surface-enhanced Raman scattering for molecules on colloidal gold clusters,” Applied Spectroscopy 52, 1493–1497 (1998)
13. K. Kneipp, H. Kneipp, R. Manoharan, I. Itzkan, R. R. Dasari, and M. S. Feld “Surfaceenhanced Raman scattering (SERS) - a new tool for single molecule detection and identification,” Bioimaging 6, 104–110 (1998)
14. V. M. Shalaev, R. Botet, J. Mercer, and E. B. Stechel Physical Review B 54, 8235 (1996)
15. H. Ditlbacher, N. Felidj, J. R. Krenn, B. Lambprecht, A. Leitner, and F. R. Aussenegg “Electromagnetic intereaction of fluorophores with designed 2d silver nanoparticle arrays,” Applied Physics B 73, 373 (2001)
16. N. Felidj, J. Aubard, G. Levi, J. R. Krenn, A. Hohenau, G. Schider, A. Leitner, and F. R. Aussenegg “Optimized surface-enhanced Raman scattering on gold nanoparticle arrays,” Applied Physics Letters 82, 3095–3097 (2003)
17. J. Malicka, I. Gryczynski, Z. Gryczynski, and J. R. Lakowicz “Effects of fluorophore to-silver distance on the emission of cyanine-dye-labeled oligonucleotides,” Analytical Biochemistry 315, 57–66 (2003)
18. T. W. Ebbeson, H. J. Lezec, H. F. Ghaemi, T. Thio, and P. A. Wolff “Extraordinary optical transmission through sub-wavelength hole arrays,” Nature 391, 667–669 (1998)
19. Y. Liu and S. Blair “Fluorescence enhancement from an array of sub-wavelength metal apertures,” Optics Letters 28, 507–509 (2003)
20. Y. Liu, S. Blair, and J. N. Herron “Biosensing based upon molecular confinement in metallic nanocavity arrays,” submitted to Biosensors and Bioelectronics (2004)
21. E. Prodan, P. Nordlander, N. J. Halas, “Effects of dielectric screening on the optical properties of metallic nanoshells,” Chem. Phys. Lett. 368, 94 (2003)
22. O. J. Rolinski and D. J. S. Birch, “Structural sensing using fluorescence nanotomography,” Journal of Chemical Physics 116, 10411 (2002)
23. H. Ditlbacher, J. R. Krenn, B. Lamprecht, A. Leitner, and F. R. Aussenegg, “Spectrally-coded optical data storage by metal nanoparticles,” Optics Letters 25, 563 (2000)
24. B. Dubertret, P. Skourides, D. Norris, V. Noireaux, A. Brivanlou, and A. Libchaber, Science 298, 2048 (2000)

25. D. Iacopino, A. Ongaro, L. Nagle, R. Eritja, and D. Fitzmaurice, "Imaging the DNA and nanoparticle components of a self-assembled nanoscale architecture," Nanotechnology 14, 447 (2003)
26. S. Schultz, D. R. Smith, J. J. Mock, and D. A. Schultz, Proceedings of the National Academy of Sciences 97, 996 (2000)
27. D. Yelin, D. Oron, S. Thiberge, E. Moses, and Y. Silberberg, "Multiphoton plasmon-resonance microscopy," Optics Express 11, 1385 (2003)
28. K. Kneipp, "Surface-enhanced Raman spectroscopy in single living cells using gold nanoparticles," Applied Spectroscopy 56, 150 (2002)
29. D. Pouliquen, H. Perroud, F. Calza, P. Jallet, and J. J. Le Jeune, "Investigation of the magnetic properties of iron oxide nanoparticles used as contrast agent for MRI," Magnetic Resonance in Medicine 24, 75 (1992)
30. L. Cognet, C. Tardin, D. Boyer, D. Choquet, P. Tamarat, and B. Lounis, "Single metallic nanoparticle imaging for protein detection in cells," Proceedings of the National Academy of Sciences 100, 11350 (2003).
31. L. R. Hirsch, R. J. Stafford, J. A. Bankson, S. R. Sershen, B. Rivera, R. E. Price, J. D. Hazle, N. J. Halas, J. L. West, "Nanoshell-mediated near-infrared thermal therapy of tumors under magnetic resonance guidance," Proceedings of the National Academy of Sciences 100, 13549 (2003)
32. V. P. Zharov, "Far-field photothermal microscopy beyond the diffraction limit," Optics Letters 28, 1314 (2003)
33. V.G. Veselago, "The electrodynamics of substances with simultaneously negative values of ε and μ," Sov. Phys. Usp. 10, 509 (1968)
34. R. A. Shelby, D. R. Smith, and S. Schultz, "Experimental verification of a negative index of refraction," Science 292, 77 (2001)
35. J. B. Pendry, "Negative refraction makes a perfect lens," Physical Review Letters 85, 3966 (2000)
36. V. A. Podolskiy, A, K. Sarychev, and V. M. Shalaev, "Plasmon modes and negative refraction in metal nanowire composites," Optics Express 11, 735 (2003)
37. C. R. Martin and P. Kohli, "The emerging field of nanotube biotechnology," Nature Reviews Drug Discovery 2, 29 (2003)
38. C. Zhou, M. R. Deshpande, M. A. Reed, L. J. II, and J. M. Tour "Nanoscale metal/selfassembled monolayer/metal heterostructures," Applied Physics Letters 71, 611 (1997)
39. G. Timp, Univ. of Illinois.

[LC]

[Aizenberg, 2001], J. Aizenberg, A. Tkachenko, S. Weiner, L. Addadi and G. Hendeler, Calcitic microlenses as part of the photoreceptor system in brittlestars , *Nature*, vol. 412, 819-822, 2004

[Balya, 2002] D. Balya, B. Roska, T. Roska, F. S. Werblin, A CNN Framework for Modeling Parallel Processing in a Mammalian Retina, *International Journal of Circuit Theory and Applications*, Vol. 30, 363-393, 2002.

[Chua,2002], L. O. Chua and T. Roska, *Cellular Neural networks and Visual Computing*, Cambridge University Press, Cambridge, 2002.

[Jortner, 1997], J. Jortner and M. Ratner. *Molecular Electronics*, Blackwell Science, 439-472, 1997.

[Ratliff, 1965] F. Ratliff, *Mach Bands: Quantitative studies on neural networks in the retina*, Holden day, 1965.

[Roska, 2001], B. Roska and F. S. Werblin, Vertical Interactions across Ten Parallel, Stacked Representations in the Mammalian Retina, *Nature*, Vol. 410, 583-587, 2001.

[Wagner 2004] R. Wagner, A. Zarandy and T. Roska, Adaptive Perception with Local-Adjustable Sensor Array, *IEEE Trans. On Circuits and Systems I*, Vol 51. May, 2004.

[CP]

[1] **Near-field scanning optical microscopy studies of electronic and photonic materials and devices**, J. W. P. Hsu, Materials Science and Engineering Reports 33 (2001) 1-50

[2] Material-specific mapping of metal/semiconductor/dielectric nanosystems at 10 nm resolution by backscattering near-field optical microscopy, **Hillenbrand, R., Keilmann, F., *Applied Physics Letters*, v 80, n 1, 7 Jan. 2002, p 25-7**

[3] **Enhancing the resolution of scanning near-field optical microscopy by a metal tip grown on an aperture probe,** Frey, H. G., Keilmann, F., Kriele, A., Guckenberger, R., *Applied Physics Letters*, v 81, n 26, 23 Dec. 2002, p 5030-2

[4] **High-frequency near-field microscopy,** B. T. Rosner, D. W. van der Weide, Rev. Sci. Instrum., 73, No. 7, July 2002; **Microfabricated silicon coaxial field sensors for near-field scanning optical and microwave microscopy**, B. T. Rosner, T. Bork, V. Agrawal, D. W. van der Weide, Sensors and Actuators A 102 (2002) 185–194

[5] **A microfabricated tip for simultaneous acquisition of sample topography and high-frequency magnetic field,** V. Agrawal, P. Neuzil, D. W. van der Weide, Appl. Phys. Lett. **71** (16), 20 October 1997

[6] **Atto-newton force detection using ultrathin silicon cantilevers**, T. D. Stowe, K. Yasumura, and T. W. Kenny, D. Botkin, K. Wago, and D. Rugar, Appl. Phys. Lett. **71** (2), 14 July 1997

[7] **Towards atomic force microscopy up to 100 MHz,** H. Kawakatsu, S. Kawai, D. Saya, M. Nagashio, D. Kobayashi, H. Toshiyoshi, and H. Fujita, Rev. Sci. Instrum., Vol. 73, No. 6, June 2002

[8] **Stretching single molecules into novel conformations using the atomic force microscope,** T. E. Fisher, P. E. Marszalek, J. M. Fernandez, Nature Structural Biology, Vol. 7 number 9, September 2000

[GB]

1. E. Kim, A. Madhukar, Z. M. Ye, and J. C. Campbell, App. Phys. Lett. (April 26, 2004 issue; In Press)

[PE]

[1] DFT calculations of organics at surfaces
[2] Vashishta (Argonne, USC), statistics and structural
[3] Dislocations in metals
[4] P. Weiss
[5] Raman, ellipsometry, etc.