

Perspective

Perspective on Optical Biosensors and Integrated Sensor Systems

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Optical biosensors have begun to move from the laboratory to the point of use. This trend will be accelerated by new concepts for molecular recognition, integration of microfluidics and optics, simplified fabrication technologies, improved approaches to biosensor system integration, and dramatically increased awareness of the applicability of sensor technology to improve public health and environmental monitoring. Examples of innovations are identified that will lead to smaller, faster, cheaper optical biosensor systems with capacity to provide effective and actionable information.

In the 1980s, only a limited number of groups were publishing data on optical sensors with integrated biological recognition molecules.^{1–5} The possibility of moving a biosensor off an optical bench was still a long-term goal primarily because of the bulky optics available at the time. Moreover, reagent manipulations were all performed manually. The primary challenges being addressed were maintaining the activity of the recognition molecules after immobilization or entrapment, collecting the relatively weak fluorescent or absorbance signals, and discriminating a recognition event from nonspecific adsorption. Only after these problems were well understood and the manner in which they needed to be

addressed was better appreciated could the next level of challenges be undertaken: consideration of binding kinetics at surfaces; operation under flow as opposed to static equilibrium conditions; utilization of new solid-state optical devices, recognition molecules, enzymes for signal amplification, and near-IR and long-lifetime fluorophores; multiplexed analyses; system automation; and constraints for utility at the point-of-use. Both as a result of this foundational work and advances in other fields, a number of new devices and techniques evolved including a wide variety of solid state optical elements, immobilization chemistries, genetically engineered recognition molecules, microarrays of capture molecules, and fluidics for continuous monitoring. The result has been a variety of relatively expensive but commercially available optical biosensors for specific application areas including medical diagnostics, environmental testing, and food safety.⁶

In 20 years from now, will we have the Star Trek Tricorder that tells us at a distance the identity of a target of interest, be it chemical, biological, or mineral? Current users of optical biosensors clearly want a device usable anywhere by anyone that tests for everything of interest, in real-time, and at trivial expense. While it is unlikely that this goal will be accomplished, optical biosensors will be constructed to meet the needs of operators in various fields of use in cost-effective packages. For example, in 10 years, biosensors with capacity to test for all common food pathogens in vegetable or carcass washes, beverages, or homogenized food samples could be in place. Point-of-care systems for identifying common infectious diseases could be in every doctor's office in 20 years: the limitations of cost, reimbursement, and regulation are greater than those of technology. Integration of biosensors into environmental monitoring systems will increase as costs are reduced, and biosensor usage will expand from homeland security and pollution control applications to analysis of natural processes

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(e.g., the role of soil bacteria in the evolution of plants, biomarkers in wild animals that indicate environmental stress, and biological adaptations to volcanic activity or global warming).

Progress in optical biosensors is not just a function of the invention of smaller, cheaper, better optical components. Optical biosensors amalgamate discoveries in optics, fluidics, electronics, and biochemistry. The remainder of this article discusses emerging science and technology that will enable the creation of more efficient application-specific optical biosensors. Commercial biosensors have already been introduced into a number of application areas mentioned above, but they are generally expensive and limited in the number of targets for which they can test. Rapidly evolving science and technology will contribute to producing optical biosensors useful as everyday analytical tools. Biological recognition and signal amplification strategies, nanotechnology for geometric control of the biochemistry and signal enhancement, microfluidics for automated reagent delivery and reaction control, and emergence of optical elements amenable to improved systems integration will play a critical role in this evolution.

"BIO" IN THE OPTICAL BIOSENSOR

Most of the early optical biosensors used antibodies or lectins as biological recognition molecules. The molecular biology tools developed for identifying genes using complementary oligonucleotides and for in vitro creation of antibodies provided methods for de novo creation of new or improved recognition molecules. New recognition paradigms evolved, and the capabilities provided by multiplexed recognition systems became apparent. High-density arrays of DNA, antibodies, carbohydrates, and peptides have been validated with optical readout systems for simultaneous detection of large numbers of targets. Low-density arrays have been implemented in inexpensive optical biosensor assays for limited numbers of biomarkers with the extremely valuable capacity to run positive and negative controls in the same test.

Antibodies can now be synthesized in vitro using cells, cell-free systems, and bacteriophages and selected for unique specificity. After the initial selection of antibody-producing clones, subsequent molecular modifications, including random mutations to increase affinity or selected mutations to increase stability or provide sites for purification or labeling (e.g., integration of histidine tags or biotin) can be performed. For biosensor applications, the development of small, single-chain antibodies from camelids and sharks is a significant breakthrough because of the incredible stability of these molecules after exposure to heat or solvent.^{7–9} Not only is this stability important for storage and use in harsh environments, but the single-chain antibody's capacity to denature and renature rapidly and repeatedly makes it invaluable for continuous monitoring applications.

The introduction of microarrays in the 1990's provided the capability for detecting thousands to millions of targets simultaneously. The limitation imposed by having to provide a specific

nucleotide sequence to match each potential target has been partially moderated, as DNA arrays have been demonstrated to be capable of sequencing not only anticipated infectious disease targets but also near neighbors. Resequencing arrays are capable of detecting hundreds of pathogen strains on a single chip.¹⁰ Utilization of DNA-binding probes also sparked the invention of aptamers which can bind to targets other than nucleic acids.^{11–14} Aptamers have already evolved so that they can be tailored both to recognize a target and to generate a signal upon binding. Such signals include enzyme activity and fluorescence as molecular beacons are turned on.¹⁵ Willner and his colleagues have developed a DNA construct as a molecular machine that binds a target, turns on a replicating enzyme, and generates a signal in a self-replicating cascade. This scheme provides exquisite sensitivity in a homogeneous system, with a signal measurable using the simplest of optical components.¹⁶ Such oligonucleotide-based technologies are evolving in directions that can eventually simplify the demands on the optics while providing increased information content or sensitivity.

Both DNA and antibody-based sensors tend to be specific for an anticipated target. A number of approaches for detecting harmful unknowns without prior assumptions about identity are also being explored using optical signal transduction. Cells,¹⁷ cell receptors,^{18–20} carbohydrates,^{21–23} antimicrobial peptides,^{24,25} and siderophores²⁶ have been used to detect physiologically harmful toxins or families of pathogens without having to anticipate the exact target. Combining such generic recognition approaches with integrated optics, pattern recognition software, and stochastic sensing paradigms may provide simpler optical biosensors with multiplexing capabilities compared to biosensors that require a unique recognition molecule for every target of interest. Such biosensors could provide actionable information (e.g., drug sensitivity, pathogenicity) without an exact target identification,

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reducing the level of multiplexing required and thus the demands on the optics for spatial or spectral discrimination.

NANOTECHNOLOGY: ENHANCING OPTICAL DETECTION

Nanotechnology is providing new tools for integrating biorecognition molecules with the mechanisms for signal generation, altering the geometric distribution of the optical power, and controlling nonspecific surface interactions. As molecular interactions, molecular transport distances, and optical energy fields approach similar dimensions, it becomes more and more natural to take an integrative view of the biochemical and physical interactions of molecules and forces.

While the function of biosensors has always been at the “nano” level in terms of molecular recognition and optical signal generation, the first application of nanoparticles for biosensing was the development of “PEBBLES” by Kopelman and colleagues.²⁷ These nanoparticles included dyes and/or enzymes for chemical and biological sensing after insertion into cells to make measurements in situ. Quantum dots and metallic nanoparticles have also been employed for making intracellular measurements.^{28,29} In addition to the information provided by virtue of their localization in the cell, such particles can exhibit fluorescence energy transfer or other changes in optical properties in the presence of the target.^{30–32} These approaches will yield new information about localized concentration changes for molecules within cells, but the utility for intracellular measurements is limited currently by the requirement for a high-resolution fluorescent microscope or imaging system. Inventions such as the confocal microscope-on-a-chip³³ or even cell-phone camera technology may make such analyses easier and cheaper, but utility will still be limited to venues where examination of cells is possible.

For multiplexed analyses, coded particles are changing the way we think about microarrays.^{32,34} In coded-particle assays, one or two sets of particles specific for each target are added to the mixture of particle sets, and assays for all targets are processed in a single batch. Adding assay capability for one more target is generally just a matter of adding an additional particle set to the mixture rather than completely reformatting a planar microarray. Each particle provides a discrete recognition surface, and statistics of large numbers can be used to increase the signal-to-background discrimination. Furthermore, when compared to passing the sample solution over a planar microarray, mixing the particles in the sample solution minimizes the diffusion limitations, speeding up the reaction. The utilization of magnetic coded particles further facilitates the concentration of trapped target, with concomitant increases in sensitivity and in the potential for separating the target

from interfering agents. While equipment for sequencing from coded particles is complex and expensive,³⁵ relatively compact equipment to read out affinity reactions on particle arrays is available.^{36–39} The next sensor development in this area will involve the integration of microfluidics and micro-optical components to translate the sample processing and particle interrogation into a single hand-held device. In addition to providing tags, magnetic and nonmagnetic nanoparticles provide the opportunity for manipulation of target and reagents within microfluidic devices for automated sample processing.

Nanoparticles are also beginning to be appreciated for the role that their size and shape can play in terms of optical excitation in a biosensor.^{40,41} Nanoparticles with varying size and shape have been used to modify planar sensing surfaces to make them generate bigger signals and obviate the need for labels. It has long been known that a lawn of gold or silver nanoparticles can enhance surface plasmon resonance (SPR), but only recently has this effect become reproducible as the methods for making uniform particles and for fabricating the modified waveguides have been defined.⁴² Homola and collaborators have increased sensitivity of SPR sensors by an order of magnitude after modifying the waveguide with gold nanoclusters.⁴³ Similar studies have used carbon nanotubes or metal nanorods to modify surfaces for surface enhanced resonance Raman (SERR) measurements with similar increases in sensitivity.^{44–46} As the ability to control the size, shape, surface chemistry, and deposition of such nanostructures advances, the boundary between whether the particle is an integral part of the optical configuration or a label on the target is going to become less clear, i.e., the particles may serve both functions.

A major problem with label-free optical biosensors such as SPR or SERRs is that the assay background from nonspecific adsorption of other sample components is also detected; improving sensitivity also increases the nonspecific signal. Simple surface treatments such as blocking with casein or bovine serum albumin or covalent attachment of polyethylene oxide may not be sufficient to prevent nonspecific binding. Electrophoresis,⁴⁷ mag-

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netic force,^{48,49} and flow⁵⁰ have been used as active measures to expedite target binding, remove nonspecifically bound components, and improve signal-to-background. Nanotechnology provides a more subtle approach to counter the problem caused by nonspecific binding: superhydrophobic and superhydrophilic surfaces. Nanostructures on such surfaces control the wettability and potential for fouling,⁵¹ and electrowetting materials are under development that potentiate the cycling from hydrophobic to hydrophilic surfaces for self-cleaning regimens.^{52,53} Label-free optical biosensors are attractive from the point of view of reduced reagent cost and assay complexity. Elimination of nonspecific binding, along with increases in signal generation, would make them far more useful for detection of targets in complex, real-world samples.

AUTOMATION AND MICROFLUIDICS: MOVING OPTICAL BIOSENSORS OUT OF THE LABORATORY

For a biosensor to be used outside the laboratory, it either has to be as simple as a hand-held pregnancy test strip or automated with regard to sample processing and reagent addition. In most cases, microfluidics will provide the platform for automated sample manipulation. Microfluidic systems are well recognized for their ability to move small volumes of fluids through different processes and over a sensing surface, their importance in cost reduction because of reduced fabrication expense and decreased requirements for costly reagents, and their role in reducing processing and assay times that are proportional to liquid volumes.^{54,55} Microfluidics will be extremely important in the development of automated portable optical biosensors for several other reasons as well. First, microfluidic devices can be used for target preconcentration^{56,57} and target separation from other sample components.^{58–60} Second, cell disruption or sample homogenization can be performed in a microfluidic system.^{61,62} Third, both active and passive mixers are available for combining

sample and assay reagents.^{63,64} Fourth, techniques for using solid-phase materials for separations in microflow have been identified.^{65–68} Finally, on-chip temperature control is available for temperature-dependent reactions such as PCR or simply for maintaining stability of the system in harsh environments.^{69–72} Conversion of these procedures to automated, on-chip manipulations can be a major step forward in eliminating the requirement for a technically trained operator, but microfluidic systems must first be developed that deal with real-world samples.⁷³

Researchers are just beginning to exploit the power of fluid focusing, a technology that will be very important for manipulating complex samples. Instead of having a wall for each flow stream, one fluid can be used to confine another. Fluid focusing has been used for separations,^{74–76} target delivery to a sensor surface,^{77,78} flow cytometry,^{79,80} and constraint of light propagation (Figure 1).⁸¹ In another incarnation of fluid focusing, a droplet is manipulated on a surface surrounded by air, moving the target through the different steps in the reaction process.^{82–84} If the relative positions of different fluids can be controlled by manipulating fluid streams or surface characteristics, complex reactions can proceed without a complex network of solid capillary walls, loss of sample components on capillary walls can be avoided, and targets and reagents can be directed to a sensing surface to negate mass transport limitations that increase time and decrease sensitivity.

The technology for fabricating microfluidic subsystems is becoming increasingly varied and user-friendly. In addition to sophisticated silicon and glass etching methods, laser ablation,

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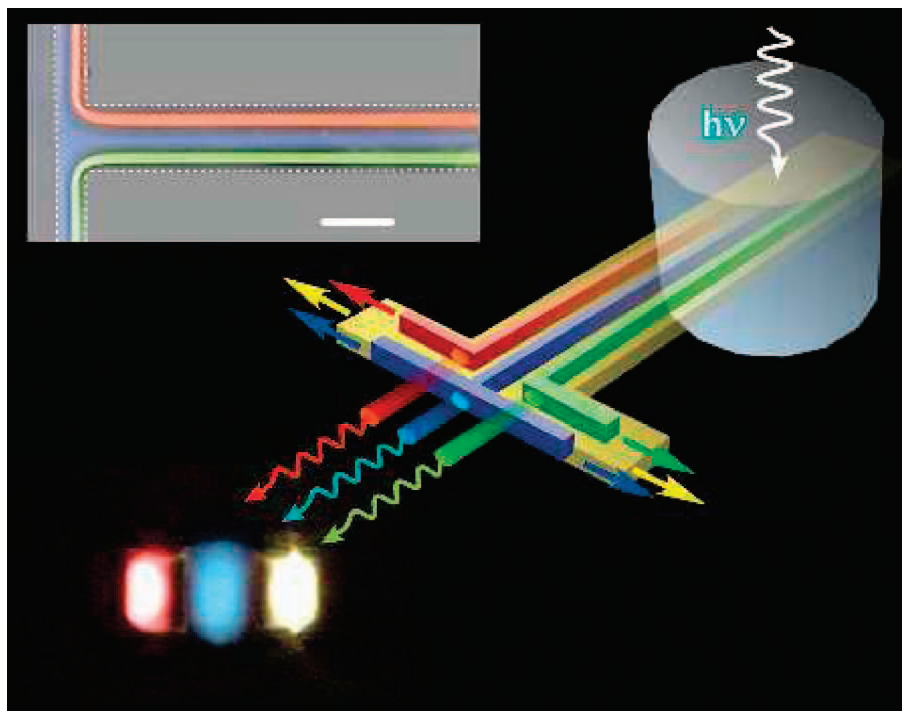


Figure 1. Three parallel waveguides formed with liquid core and cladding in laminar flow systems.⁸¹ The direction of the light propagation can be altered by differential flow rates of the adjacent fluids. (Reprinted with permission from G. Whitesides. Copyright to this figure retained by *Proc. Natl. Acad. Sci. U.S.A.*).

and injection molding, techniques such as soft lithography⁸⁵ and hot embossing^{86–88} are becoming widely used in research laboratories. Devices exhibiting three-dimensional complexity are becoming more common as investigators shift from glass and silicon to plastics, which provide potential for more shapes at lower cost. Furthermore, plastics resistant to organic solvents can enable devices for additional applications and procedures. The understanding of the interaction between biomolecules and plastic materials is currently based primarily on empirical data: making assays work in plastics has been a matter of trial-and-error or surface modification to cloak problematic surfaces with a biocompatible film. Nonetheless, optical biosensors are already being marketed with plastic cassettes to house the fluidics and the surfaces or reservoirs where the sensing is performed. Increasing sample processing and manipulation in such cassettes is an area of intensive R&D activity, but the material and surface chemistries deserve more attention.

SYSTEMS INTEGRATION AND ADVANCED OPTICS: APPROACHING GESTALT

Biosensors need to be envisioned first as a system and appropriate components selected or invented to support the system requirements.^{89,90} Currently, most biosensors are developed because the inventors are intrigued with one particular component, and the rest of the device is jury-rigged around that

entity. Proper system design can achieve “gestalt”, a whole that cannot be derived from the sum of the parts. However, one has to appreciate the potential of component parts, including biochemistry, fluidics, optics, electronics, and packaging before *ab initio* system design is feasible. In addition, the designer needs to appreciate sample characteristics (e.g., volume, complexity, interfering agents, viscosity, target concentration range, component stability) and user constraints (e.g., technical competence, assay time, cost, size, weight, assay frequency, environmental conditions, ease of maintenance, power access).

Sampling for biosensor analysis is usually a separate function at this time. However, for continuous or periodic monitoring, automated sample collection and introduction is far preferable. Samplers that preconcentrate the target are particularly useful for reducing sample volume. Currently, wetted wall cyclones or electronic impactors concentrate particulates from air into a liquid sample that can be automatically transferred into a biosensor,⁹¹ whereas filtration and centrifugal systems concentrate samples from liquid sources. These technologies all take the form of a separate device from which the optical biosensor draws sample. There is a continuing need for more efficient, small, automated concentrators for targets in a wide variety of sample matrixes that can be effectively integrated with the biosensor. Why not integrate the biosensor into the sampler?

The use of microfluidics for sample processing can eliminate the manual operations, reducing variability and expediting the assay as discussed previously. Design software to create microfluidic systems, as opposed to characterizing existing systems, is

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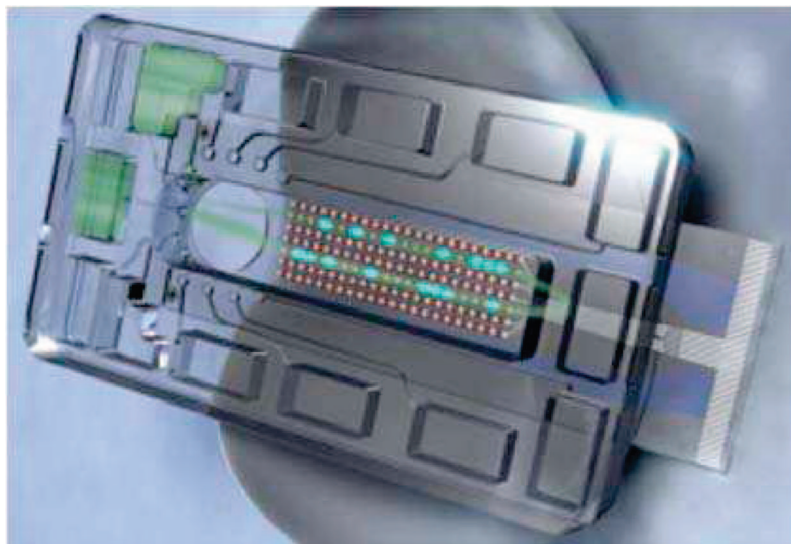


Figure 2. Concept for a biosensor with automated sample processing unit (developed by the author) and a polymer photodiode array (developed by Biolident).¹²¹

just beginning to appear.^{92,93} Currently, the biggest problem is to integrate small pumps and valves into the system, either as miniature devices hooked up to the main substrate or integrated into the substrate along with the sensing elements. Finding or fabricating reliable pumps that provide the right amount of fluid at an exact and steady flow rate is extremely difficult. Many of the on-chip pumps and valves reported in the literature are appropriate only for use with relatively clean, well-defined fluids. Pumps and valves can also consume the largest portion of the power required by a system. When the biosensor must run on batteries, energy consumption is a significant issue. Both reducing energy requirements and improving miniature energy sources, such as a microfluidic fuel cell or a biomimetic photocenter,^{94,95} will be critical for long-term acceptance and practicality of automated biosensor systems.

In addition to enabling automation, the microfluidic components can be integrated with the optical components.^{96,97} Several examples of such integration have already been demonstrated: Capillary walls can constrain the flow of sample and reagents, provide a surface for the attachment of biorecognition molecules, and serve as waveguides for excitation of bound fluorophores and collection of fluorescence emission.^{98,99} Avalanche photodiodes can be embedded in a waveguide along with a laser-emitting diode so that all the optical components are integrated with the sensing surface. Photopatterning of glass has resulted in the fabrication of both microchannels and optical waveguides in a single substrate.¹⁰⁰

To date, miniaturization and integration of the fluidics and optics has depended on the development of microfluidic fabrication techniques and the miniaturization of optical components such as CCD and CMOS detectors, avalanche photodiodes, and light emitting diodes. While integration of miniaturized silicon devices into biosensors has begun, there is an entire generation of new polymer optical components that will be even more suited to integration with microfluidics and sensor substrates: flexible organic filters,¹⁰¹ tunable organic microlenses,¹⁰² organic light emitting diodes (OLEDs),¹⁰³ and organic photodiodes (OPDs).¹⁰⁴ OLEDs have already been demonstrated in high-density arrays, and the potential for using OPDs as detectors in biosensors is

acknowledged (Figure 2).¹⁰⁵

As optical biosensor systems become smaller and more automated, new capabilities can be achieved by combining two or more analytical technologies. For example, on-chip DNA amplification has been combined with fluorescence detection following capillary electrophoresis of the products.^{106–108} On-chip high-pressure liquid chromatography and capillary electrophoresis are well suited for coupling to multispectral imaging and optical spectrometry on-chip. Photonic crystal spectrometers might, for instance, be combined with on-chip chromatography to look at reaction rates for ligand–receptor or protein–protein interactions as part of a general trend to develop systems providing both complex biochemical and optical information.

OPTICAL BIOSENSOR APPLICATIONS, PRESENT AND FUTURE

Optical biosensors have proven advantages over other types of sensors for multitarget sensing and continuous monitoring.

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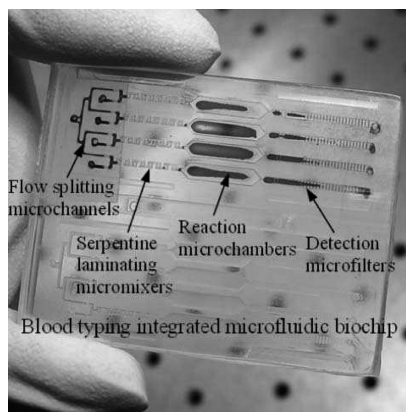


Figure 3. A biosensor chip for blood typing.¹²⁰ A single droplet of blood is split into four paths through a micromixer, reaction chamber and detection region. The blood type is read by eye. (Printed with permission from The Royal Society of Chemistry).

These advantages have highlighted the potential of optical biosensors to address the analytical needs for medical and veterinary diagnostics, food processing, environmental protection, and homeland security. Increased awareness of the capabilities of optical biosensors for on-site, multianalyte sensing is encouraging continued public investment as well as attracting larger amounts of private development funds.

The largest initial market for commercial optical biosensors was the research community. Rich and Myszka documented the number of papers published over the 6 years beginning in 2000 that used commercial optical biosensors.^{109,110} The number nearly doubled from 600 to over 1100 in this short period. In general, the commercial “biosensors” referenced are benchtop devices that are not fully automated but usable by a skilled operator. Already, smaller, less expensive, and more user-friendly systems are appearing, particularly for nucleic acid amplification and identification, affinity microarray analysis, and flow cytometry.

Medical applications are currently attracting the most commercial interest, particularly in terms of implementing the capacity of optical biosensors for multiplexed diagnostics. However, unless the diagnostic test is appropriate for screening large populations (Figure 3) or is tied to a high-value drug, then it is difficult to generate sufficient profit to motivate a company to go through the regulatory process, assume liability, and expend marketing capital. Diagnostic biosensors that simultaneously test for large numbers of infectious diseases or biomarkers face the additional regulatory challenge of demonstrating that the information provided is of clinical significance. In many of these highly multiplexed tests, there are not sufficient patients with each of the diseases included in the panel to get statistically significant information and comprehensive clinical trials would be prohibitively expensive. In the case of biomarkers, the etiology of the appearance of these markers in the disease may not yet be well understood or indeed the importance of each marker well validated. Biomarker analysis could be especially valuable in prognosis and risk analysis (e.g., newborn screening, thyroid

disease, genetic disorders), but the biology needs to be solid and health care payers must have the statistics to confirm the value of prevention and early diagnosis. As more and more diagnostic techniques become available for point-of-care and self-testing,^{111,112} physicians and patients must be educated to use such tools effectively. Already, optical biosensors have been commercially developed to test for infectious disease, alcohol, drugs of abuse, and heart attack; feedback from physicians and patients will pave the way for improved biosensors.

Surprisingly, the goal of using optical biosensors for diagnostics in developing countries has become an important driver for engineering more cost-effective systems (Table 1).^{113,114} Technologies for cheap, robust, low-cost, user-friendly diagnostics with minimal requirements for external energy sources are in the development and clinical testing phase. Successful approaches will work just as well in technologically advanced cultures and be more rapidly accepted due to the lower cost of use. However, again it must be emphasized that in order for such biosensors to be accepted, the information they provide must be actionable.

Optical biosensors are also being used to a growing degree in other application areas. Homeland security applications have pushed the development of biosensors for decades, but that momentum drastically increased after 9/11.¹¹⁵ Optical biosensors have proven to provide the most effective means for identifying biothreats, and similar technologies are being tested for explosive detection and tracking. Environmental concerns are driving the development of on-site monitoring systems to reduce the response time and cost of pollution control in comparison to shipping samples to a central laboratory. Optical biosensors are being tested for monitoring air, water, and soil, with the primary interest coming from environmental regulatory agencies.^{116,117} Again, the issues relevant for the acceptance of optical biosensors for pollution monitoring are cost of operation and actionable results. Food testing applications have been clearly demonstrated,¹¹⁸ but the regulatory agencies responsible for monitoring food safety are generally too underfunded and understaffed to devote significant resources to implementing new technology. Food processing companies are interested in automated monitoring systems to promote safer products and reduce liability, but sampling presents a major challenge. While a few companies have emplaced optical biosensors for food testing, the efficacy of these systems for process monitoring is just beginning to be confirmed.

FUTURE OPTICAL BIOSENSORS: CRITICAL ISSUES BEYOND ANALYTICAL TECHNOLOGY

While the technical future of optical biosensors is in the hands of clever scientists and inventive engineers, the rate of transition

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Table 1. Laboratory Structure Constraints in Low-Resource Settings Informing Product Attributes^a

laboratory infrastructure constraints in low-resource settings	implications on point-of-care diagnostic product attributes
wide disparity of laboratory facilities and capacities within a country and among countries	Careful consideration for the final user of the test is required.
poor or nonexistent external quality control and laboratory accreditation systems	The test should be reproducible and provide clear and easy to interpret internal and process controls.
unreliable procurement system leading to stock outs of key laboratory supplies	The test should require as few external reagents and supplies as possible.
unreliable quality of reagents and supplies procured through national channels	The test should require as few external reagents and supplies as possible.
lack of basic essential equipment	The test should require as little instrumentation as possible or provide its own instrumentation.
lack of laboratory consumables	No assumptions should be made regarding supplies for specimen collection, storage, and handling.
unreliable water supply and quality	This is extremely variable in different regions and seasons, and a device should not require external water if high quality is needed.
unreliable power supply and quality	This is often tied to water supply. Devices requiring external power should account for long periods of time without network electricity supply and high variability as well as frequency of surges from the network electricity supply.
inconsistent refrigeration capacity	This is associated with unreliable power supply. A test should be able to withstand large fluctuations in temperatures (from 40 to 10 °C) during transportation as well as sustained storage at 30 °C.
insufficiently skilled staff	The test should be easy to use and interpret.
limited training opportunities	Any training requirements should be given special consideration for the introduction strategy.
limited access to distributors' service maintenance staff	Any device should be robust with over 1 year half-life.
poor waste-management facilities	The environmental impact of disposable, chemical reagents, and biohazardous materials should be considered.

^a Reprinted with permission from *Annu. Rev. Biomed. Eng.* www.annualreviews.org.¹¹³

to the user community will be controlled by a wide variety of nonscientific factors.¹¹⁵ Ethical concerns have been expressed with regard to the use of genetic information and the safety of nanomaterials,¹¹⁹ and such concerns of the public will ultimately drive regulation. Social concerns over problems such as resource depletion will also drive priorities for system design as well as for application areas. For example, as energy becomes more and more expensive, on-chip power generation becomes more attractive. As clean water becomes more and more of a problem, testing of drinking water will assume a higher priority and more thorough testing will be publicly demanded than is currently the case. Both public and private funding priorities will react accordingly to public concerns.

For those of us working to develop optical biosensors, the number of opportunities to incorporate new science and technology into our systems is almost overwhelming. The only limitations

seem to be our ability to integrate basic and cutting-edge information from disciplines other than our own, to find colleagues willing to work with us who have the skills we lack, and to find the financial and physical resources to create and test new optical biosensors. However, we must also consider the ultimate user, the reliability of the data produced, and the impact of any reaction to that data, positive or negative. Such considerations can focus our research and development efforts into the most productive paths to produce optical biosensors that can solve real problems in everyday life.

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