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Perspective

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Policy Considerations for Mobile Biosensors

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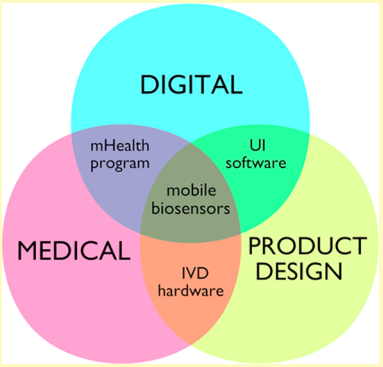
ABSTRACT: Meeting policy requirements is essential for advancing molecular diagnostic devices from the laboratory to real-world applications and commercialization. Considering policy as a starting point in the design of new technology is a winning strategy. Rapid developments have put mobile biosensors at the frontier of molecular diagnostics, at times outpacing policymakers, and therefore offering new opportunities for breakthroughs in global health. In this Perspective we survey influential global health policies and recent developments in mobile biosensing in order to gain a new perspective for the future of the field. We summarize the main requirements for mobile diagnostics outlined by policy makers such as the World Health Organization (WHO), the World Bank, the European Union (EU), and the Food and Drug Administration (FDA). We then classify current mobile diagnostic technologies according to the manner in which the biosensor interfaces with a smartphone. We observe a trend in reducing hardware components and substituting instruments and laborious data processing steps for user-friendly apps. From this perspective we see software application developers as key collaborators for bridging the gap between policy and practice.



KEYWORDS: *mHealth, telemedicine, smartphone, diagnostics, paper-based analytical devices*

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Global health is multifaceted, with stakeholders at international, regional, and local levels in both public and private sectors. As such, the perspectives of international organizations and national regulators, down to frontline healthcare workers and individual patients, all influence how policy is set at each level. With this range of stakeholders in mind, policymakers are tasked with mapping out the best path toward holistic improvements for healthcare systems for both patients and providers. The prevailing trend in global health policy over the past 40 years has been focused on the decentralization of healthcare services and infrastructure.[1−3] Decentralization promised to be more democratic, to reduce costs, and to be more efficient than centralized models by providing greater patient involvement at regional and community levels. In practice, however, decentralization has led to new problems such as higher costs, limited access to highly specialized services, inefficient management of patient records among decentralized facilities, and the inequities of access and quality standards among economically disparate communities.[2] A second wave of decentralization strategies have sought to overcome these problems, including renewed calls for universal health coverage,[4,5] personalized medicine,[6] and developing more sustainable practices in the healthcare industry.[7] Even more recently, over the past 10 years a third wave of decentralization strategy has emerged that leverages the ubiquitous status of digital communication devices.[5,8−10]

Leading organizations such as the World Health Organization, the International Medical Device Regulators Forum, the European Union, and the National Institute of Health are now looking to mobile health, or mHealth, as a promising future direction for decentralized healthcare not just at the local or national level, but globally. mHealth is defined as the use of mobile devices—such as mobile phones, patient monitoring devices, personal digital assistants (PDAs), and wireless devices—for medical and public health practice.[8,11] With mobile communications networks already available worldwide, even in severely resource-restrained areas and the most remote locations on earth,[5] each mobile communications device is a potential access point for decentralized healthcare provision. Consequently, mHealth can be used to bolster previous decentralization efforts and bypass some of its former limitations. Increased equity of access to healthcare, one of the half-fulfilled promises of first-wave decentralization efforts, has been measurably improved with mHealth globally between 2011 and 2016.[5] The digital platform of mHealth also offers a viable solution to efficient data management. For example, data from patient records can be uploaded to a cloud storage service from any location and be retrieved at any location when needed. Combined with blockchain encryption, mHealth could also offer the data security that is required to handle confidential health information more efficiently than other methods.

Despite these advancements, a long-standing impasse to decentralized healthcare has been the question of how to provide local access to specialized services such as molecular diagnostics. Even under robust decentralization efforts, these services often remained centralized due to large and expensive diagnostic equipment and the paucity of specialized healthcare workers to operate it. However, the development of mobile biosensors has the potential to solve these issues by substituting

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bulky instruments for the nearly ubiquitous smartphone. This is especially the case now because recent developments have sought to dramatically lower costs associated with mobile biosensors by using the smartphone as a user-interface platform[12,13] and by fabricating biosensors on disposable paper substrates.[14,15] With these developments, mobile biosensing is becoming more suitable for decentralized healthcare that is personal, sustainable, and available universally.

However, integrating new technology into existing healthcare systems and unlocking the potential of mobile biosensors requires considering the policy surrounding traditional in vitro diagnostics and the policy surrounding the use of digital devices in healthcare. Moreover, because the digital devices being used are personal communications devices, additional policy regarding product design and the protection of patient confidentiality must be considered as well. Developing mobile biosensors that can fulfill these policy requirements is an essential step toward introducing these technologies into everyday health care.

POLICY GUIDE

Policy that stems from all levels of healthcare organizations is often presented to stakeholders in the form of gray literature such as white papers, green papers, market analysis reports, or legislation. The policy documents that are applicable to mobile biosensors generally fall into three domains: medical, digital, and product design. As mentioned above, the medical domain includes safety regulations for medical devices and quality standards for in vitro diagnostics. Policy in the digital domain includes regulations for software applications (apps), and legislation concerning data security. The domain of product design includes gray literature that aims to ensure that mobile biosensors are appropriately accessible for the end-user, whether it be a doctor, a frontline healthcare worker, or the patients themselves. It also includes information about costs, funding, and management issues for deploying large-scale mHealth programs, as well as regulations concerning certain types of fabrication methods. Overall, researchers are challenged to meet these medical, digital, and product design policy demands.

Figure 1 shows the overlap among these policy domains in the context of mobile biosensors. At the intersection of the medical and the product design domains there are well-established policies related to the development of in vitro diagnostic tests. At the intersection of the medical and the digital domains, there is a newer subset of policies related to mHealth programs. At the intersection of the digital and the product design domains, there is policy related to software that aids in the user interface. A mobile biosensor designed for use in global health is found in the center. Table 1 lays out a reference guide to specific policy documents, the organizations from which they originate, and the policy domains they cover. In addition to these policies, the specific region where a mobile biosensor is intended to be used also has a bearing on the applicable policy. Below we offer policy summaries from some of the main players in global healthcare that detail particularly influential policy documents and region-specific interests.

World Health Organization (WHO). Originating in the literature concerning diagnostics tests in low income areas, the WHO has a set of criteria that uses the acronym ASSURED (affordable, sensitive, specific, user-friendly, rapid and robust, equipment-free, deliverable to end-users) for developing diagnostic tests.[16,17] While ASSURED was developed before the advent of smartphones, this technology offers a particularly well-suited platform for meeting these criteria.

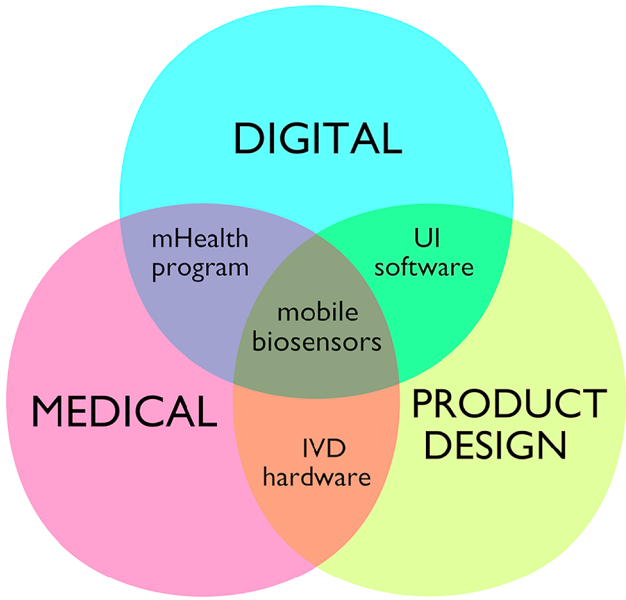

Figure 1. Overlapping policy domains applicable to mobile biosensors, including in vitro diagnostic (IVD) hardware, user-interface (UI) software, and mobile health (mHealth).

More recently the WHO has been monitoring the global status of mHealth. While there is no unique category for mobile biosensing, a related topic is currently included under the rubric of health surveillance and patient monitoring.[5,8] It involves installing remote sensors in a patient's home to check the status of a chronic illness. The WHO has observed that the number of countries that report having this type mHealth program has nearly doubled in 5 years, with interest in wearable sensors increasing, showing a trend from remote sensing toward mobile sensing. However, the report also states that these developments are confined to high-income areas, as the technology is still too expensive for global mHealth applications.[8,10]

The WHO also provides a toolkit for mHealth projects already underway that aims to take them from the pilot stage and scale them up to independent enterprises. The MAPS toolkit names six axes (Figure 2) to consider and includes advice on how to assess, plan, and improve mHealth projects as they grow and evolve in response to the feedback of stakeholders.[18]

World Bank/Advanced Development for Africa (ADA). Targeting an appropriate medical need, as well as funding and sustainability policies, is emphasized by the World Bank when a mobile biosensor is intended to be used in Africa. In a white paper concerning mobile applications for the health sector, the World Bank focuses on economic and market demands for mHealth projects. From their point of view, for any mHealth program to be successful it will need to address a specific problem for which there is a large demand to solve. They identify the largest problems in the developing world as infectious diseases, chronic disease monitoring, and maternal health, all of which directly relate to mobile biosensing.[19,20]

The ADA states that one of the largest barriers to a successful mHealth program is sustainability. Nonprofit models initiated by large organizations account for most mHealth programs, but of the many pilot projects that have been started in African countries, the vast majority of them are halted when the initial

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Table 1. Guide to Main Policy Documents and Their Policy Domain[a]

organization	policy document	policy domain
World Health Organization	Global Diffusion of eHealth: Making Universal Coverage Achievable[5]	M/D
	mHealth: New Horizons for Health through Mobile Technologies[8]	M/D
	Mapping the Landscape of Diagnostics for Sexually Transmitted Infections[16]	M
	Rapid tests for sexually transmitted infections (STIs): the way forward[17]	M
	Decentralization in Healthcare[2]	P
	The MAPS Toolkit: mHealth Assessment and Planning for Scale[18]	P
United Nations	Health Information as Healthcare: The Role of Mobiles in Unlocking Health Data and Wellness[10]	M/D
UNICEF etc.	Principles for Digital Development[88]	D
European Union	eHealth Action Plan 2012−2020 - Innovative healthcare for the 21st century[9]	M/D/P
	Green Paper on mHealth[11]	M/D
	Study on Cross-border Health Services: Potential Obstacles for Healthcare Providers[85]	P
Advanced Development for Africa	Scaling Up Mobile Health[20]	P
Food and Drug Administration	Digital Health Innovation Action Plan[89]	M/D
	21st Century Cures Act[25]	M/D
	Mobile Medical Applications[86]	M/D
	Technical Considerations for Additive Manufactured Medical Devices[24]	P
	Design Considerations for Devices Intended for Home Use[23]	P
	Molecular Diagnostic Instruments with Combined Functions[91]	M/D/P
	Content of Premarket Submissions for Management of Cybersecurity in Medical Devices[22]	D
	Breakthrough Devices Program[31]	M/D/P
	Digital Health Software Precertification (Precert) Program[87]	D/P
Federal Trade Commission	Start with Security: A Guide for Business[82]	D/P
	Mobile Health App Developers: FTC Best Practices[93]	D/P
Federal Communications Commission	Federal Regulations for Radio Frequency Devices[84]	P
Health and Human Services	Summary of the HIPPA Privacy Rule[92]	M/P

[a]M: medical, D: digital, P: Product design.

Figure 2. The six axes of planning a sustainable mHealth program. Reprinted with permission from ref 18. Copyright 2015 World Health Organization Press.

funding runs out.[20] For mHealth to grow into an industry, for-profit and hybrid models should be explored.[19] This could take the form of teaming up with public health agencies financed by governments or by teaming up with corporate sponsors in the mobile telecommunications industries. For example, a recent mHealth program from the Vodafone Foundation that was implemented in Lesotho cites its funding partners as USAID, ViiV Healthcare, the Elton John Aids Foundation, the Elma Foundation, and Vodacom Lesotho Foundation.[21] These funding partners are a mix of public sector, private company, and nonprofit charitable organizations.

European Union (EU). If a mobile biosensor is intended to be used in the EU, there is an emphasis on developing the digital single market as a way to integrate national health systems in the block. At the same time, there is also an emphasis on personalization, which includes offering a multilingual user-interface, and in particular, one that is designed for the aging population. While the WHO and the World Bank/ADA focus on developing countries and low-resource areas, the European Union is more concerned with improving their current healthcare systems. Faced with an aging population putting a strain on traditional modes of healthcare provision as well as the free-movement of patients and providers across national borders throughout the block, the EU is embracing digital solutions.[9] Providing integrated, sustainable, and citizen-centered care is their stated objective that they hope to accomplish through mHealth strategies.[11]

Citizen-centered care is twofold. It involves providing personalized care to the patient as well as patients monitoring their own health. Personalized healthcare requires stratifying patients as a function of shared biological characteristics. To achieve this, healthcare professionals require tests for the rapid detection of biomarkers at the point of care. Mobile biosensors are ideal to achieve this goal because the test results can be easily uploaded to a cloud service, therefore enabling their analysis with big data approaches that are ideal for patient stratification. At the same time, the policy goal of patient-centered care could be reached if patients were provided with diagnostic tests for checking their health status autonomously. Mobile biosensors are best suited to meet this demand; however, this requires biosensing platforms and apps that are accessible in various languages, and that are easy to use for all ages and educational backgrounds.

Food and Drug Administration (FDA). If a mobile biosensor is intended to be used in the USA, policy related to the safety of product design is paramount. The FDA is the regulatory agency that oversees the safety of medical devices, in vitro diagnostics, and digital health solutions that are available on the consumer market.

All medical devices are subject to Class 1, General Regulatory Controls. This entails regulation about registering with the agency, record keeping, and accurately representing the device function and intended use.

Depending on the reagents used, the medical device may also qualify for Class 2, Special Controls. This includes the general control as above, but with case-by-case specifications for different reagents. Finally, if the medical device is used to diagnose a life-threatening condition or highly contagious disease, then it is subject to Class 3 regulatory controls, which in addition to the general controls also requires a premarket approval process. The premarket approval process requires satisfying their policies for laboratory quality standards, scientific data integrity, and approved protocol for clinical trials.[22]

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For diagnostic tests that are developed for use outside of traditional clinical settings, the FDA has compiled a document of design considerations. It contains useful information about conditions that may occur outside of a laboratory setting, including environmental variables such as temperature, dampness and humidity, atmospheric pressure, and airflow, as well as user-related variables such as mobility, dexterity, coordination, and strength. Design specifications for maintenance, security, and calibration are also included, as are issues concerning possible electrical problems, such as power supply during outages, and warning systems for low batteries in medical devices The skill level of the intended user and proper disposal of these devices is also discussed.[23]

As mobile biosensor technology advances, so too do their software components and fabrication methods. The FDA has issued a guidance document on the use of 3D printing for medical devices. It covers topics such as approved material types, and protocol for software file formats, as well as issues of sanitation and cleaning requirements for 3D printed medical devices.[24] Software that is used for healthcare purposes is increasingly sophisticated and is regulated depending on its function in the mobile platform. Mobile medical apps that are used to operate a sensor by acting as a control panel or display screen, or apps that turn a smartphone into a medical device by leveraging its built-in sensors are the focus of FDA regulations.[25] Finally, software as a medical device, that is, software that calibrates or analyzes medical data and provides a diagnosis, has its own regulatory review process.[25]

From Policy to the Lab. These policy frameworks have caused a reassessment of traditional diagnostic methods and are still guiding the development of new mobile biosensors. Since one of the recurring policy goals is to increase access to health care without increasing costs, researchers have felt compelled to design biosensors that are both portable and inexpensive in order to ensure that anyone can use them regardless of geographical location or socioeconomic status. This has spurred a new wave of biosensors that do not require expensive materials or high-end facilities in their fabrication.[26−28] The end product also needs to be lightweight and small in order to be feasibly couriered to remote locations should this be required.[29,30] This not only involves the biosensor itself but also any fluidic system required for handling liquids, which often requires heavy pumps. With regard to the instrumentation, mobile biosensors that interface with smartphones offer alternatives to bulky or expensive equipment that could improve the portability of the assay.

While it is true that policy influences the design of mobile biosensors, the design of novel mobile biosensors can also be the driving force behind new policy. The field of mobile biosensors is developing rapidly, and policymakers such as the FDA and the EU actively seek input from stakeholders as they draft new policy in this area.[11,31] The opportunity for researchers to exert their influence as stakeholders in this area provides a timely opportunity to look at recent developments in order to better chart the course for the future direction of mobile biosensors for global health.

CATEGORIES OF MOBILE BIOSENSORS

When it comes to mobile biosensors, their overarching commonality is the use of a mobile communications device, predominately a smartphone, as a platform. In the following sections, we categorize mobile biosensors according to the manner in which they interface with a smartphone. The categories include using the smartphone to receive and transmit data from a biosensor, biosensors that are remotely controlled with a smartphone via wireless communication, directly connecting a biosensor to a smartphone for use as a power source, and using a smartphone's camera, a CMOS sensor, to detect or interpret signals as part of the biosensor. For evaluating these categories, we use their suitability for meeting the broadest amount of policy for global health applications as the main criterion.

Smartphones for Transmitting Data. Focused on the communications aspects of smartphones, this type of interface is employed to report the results of a biosensor to a healthcare professional or directly to the user. It also facilitates basic mHealth services such as receiving a consultation from a healthcare professional based on the results of a biosensor via telemedicine.[5−8] A notable characteristic of this type of interface is that it does not use the smartphone for any part of the biosensing process, but rather to collect and relay data. This type of interface can be found in some wearable biosensors, that is, biosensors that are in direct contact with the body, whether in the form of bandages, clothing, or other accessories. Wearables can use smartphones to relay data from the biosensor to a healthcare provider.[32−35] In some cases, the biosensors upload data to a cloud service for analysis and monitoring from a hospital.[36] Should the biosensor data indicate an urgent medical condition, then the use of a smartphone or other mobile communications device allows a healthcare provider to inform a patient that they should come in for treatment.

A potential drawback of this strategy is that relies heavily on healthcare professionals, who may become overloaded with data. It may also put a strain on healthcare providers that are understaffed and therefore unable to keep up with the demand for the service.[5,8] Fortunately, with the advent of big data analysis and cloud computing for managing large quantities of data, the strain on human resources for healthcare providers could be reduced.[8,36] A scheme for this type of data transmission system is shown in Figure 3.

Figure 3. Wireless data transmission from a mobile biosensor for acute myocardial infarction (AMI) to a smartphone using a standard protocol for health data (IEEE11073). From the smartphone, data is transmitted to a server at a healthcare facility where it can be securely accessed by a doctor for review. Reprinted in part with permission from ref 35. Copyright 2015 Wiley Online Library.

For example, Jung et al. have developed a wearable biosensor, shown in Figure 4, to check four protein biomarkers for acute myocardial infarction, or a heart attack. To check for these biomarkers, the patient holds down a button for ten seconds which activates the device in a single step. The device collects a blood sample, filters the serum, and then detects the biomarkers by passing the serum over antibody coated electrodes. The device processes the signals and relays the results to a healthcare professional all in 14 min.[35]

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Figure 4. Wearable biosensor with manual controls and display screen that detects four biomarkers related to heart attack risk. Results are transmitted to a smartphone and then relayed to a doctor. Reprinted in part with permission from ref 35. Copyright 2015 Wiley Online Library.

This intersection of biosensors and telemedicine makes communicating with healthcare providers more accessible to people in remote locations and also allows for patients to monitor chronic health conditions from the comfort of their homes, thus helping to decongest hospitals and clinics and foregoing the burden of traveling to a healthcare facility unless urgently needed. However, these technologies are mainly aimed at consumers with the resources to purchase sophisticated medical devices and for patients in areas that already have strong healthcare infrastructures. Because of this, its application for global adoption is currently limited.

Smartphones as Displays and Controls. In this approach the smartphone is used to wirelessly control a mobile biosensor via Bluetooth,[32,37−45] radiofrequency identification (RFID), or near-field communication (NFC).[46,47] For example, Liu et al. developed a mobile electrical impedance spectroscopy device for the detection of *E. coli*.[43] The device connects to a smartphone via Bluetooth with which it can be controlled using a custom software application (app). The mobile biosensor has all of the functionality of a commercial LRC meter to measure the inductance (L), capacitance (C), and resistance (R), but at lower cost and smaller size, as shown in Figure 5. The benefit of

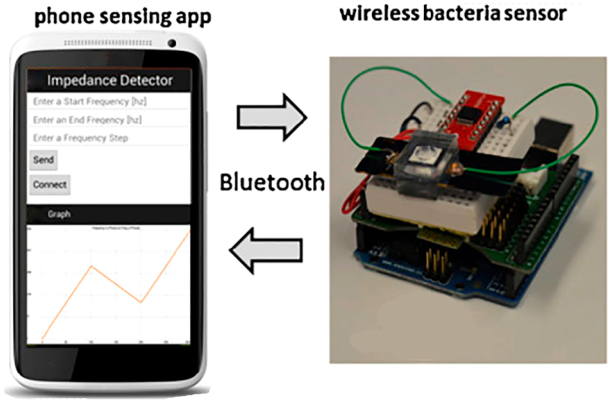

Figure 5. Small, low-cost biosensor that connects to a smartphone app via Bluetooth in order to control the device and display the results. Reprinted in part with permission from ref 43. Copyright 2014 Elsevier.

this type of interface is that the mobile biosensor does not need to include its own display screen or control panel, making it lighter, less expensive, and more portable than previous devices. It also includes the telecommunication benefits as before, paving the way for using the platform in large-scale mHealth programs. However, devices such as this rely on their own internal power source. Including a battery in the design may make it more expensive to fabricate easily disposable, single-use devices. A battery also accounts for extra weight and additional shipping requirements for international couriering, causing logistical complications for implementation in a global mHealth program.

Smartphones as Powering Devices. Another way to interface biosensors and smartphones is in the form of a dongle. In this way the mobile biosensor uses the smartphone as a power source in addition to a control/display screen for the device. Some have exploited the smartphone's mini USB to this end,[48−51] while others have opted for the smartphone's audio jack.[52,53] For example, Hall et al. report the development of a mobile biosensor for the electrochemical detection of SLPI (secretory leukocyte protease inhibitor), a biomarker for lung infections for people living with cystic fibrosis.

The device, shown in Figure 6, was designed in order to exploit as much of the smartphone's hardware as possible, thus

Figure 6. Biosensor dongle that connects directly to a smartphone and harvests power via the headphone jack, eliminating the need for a separate battery. Reprinted in part with permission from ref 52. Copyright 2016 Elsevier.

making it lighter and less expensive than standalone devices. By using the audio jack, the device is compatible with a wider range of smartphones and requires fewer components than those that use Bluetooth or a USB to connect. It is also more convenient to the end user, as they do not have to recharge or dispose of the battery.[52]

Smartphones as Optical Readout Devices. Smartphones can also interface with biosensors by using the smartphone's camera, a CMOS sensor, to capture and process signals from biosensors. Mobile biosensors of this kind broadly fall into two subsets: those which modify the camera with an accessory, and those which leave the camera unmodified. Accessories that modify the camera can be microscopes,[54−59] microplate readers,[48,60−63] or what is described in the literature as a "cradle", that is, a small box that is used to control photographic conditions such as lighting, distance, and the angle of the camera.[64−70] Figure 7 shows an example of this type of accessory.

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Figure 7. Cradle accessory for a smartphone used to control photographic conditions for optical sensing. Reprinted in part with permission from ref 69. Copyright 2013 Royal Society of Chemistry.

Using the smartphone's built-in CMOS sensor instead of a separate electronic device further reduces the cost and weight of the diagnostic platform. Nevertheless, it still poses problems for point-of-care mobile biosensing. This is because in some cases the cradle requires access to a 3D printer and is made of expensive resins,[58,67] which diminishes its portability and accessibility in low-resource areas. There are also additional policy requirements for 3D printed accessories used in medical devices.[24] In other cases, the accessory includes a separate power source to enable LED excitation of fluorescent materials.[68,70] Overall, the use of an accessory to modify the smartphone's camera reintroduces some of the limitations for global health applications described in previous sections.

There are other methods that do not require the camera to be modified with accessories. In these methods the images captured by the smartphone's camera are treated with image processing software. For example, MatLab, ImageJ, or Photoshop are often used to perform calibration calculations that compensate for variable photographic conditions.[71−74] While this approach removes the need for modifying the camera with an accessory, these calculations require a sufficient skill level to complete them, and manually processing images is laborious, resulting in a substantial time delay between performing the assay and interpreting the results. To overcome this, custom apps have been developed that can process images in real-time.[75−78] Even though custom apps can process images in real time, the results that these yield are still rather technical and would require a skilled healthcare worker to interpret them. Figure 8 shows photos of colorimetric signals, and the data extracted from those photos using image processing software.

A method that not only automatically processes images but also automatically interprets the results in a way that is easy to understand is made possible by using the smartphone's camera to scan barcodes, QR codes, and augmented reality targets that incorporate colorimetric signals in their design.[79−82] For example, an augmented reality app can be used to generate digital media as a function of the intensity of colorimetric

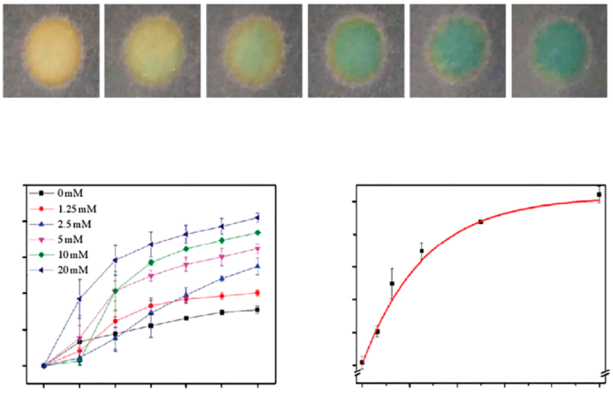

Figure 8. Photographs of colorimetric signals that are manually analyzed by splitting the red, green, and blue sensor channels with image processing software with the resulting data plotted below. Reprinted in part with permission from ref 78. Copyright 2014 Springer.

signals.[83] In this approach antibody modified nanoparticles generate colored spots on paper substrates that block the recognition of a target image overlaid on the substrate. When applied to the detection of *E. coli* this approach yielded a "hazard" message when the concentration of pathogens was equal to or higher than the safety threshold values as defined by the World Health Organization (Figure 9). This approach is

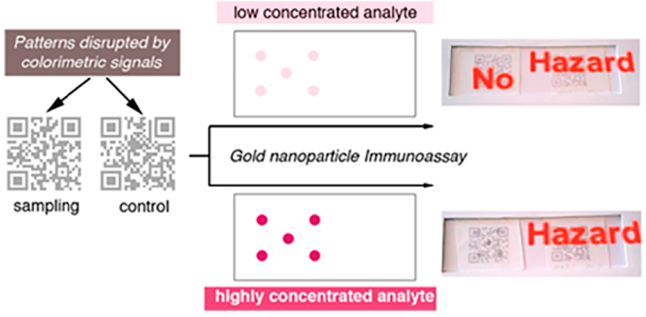

Figure 9. Colorimetric signals can block the recognition of an augmented reality target when the concentration of bacteria is above a certain threshold, yielding easy to interpret results ("Hazard" or "No Hazard") in real time. Reprinted with permission from ref 83. Copyright 2017 ACS Publications.

advantageous because the results are easy to understand by people of any skill level, including minimally trained frontline healthcare workers, or even patients themselves. The digitally augmented results could also take the form of an audio recording or a video of a healthcare professional explaining the results and offering counseling.

DISCUSSION

The four categories presented above show a trend to minimize the components required for the manufacture of mobile biosensors, from eliminating batteries to substituting external dongles with the phone sensors and exchanging signal processing software with user-friendly apps. The ideal design would then only require a smartphone and an app to enable a molecular diagnostic at the point of need. From a policy perspective, this shift in design is advantageous. Since software can be downloaded onto any smartphone regardless of location, and can be made available for free, this approach could bypass

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some logistical issues associated with using additional hardware such as fabrication costs and international shipping. Furthermore, it could bypass certain regulations that may hold back the commercialization of the mobile biosensor platform. For example, mobile biosensors that connect to smartphones via Bluetooth, NFC, or RFID are subject to additional regulations on the use of radiofrequency in electronic devices.[84] As for the biosensor, one that is easy to use, lightweight, low cost, sustainably produced, temperature resistant, and easily disposed of after use would be the most suitable for meeting global health policy. Paper-based analytical devices with wax-printed microfluidics are the most promising option, although alternatives to temperature-sensitive biomolecules are required to fully meet these demands.[14]

While chemists have focused on the design of the biosensor component and engineers have focused on the hardware aspects, in many cases the software component for the user-interface would benefit from being more fully developed in order to make mobile biosensors suitable for mHealth. Ideally, the design of the user-interface should include customizable settings for language[85] and multimedia options such as audio explanations or videos in order to accommodate a broad range of speakers, age groups, and educational backgrounds.[83] It should also preferably function in real time without having to relay data elsewhere to be processed and await a result. Here the pattern recognition-based detection platforms seem best suited because they do not require comparing the colorimetric signal with a color chart, and the signal output consists of digital media that is easier to understand that an array of numbers.[83] Because of this its adaptation for global healthcare would be relatively straightforward compared to other methods that require a high level of training to interpret the assay.

Perhaps the most significant aspect of using smartphones as a platform for diagnostics is that they are not subject to the typical regulations for mobile medical devices.[86] However, between the drafting of this manuscript and its submission, new policy has been enacted which focuses on software applications run on smartphones.[25] Additionally, the FDA has begun a certification program for software developers working with mobile medical devices, and the apps developed from those who have been certified will be preapproved for the market.[87] Despite these new policy regulations, policymakers do not want to stifle innovation or delay useful technological advances from potentially helping people in need.[90] A special category of breakthrough devices can be fast-tracked and eschew the typical policy regulations.[31] Due to mobile biosensors being at the frontier of molecular diagnostics, this may also be a possible route from the laboratory to commercialization and real-world applications. This is especially so for biosensing techniques that use the smartphone's camera interfaced with paper-based diagnostic devices, given that their lightweight, low-cost, and disposable paper-based design is suitability for global health applications.

CONCLUSION

Decentralization has been the driving force in healthcare reform, and the trend to achieve this in recent years has been through mHealth. For molecular diagnostics, this has taken the form of mobile biosensors. Influential policymakers such as the World Health Organization, the European Union, and the FDA have published policy that aims to decentralize healthcare not just at the local or national level, but globally. Developers of mobile biosensors have been trying to meet these policies by providing an easy way to share data between patients and providers and interfacing portable readers with diagnostic tests. The most streamlined approach proposed thus far just requires a smartphone and an easy-to-operate app in order to detect signals and facilitate their interpretation by nonspecialists. From our perspective we see closer ties between chemists and computer software developers on multidisciplinary teams as essential in order to further develop this trend in a way that satisfies new policy guidelines.

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Notes

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