SNAPS
PART-1 & PART-2

Shoumen Datta

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sensors

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Review

SNAPS: Sensor Analytics Point Solutions for Detection and Decision Support Systems

Eric S. McLamore [1,*], Shoumen Palit Austin Datta [1,2,3], Victoria Morgan [1], Nicholas Cavallaro [1], Greg Kiker [1], Daniel M. Jenkins [4], Yue Rong [1], Carmen Gomes [5], Jonathan Claussen [6,7], Diana Vanegas [8] and Evangelyn C. Alocilja [9,10]

1 Agricultural and Biological Engineering, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611, USA; shoumendatta@ufl.edu or shoumen@mit.edu (S.P.A.D.); tvlmorgan@ufl.edu (V.M.); ncavallaro@ufl.edu (N.C.); gkiker@ufl.edu (G.K.); yuerong@ufl.edu (Y.R.)
2 MIT Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, Cambridge, MA 02139, USA
3 MDPnP Labs, Biomedical Engineering Program, Department of Anesthesiology, Massachusetts General Hospital, Harvard Medical School, 65 Landsdowne Street, Cambridge, MA 02139, USA
4 Molecular Biosciences and Bioengineering, University of Hawaii Manoa, Honolulu, HI 96822, USA; danielje@hawaii.edu
5 Mechanical Engineering, Iowa State University, Ames, IA 50011, USA; carmen@iastate.edu
6 Mechanical Engineering Department, Iowa State University, Ames, IA 50011, USA; jcclauss@iastate.edu
7 Ames Laboratory, Ames, IA 50011, USA
8 Environmental Engineering and Earth Sciences, Clemson University, Clemson, SC 29634, USA; dvanega@clemson.edu
9 Global Alliance for Rapid Diagnostics, Michigan State University, East Lansing, MI 48824, USA; alocilja@msu.edu
10 Nano-Biosensors Lab, Michigan State University, East Lansing, MI 48824, USA
* Correspondence: emclamore@ufl.edu; Tel.: +1-(352)294-6703

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Abstract: In this review, we discuss the role of sensor analytics point solutions (SNAPS), a reduced complexity machine-assisted decision support tool. We summarize the approaches used for mobile phone-based chemical/biological sensors, including general hardware and software requirements for signal transduction and acquisition. We introduce SNAPS, part of a platform approach to converge sensor data and analytics. The platform is designed to consist of a portfolio of modular tools which may lend itself to dynamic composability by enabling context-specific selection of relevant units, resulting in case-based working modules. SNAPS is an element of this platform where data analytics, statistical characterization and algorithms may be delivered to the data either via embedded systems in devices, or sourced, in near real-time, from mist, fog or cloud computing resources. Convergence of the physical systems with the cyber components paves the path for SNAPS to progress to higher levels of artificial reasoning tools (ART) and emerge as data-informed decision support, as a service for general societal needs. Proof of concept examples of SNAPS are demonstrated both for quantitative data and qualitative data, each operated using a mobile device (smartphone or tablet) for data acquisition and analytics. We discuss the challenges and opportunities for SNAPS, centered around the value to users/stakeholders and the key performance indicators users may find helpful, for these types of machine-assisted tools.

Keywords: sensor; smart systems; data analytics; cyber-physical systems; artificial reasoning tools; ART; drag and drop analytics; DADA; sensor-analytics point solutions; SNAPS; sense-analyze-respond-actuate; SARA; machine-assisted tools; MAT; machine-assisted platform; MAP; knowledge graphs; trans-disciplinary convergence

1. Overview

A plethora of literature reviews describe the historical context [1], recent advances [2–4], and futuristic ideas [5–7] related to development and application of chemosensors, biosensors, physical sensors, and nanosensors [8,9]. These diagnostic tools have important applications across the medical, agricultural, and environmental domains, and in some cases overlap multiple areas. Chemosensors, physical sensors, biosensors and nanosensors (collectively referred to as sensors herein) have enormous potential as point of care (POC) devices [10,11], also known as point of need devices [12,13]. The majority of POC sensor applications are in the medical and public health fields, although recently the library of tools for agricultural and environmental applications has been expanding rapidly [14–16]. The expansion of data connectivity within POC devices [17] is a catalyst for divergent application of sensors into otherwise restricted domains. In agricultural and environmental applications, enhancing mobility through data connectivity is paramount, and many current efforts are focused on wireless sensors connected to mobile devices. However, in most cases there are no analytic tools directly embedded into the mobile device and post hoc analysis is required using a laptop or computer. In this review, we discuss select POC systems and introduce sensor-analytics point solutions (SNAPS) as a platform for aggregating sensor data for analytics. SNAPS illustrates a confluence of ideas, including sensing, mobile devices, connectivity and cyber-physical systems, which may be combined with artificial reasoning tools (ART) and data-informed decision support systems. SNAPS serves as a proof of concept for ensuring the appropriate hardware/software tools are matched, ensuring diverse stakeholder needs are matched with sensor data and analytics.

This review provides an overview of sensor engineering related to the recognition-transduction-acquisition triad as it relates to basic design decisions for SNAPS, followed by a discussion of hardware and software elements which may be necessary for SNAPS. We then introduce elements of autonomy, provide specific examples of SNAPS, and we point out a few of the challenges and opportunities. We conclude by discussing the importance of making sense of data and how to deliver information on demand from data to users and stakeholders, before the quality of service perishes, in the context of actionable information which possesses transactional value (see Figure S1).

2. Sensor Engineering

Sensor engineering is rooted in material choice, and development of practical protocols that enhance device accuracy without sacrificing temporal resolution. The fundamental sensor working mechanism established by the International Union of Pure and Applied Chemistry in the 1990's has consistently served as the design backbone for research groups (see Figure S2). The coating on the sensor surface selectively binds the target, a transduction event produces measurable signal, and the signal is acquired using specialty equipment. This sensing process, based on the recognition-transduction-acquisition (RTA) triad, has been enhanced through the use of nanomaterials that improve detection limit, speed and/or reversibility [18,19]. In biosensors, biomaterials are commonly employed to improve selectivity, bandwidth, or facilitate actuation [20–22]. Recent progress in engineering nanoscale materials has paved the way for development of non-biological chemical and physical sensors that accomplish some of these same improvements [23,24]. Whether the nature of the recognition event is chemical, biological, or physical, these molecular scale interactions are the initial step in sensing, and the material choice governs the efficacy of this RTA triad.

The affinity of the sensor coating for the target is the limiting factor for device function, and the importance of this first step in the RTA triad cannot be over-emphasized. Given that binding affinity and selectivity are the architects of the RTA triad, transduction is the platform for innovation. Intuitively, material choice dictates classification of device as either a sensor (use of abiotic materials), biosensor (biological or biomimetic materials), nanosensor (nanomaterials), or nanobiosensor (hybrid nano/biomaterials). In addition to establishing these commonplace definitions, sensor material choice dictates critical performance factors such as durability, cost and ultimately quality of service. In its most basic definition, transduction is defined as a change in energy state. There are two major classes of transduction that lead to the evolution of quantitative data or qualitative data, namely inherent transduction and engineered transduction, respectively (Figure 1).

Engineered transduction (Figure 1A,B) involves highly specific binding of the target by the receptor but cannot be used for reversible, continuous measurement due to the need for an exogenous reagent or engineered process for at least one of the following: (i) facilitation of the transduction step, or (ii) promoting release of target from binding site. In either case, the sensor cannot autonomously produce a measurable product without an engineered process or exogenous reagent. In this type of sensor (often referred to as a dosimeter), the thermodynamics do not lead to favorable production of an active compound which can be directly quantified using acquisition equipment. There are generally two situations which require addition of exogenous reagents and/or engineered processes: compound(s) which facilitate a change in activation energy that can be measured, or compound(s) which promote desorption of the target from the receptor binding site for sensor reuse. Examples of exogenous reagent(s) and engineered processes include: fluorescent labels [25], heating elements [26], supporting material(s) in close proximity to the recognition structure such as a coloring enzyme [27], strong acid/base to denature target-receptor bonds [28], among other examples. For example, sensors based on binding between H_2 (*g*) and Ag^+ nanoparticles or Ag^+ films are not reversible without external heating of the sensor surface (Figure 1A). In a biotic example, biosensors based on covalent binding between antibodies and antigens are commonly used in lateral flow assays (Figure 1B). In most cases the binding between the target and receptor material is covalent and cannot be reversed without considerable additional cost. In the case of lateral flow assays, the recognition structure is co-immobilized with a secondary structure that, upon binding of the target, undergoes a specific reaction and leads to a visible color change [29]. In this type of transduction, covalent bonds between the target and recognition structure are typically intact after the signal is acquired, leading to a significant amount of hysteresis. Due to the hysteric binding between target and receptor, devices based on engineered transduction are typically not reusable as attempts to recover the native binding chemistry of the receptor are not known, at this time. There are examples of reversible covalent bonds for sensing based on chiral nematic liquid crystals [30], and other recent work has demonstrated re-usability using allosteric triggers engineered within the recognition mechanism [31,32]. At present, semi-quantitative data can be obtained using engineered transduction approaches, if a sensor array is developed but the hysteric molecular interactions restrict the data from being truly quantitative.

Sensors which autonomously produce quantitative data are classified as inherent transduction (Figure 1C,D). For example, an abiotic sensor based on non-covalent metal coordination between O_2(*g*) and platinum porphyrin is shown in Figure 1C. An example of a biosensor based on enzyme-ligand interaction is shown in Figure 1D. In this type of transduction, binding of the target by the receptor leads to the production of a measurable by-product with little or no hysteresis. No additional engineering is needed to obtain useful signal correlated to the binding event, as the thermodynamics of the system indicate that the presence of the target alone is the rate limiting step for energy state change. The formation of the product can be directly correlated to the presence of a specific concentration of target, with the product formation well described by stoichiometry. The most common example of inherent transduction is the glucose biosensor for blood analysis, where glucose and oxygen are both present in blood, and serve as activators of the enzyme-catalyzed oxidation due to GOx, or glucose-1-oxidase (beta-D-glucose:oxygen-1-oxidoreductase, EC 1.1.3.4). In this reaction, the oxidation of glucose on the sensor surface results in the production of electrons, which are measured using oxidative amperometry [33]. There are many examples of non-contact sensors which are reusable, such as pulse oximeters for blood O_2 inference [34] which are critical for vital sign monitoring but lack the specificity of quantitative tools such as the GOx sensor. Optimizing performance tradeoffs between quantitative sensitivity, response time, selectivity, and range is a task which begins with the user in mind [35], and requires a detailed understanding of the problem context prior to design considerations which are based on material choice. One major advantage of inherent transduction over engineered transduction is that the bonds between the target and receptor are inherently destabilized during the transduction process, leading to diffusion of reaction by-products away from the binding site after by-product formation. Reducing sensor hysteresis facilitates development of reusable sensor chemistry, allowing continuous or in line sensing.

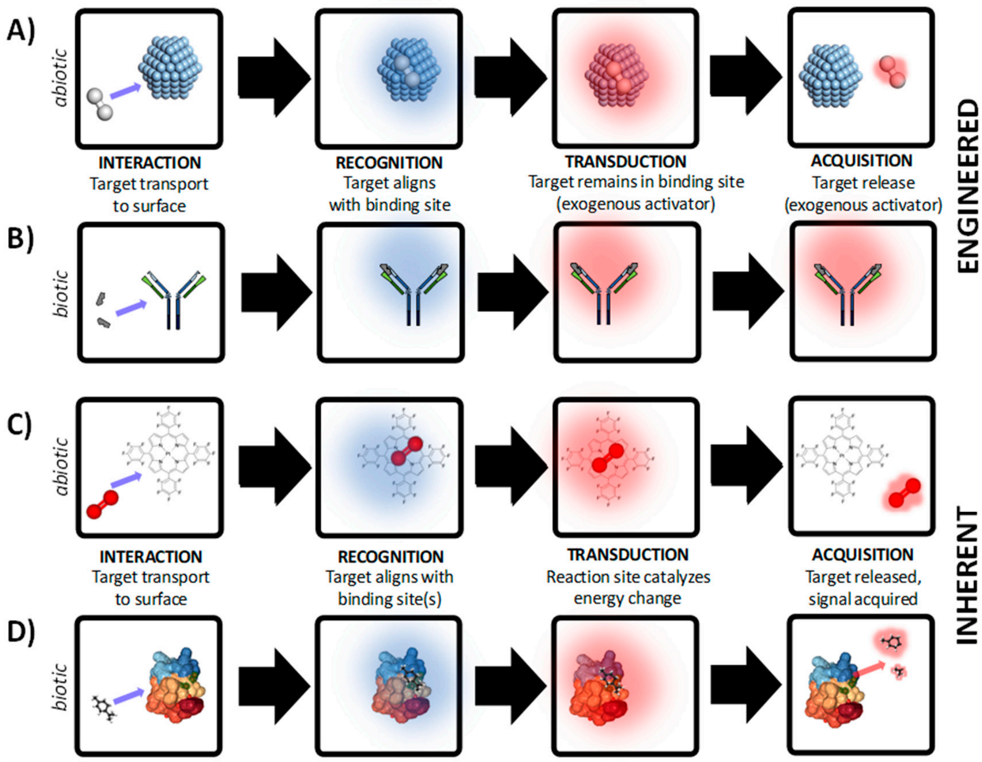

Figure 1. Development of chemical/biological/physical sensors is based on either engineered transduction where an external process is engineered to control transduction and/or acquisition for reversible sensing (panels A–B) or inherent transduction where (panels C-D) where activation energy is supplied by target and ambient environment for reversible sensing. In both examples, abiotic and biotic examples are demonstrated. (**A**) Abiotic sensing of H_2 (g) with Ag+ particles. (**B**) Biotic sensing in a lateral flow assay based on antigen-antibody interactions. (**C**) Abiotic O_2 (g) sensing based on the luminescent dye platinum porphyrin dyes. (**D**) Odorant sensing based on chemosensory proteins. Structure of protein in panel D courtesy of Mosbah et al [36]. The examples shown here are for demonstration purposes, and do not represent all chemical, biological, or physical RTA mechanisms.

Whether the recognition involves a biomaterial, abiotic, or nanophase material, in most cases multiple chemical bonds occur between the target and the receptor material, and the strength of these bonds governs the specificity, limit of detection, response time, and hysteresis of the sensor. Mismatch between material choice and intended application (see Figure S3) results in loss of quality of service, and in some cases a complete lack of technology acceptance. Assays and sophisticated *post hoc* analysis techniques can resolve some of this mismatch, but there are limits. To preserve and elevate the quality of the outcome, selection of appropriate material(s) should be paired with sensing protocols and analytical techniques, discussed in the following section.

Point of Need Sensing and Smartphones

Point of need sensors are a critical tool for medical, agricultural, and environmental monitoring, and the applications of these tools has been diversifying over the last few decades. The primary application space for point of need sensors has been the analysis of unique targets using relatively low cost, rapid detection platforms [37], including small molecules [38,39], viruses [40,41] and cells [42,43] (amongst other targets). Recent works have focused on enhancing the mobility of point of need sensors for rapid on site applications [44] by limiting the requirement for equipment or *post hoc* methodologies that depend on a formal laboratory. Most portable/handheld sensors are not designed to compete with standard analytical laboratory diagnostics, but rather as a parallel tool to trigger new questions or provide additional sampling to improve resolution. Attempting to use a handheld sensor to produce the accuracy and precision that is commonplace in laboratory-based analytical techniques is in most cases not realistic, and often cost prohibitive. What is realistic, on the other hand, is the development of low cost, light weight, rapid diagnostic tools that can provide point solutions to match the specific context of urgent questions. These urgent questions are posed by millions of people in remote rural communities every day, but from a technology point of view may represent the "lower hanging fruit" from the tree of complex problems. Mobility of customized/personalized sensors in an open-access format may prove to demystify the complexity of certain intractable problems, increasing knowledge while providing service to communities in need, and in turn enabling science to serve society. Mobile phone-based data acquisition systems are primary catalysts for mobility of sensor data in this context [45].

Smart phone point of need sensors are available for optical transduction techniques such as fluorescence [46] and surface plasmon resonance [47], in addition to electrochemical transduction techniques such as voltammetry [48] and impedance spectroscopy [49]. While analytical capabilities have grown exponentially in the last decade due to the rapid diffusion of tools such as machine learning [50–52], there are only a few examples of mobile phone-based data analysis tools in the literature [53] as most data analysis occurs on computers and not on mobile devices. To maintain the integrity of user/stakeholder needs and ensure quality of service, mobile phone-based sensors may be connected to remote analytics which most modern mobile devices are capable of supporting. SNAPS is a platform approach for transforming sensor data into actionable information using the mobile phone for data acquisition and performing near real-time, on-site, edge analytics on a mobile device such as a smart phone or a tablet (Figure 2).

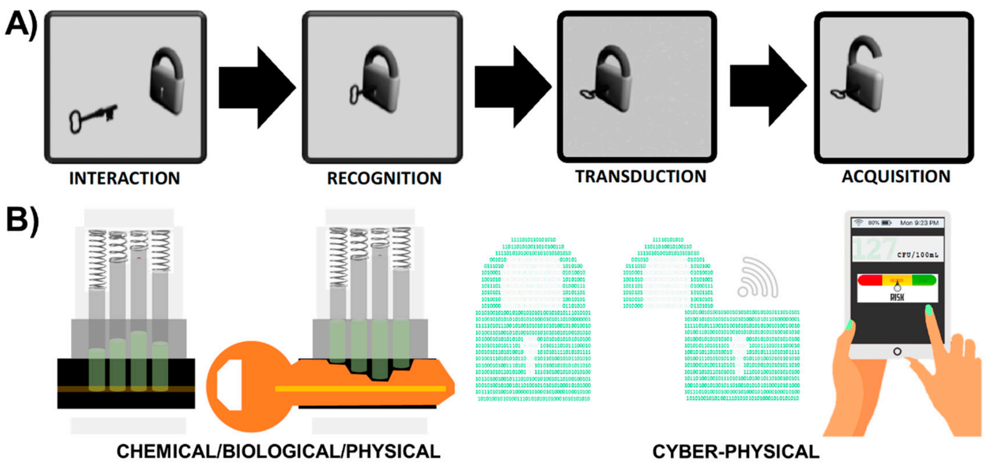

Figure 2. Sensor-Analytics Point Solutions (SNAPS) optimize synergistic integration and connectivity between chemical/biological/physical sensing with cyber-physical systems. (**A**) Classical "lock and key" metaphor for sensor/biosensor/nanosensor design. (**B**) Sensor signal transduction (physical/chemical/biological component) and transmission to a mobile device coupled with in-network processing and on-site edge analytics (cyber component).

3. Sensor-Analytics Point Solutions (SNAPS)

SNAPS consist of a biological/chemical/physical sensor directly interfaced with an analytical tool on a mobile device. The general concept of sensors using mobile devices is not new (for example see review by Quesada- González and Merkoci [45], but to date this may be the first review that focuses on convergence of sensing and analytics on mobile device platforms with an equal balance on the two domains. In this section we provide a roadmap for matching transduction type to analytics (Figure 3) and then we review a select number of recent advances in hardware and software used for SNAPS (Figure 4). The green box in Figure 3A summarizes the RTA triad and displays a choice between the two types of transduction discussed in Section 2. Once a receptor material is selected and the appropriate transduction scheme is engineered, the process is coupled with acquisition equipment to obtain signal (data). The blue box in Figure 3B shows the post hoc data analysis phase of SNAPS, which aims to extract actionable information from sensor data. Contrary to the standard used in sensor design, the analysis phase is less standardized, primarily due to lack of platform(s) for data diagnostics, data quality, context, problem space, and query semantics [54]. As an example of a common framework, Marr's framework is shown, which is a learning principle grounded in Bayesian inference. Marr's analysis process flow has three interconnected steps: (i) a computational stage, (ii) an algorithmic or heuristic step, and (iii) an implementation step [55]. Analogous to the two types of transduction previously discussed in Section 2, the choice of a heuristic or algorithmic approach should be directly linked to the problem context in order to maintain quality of service (QoS). The implementation step deconvolutes processed data using a relevance filter for producing actionable information. An important *a priori* consideration for SNAPS is that the context of the problem should drive the design of both the sensor performance and the type of analytics to extract information.

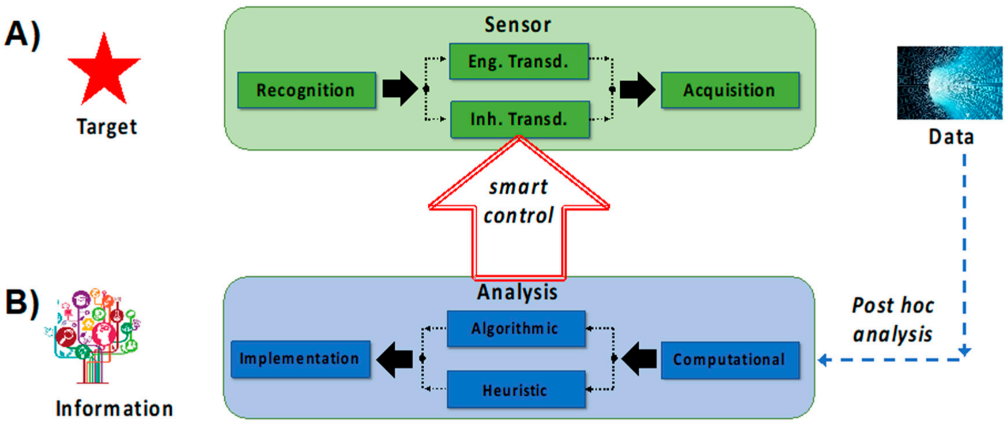

Figure 3. SNAPS attempts to transform data into information based on convergence of two distinct areas, namely sensing and analytics. The framework for these two areas is described by: (**A**) standard sensor development guided by RTA logic, and (**B**) data analysis using the usual tools (computational, algorithmic, statistical). Smart control can be achieved when data from the analysis step actively controls (auto-actuates) at least one process within the RTA sensor triad.

In advanced SNAPS, the analysis phase may have an optional feedback control loop with the sensor transduction step, which may be referred to as smart SNAPS. For example, the temperature, pH, electrical potential, or light intensity can be modulated to influence the sensor transduction step based on information obtained from the data analysis phase. Active control of any phase in the RTA triad qualifies as a smart SNAPS but interfacing with the transduction step is the most logical route for adding value. This concept is broadly referred to as sense-analyze-respond-actuate (SARA), which offers tremendous opportunity for controls systems (a detailed discussion is beyond the scope of this manuscript). In SNAPS, acquisition and analytical processing occurs at the edge by deploying a mobile platform of tools using a smartphone or a tablet, or other similar devices as mobile hosts. The next section demonstrates a few examples of these hardware and software tools in the current literature.

SNAPS Hardware and Software

Figure 4 shows an example of the hardware and materials that may be used for the development of SNAPS. There are many other examples in the literature [46–49], but these two cases overview engineered and inherent transduction as proof of principle. There are a myriad of other approaches for optical smartphone sensing [47,56,57] as well as electrochemical sensing [48,58], and each has value. The examples in this review are by no means comprehensive (see Table S1 for summary).

An example of engineered transduction (top of Figure 4) demonstrates engineered transduction for diagnosis of tuberculosis (TB) via detection of acid-fast bacilli in sputum samples. Biorecognition is grounded in principles of glycobiology, where target cells are labeled by glycan-coated magnetic nanoparticles (GMNP) [59,60]. In this example, a neodymium magnet is used to separate the particle-cell aggregates to facilitate rapid determination of acid-fastness and cording properties of captured mycobacteria. The TB test also employs Gram staining (an irreversible process) to provide visual confirmation. Smartphone-based optical systems such as the device by Wei et al [61] or the complex microfluidic system by Zheng et al [62] may be used for expanding on-site image analysis, and image processing algorithms [63–66], may be used for improving accuracy and providing decision support, among many other similar image acquisition algorithms.

An example of inherent transduction (bottom of Figure 4) is demonstrated for detection of biogenic amines using a the graphene-diamine oxidase nanobiosensor developed by Vanegas et al [67]. In this example, an enzymatic biosensor was developed based on diamine oxidase, which was tethered to a laser scribed graphene electrode (LSG) decorated with nanocopper. Upon recognition of the target ligand within the enzyme binding pocket, oxidation is carried out to produce hydrogen peroxide as a by-product. The peroxide is then deprotonated under an operating potential of + 500 mV to produce electrons, measured using oxidative amperometry. Signal acquisition is conducted using a handheld potentiostat connected to a mobile phone such as the ABE-STAT tool developed by Jenkins et al [49]. Further, the support vector machine learning (SVML) classification system developed by Rong et al [53] may be applied using the same mobile phone via the Jupyter notebook open source machine learning tools.

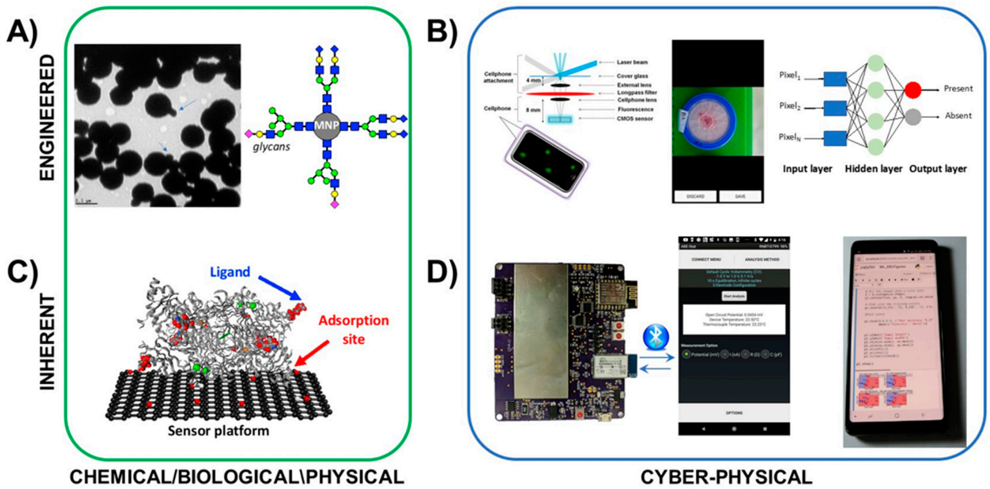

Figure 4. Examples of hardware and materials that may be used for SNAPS for engineered transduction (top) and inherent transduction (bottom). These examples are by no means comprehensive but instead demonstrate the convergence of chemical/biological sensors with cyber-physical systems for delivering computational capabilities and algorithms to sensor data. (**A**) Bacteria-specific magnetic nanoparticles provide dual functions of labeling and enhancing aggregation in detection of target cells. (**B**) Cyber-physical tools for engineered transduction may include smartphone-based microscopes for cell imaging, with the images processed by embedded algorithms for informing decision support. (**C**) Oxidase-based biosensors enable inherent transduction, limiting hysteresis and enabling reusability. (**D**) Handheld potentiostats may be used to acquire electrochemical sensor signals, and embedded or cloud-based analytics such as SVML tools (Reproduced from [53] with permission from The Royal Society of Chemistry.). may be used to provide analysis and decision support. Photograph of glycan-functionalized magnetic nanoparticles courtesy of Bhusal et al [59]. Crystal structure of diamine oxidase courtesy of McGrath et al [68]. Fluorescent smartphone sensor platform courtesy of Wei et al [61]. Image of colorimetric *E.* coli test and machine learning knowledge graph from Gunda et al [66].

Sensor data, and thus the hardware to collect the data, are core competencies required to fuel SNAPS or any equivalent tool in the portfolio of machine-assisted tools (MAT). Without data, subsequent progress from SNAPS to decision support tools is impossible. SNAPS require the point of need (i.e., mobile) platform to have near real time access to data analytics, statistical characterization and algorithms via embedded systems in mobile devices, or sourced, in near real-time, from mist, fog or cloud computing resources. In the next section we review recent advances in software applicable for SNAPS.

A wide range of commercial and custom software are available for cloud-based analytics [69–71], and the list of tools is growing. SNAPS may deliver actionable information through contextually relevant applications using combinations of machine-assisted tools (MAT) and machine-assisted platforms (MAP), enabled by user friendly innovative tools such as drag and drop systems. Drag and drop analytics [72–77] may be quite useful in this context. One example of drag and drop analytics is the tool developed for quantifying uncertainty in data exploration (QUDE). QUDE automatically quantifies different types of uncertainty/errors within data exploration pipelines [78]. The automation feature in this tool is based on the following workflow: data extraction, data integration, data processing, exploratory queries, machine learning, and finally interpretation. QUDE is not intended to represent a global solution for all problems relate to SNAPS, but rather demonstrates one approach that may serve as a starting point to connect sensors to analytics in real time based on the intuitive drag and drop interface. While this basic concept is clear, evolution of data analysis from extraction to visualization, even in a drag and drop *modus operandi*, is a process which requires a deep understanding of the context and is highly problem specific. Visualization tools (such as the volcano plots in the right side of Figure 5) are information-rich presentations of complex datasets which may facilitate use of a tool in multiple application domains, but the information is typically not comprehensible to users/stakeholders. Knowledge graph algorithms, in combination with statistical analysis and machine learning (for example, feature engineering, extraction and selection) [79,80], are elements likely to improve this aspect and facilitate evolution of the tool to enable data-informed decision support. This gradual evolution of SNAPS towards a higher order tool supports advanced features such as data-informed decision as a service (DIDA'S), as discussed in Sections 4 and 5.

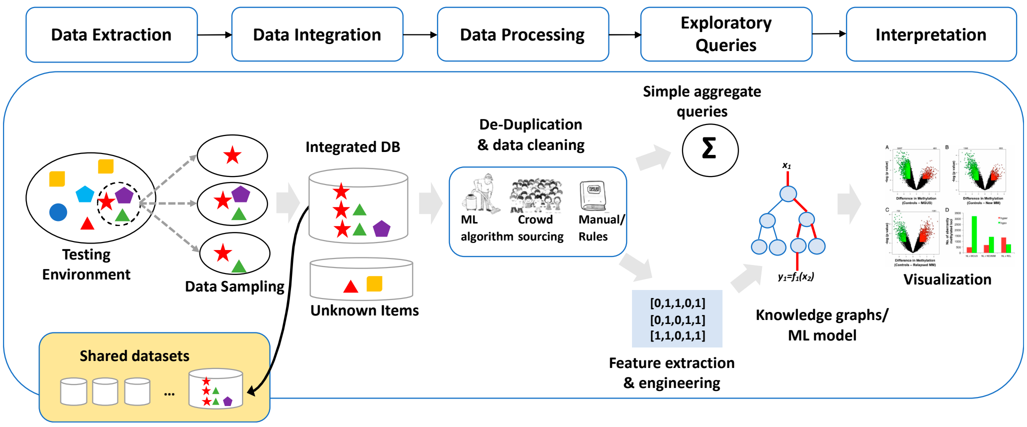

Figure 5. Example of software tools such as drag and drop analytics enable cloud-based analytics for SNAPS. The tool shown here automatically quantifies the different types of uncertainty/errors within data exploration pipelines (image from Chung et al [78] modified to match context of SNAPS). Diagram shows workflow (**top**) and an example pipeline (**bottom**). DB = database, ML = machine learning.

The plethora of tools reviewed here and elsewhere may operate in harmony in specialized facilities (such as academic research centers). However, the real value of the convergence is at the hands of the end-user, who may lack specialized knowledge of software or systems. Without lucidity as a guiding light in the design process, the applications of these tools may never be realized outside of research projects. Adoption largely depends on creating user interfaces no more complicated than a menu of choices, for example, the type of variant configuration (i.e., dashboard) that enables a user to customize a laptop. Thus, the paradigm of "plug and play" must be at the front and center of this discussion in order to hide the complexity behind simple drag and drop features which will empower the end users to efficiently interact with the tools [81,82]. Simplified drag and drop tools for SNAPS will exponentially accelerate the global demand for these sensor tools. Democratization of access through Lego-esque modular drag and drop interfaces [83], may pave the way for mobile decision support systems and partial autonomy. Drag and drop analytics coupled with SNAPS has enormous application potential, not only in the agro-ecosystem but in any domain, for example, healthcare, manufacturing [84], finance, utilities, logistics, transportation and retail. In the next section we discuss opportunities for partial automation of SNAPS.

4. Auto-Actuation and Partial Levels of Autonomy for Low-Risk Automation

In this section we introduce concepts of autonomy as they relate to SNAPS and discuss future possibilities for partial levels of autonomy in SNAPS. Autonomy is a framework that emerged from intelligent control and systems theory which dates back at least a half century [85]. The specific sensor need and problem context, predicate the architecture of the autonomous system (including both hardware and software). Not all sensors or sensor systems are required to be involved in higher levels of autonomy and there are many problems which only require partial autonomy [86,87]. For example, the purpose, architectural details, system functions, and characteristics for unmanned terrestrial vehicles are different compared to unmanned space vehicles [88]. Although these differences amongst different sensor systems are clear, one unifying attribute is the need to detect a target (sensors on the front end of the process) and then analyze the data (analytics on the back end) in near real time. Lessons from automation in the automobile or aerospace industry, among others, may serve as a knowledge base for engineering and optimization of SNAPS to deliver value, albeit in a very different context and with different specifications.

In the context of SNAPS, the traditional six levels of autonomy (see Figure S4), may inform design and serve as a guide. In the lowest level of autonomy (simple), human interaction is required for direct control of the sensor system(s) and/or manual off-loading of data for post hoc analysis. For example, deployed buoy systems are common in environmental studies of aquatic chemistry [89], which represents the current state for most sensor data. In the second level of autonomy (assisted), a high degree of human interaction is required, but at least one aspect of SNAPS (either sensing or analytics) is capable of performing task(s) without *de novo* synthesis of a pathway map. These tasks may achieve prescribed objective(s), adapt to environmental changes, or develop new objectives. For example, Rong et al [53] recently developed an open source mobile-phone based analytics protocol for analyzing impedance data acquired from a nanobiosensor without *a priori* knowledge of sensor type. The primary objective of the tool is to perform the first layer of analysis in development of a SVML classifier to analyze impedance data (in lieu of equivalent circuit analysis). The mobile phone-based tool automates selection of classifier type using principal components analysis, and subsequently automates selection of hyperplane parameters (optimizes the support vector classifier and support vector regressor functions across the selected hyperplane). While this MAT does not perform decision support or provide validation layer(s), it may qualify as machine-assisted automation, particularly if the impedance data is acquired using the same hardware and the sensing/analysis processes are linked for on-site edge analytics.

The classical third level of automation, partial autonomy, may be achieved through remote control of SNAPS related features, including sensing, data download, and some form of data analytics such as heuristic risk assessment. The outcome may trigger a low-risk set of logic tools to execute a workflow which sets into motion an auto-actuation function. By embracing and accomplishing auto-actuation, the concept of SNAPS marches forward to merge with the principle of SARA for enabling auto-actuation. For example, SNAPS may auto-adjust the water flow rate in irrigation pumps (by temporarily overriding a pre-set routine flow rate) based on updated moisture data from field sensor(s) and refreshed external weather data. Hence, smart control systems like SNAPS and SARA are derived from principles of bio-mimicry because feedback control (activation/inhibition) is the bed-rock of biological systems in maintaining homeostasis and cellular equilibrium [90].

Higher levels of automation may exceed the scope of SNAPS. If the desired outcome of a sensor involves some element of auto-actuation or partial automation, the principle of auto-actuation suggests that we must integrate elementary logic layers, relevant to the context of the event, to enable SNAPS to execute the action using/combining a set of contextually relevant output from SNAPS. For partial automation, SNAPS shall increasingly rely on integration of logic structures, for example, integrating output from SNAPS in decision support for auto-actuation. Integration of logic in the SNAPS architecture indicates a departure from simple point solutions and an upstream move toward higher levels of autonomy, a layer of convergence beyond this review.

In the next section, we focus on two major categories of SNAPS: (i) sensors with engineered transduction coupled with heuristic analysis of qualitative data, and (ii) sensors with inherent transduction coupled with algorithmic analysis of quantitative data. This organization into two categories is designed to meet user needs while maintaining an appreciable quality of service.

5. Coupling Sensor Transduction with Data Analytics for Decision Support

In this section we present two generic cases of SNAPS, each case is intended to match sensor transduction type with the appropriate class of analytics based on the logic in Sections 2 and 3. In the first case, qualitative or semi-quantitative sensors (engineered transduction) are matched with qualitative (i.e., heuristic) analytics. In the second case, quantitative sensors (inherent transduction) are matched with quantitative (i.e., algorithmic) analytics. While these two cases are not intended to cover all possibilities, we discuss the importance of ensuring that sensor data and analytic tools are appropriately coupled. In Section 6 we provide a tangible example of each type of SNAPS.

The first category of tool (Figure 6A) utilizes qualitative sensors based on engineered transduction coupled together with heuristic analysis to produce artificial reasoning tools (ART). This category, deemed SNAPS-ART, is designed to provide near real time management suggestions, such as the use of a single sensor to determine whether a particular sample is above or below a threshold set by a regulatory agency. The assumption of high fault tolerance and low risk are pivotal to development/deployment of SNAPS-ART. To maintain quality of service while optimizing development costs, acquisition of qualitative data for SNAPS-ART uses engineered transduction techniques and heuristic classification to satisfy user expectations with a binary output (for a rapid YES/NO test). In terms of active control features, the SNAPS-ART platform may be quite rudimentary, with only a few discrete and distinct actions (turn on/off a subsystem) determined by simple non-overlapping binary outputs based on input from SNAPS. SNAPS-ART is not intended to be a comprehensive diagnostic tool, but rather designed for triage or rapid screening, where additional testing is often required to confirm/validate results. It is possible to use ART for semi-quantitative purposes that depends on other combinatorial factors (e.g., flowrate control), but within reason. The layer of ART may be conceptually viewed as a holding platform for machine-assisted tools, which apply basic pseudocode with simple logic to provide an output sufficient to execute a low risk action which is highly fault tolerant.

The second category of tool (Figure 6B) utilizes quantitative sensors based on inherent transduction coupled with algorithmic analysis for providing data-informed decision as a service (DIDA'S). The tools are collectively referred to as SNAPS-DIDA'S. Contrary to SNAPS-ART, this category is designed for decision support under the assumption of low fault tolerance and moderate risk where real time, continuous monitoring is required. Rather than instantaneous results that are classified by heuristic data analysis techniques, a defining feature of SNAPS-DIDA'S is the dynamic/reiterative analysis of streaming data from sensors as well as feedback logic that interfaces with processed data. For example, active control features using a case-specific subset of tools from a super-set of MATs and MAPS (machine-assisted tools and machine-assisted platforms, respectively). Optimization based on menus of choices and ranges of values, for each variable, require computational rigor to extract context-specific variant configurations rather than workflow middleware as the control layer.

Sophisticated decision support software with decision trees executing embedded logic is one option that may be user-directed [91,92]. The latter may be enabled by a drag and drop assembly from the portfolio of modular tools under the umbrella of MAT and MAP. Another option is to present these choices to a human-in-the-loop who may exercise some form of exclusion/reduction to narrow the search space (number of choices) from the MAT/MAP menu based on experience and knowledge [93,94]. The third and the preferred long-term option is the development of a parallel agent-based system (ABS) which may be part of a multi-agent system (MAS) [95,96]. The agent is expected to be highly specific for certain pre-determined functions and endowed with the capability to replicate (reason) a few of the elementary choices and selection functions as if resembling the human-in-the-loop. ABS cannot benefit directly from human experience and/or human ability to handle exception management, which restricts the range of options to the arsenal of information and logic rules that are embedded into the ABS. One of the major limiting factors is the inability to train a software agent and invoke actual learning, especially regarding decisions such as how and when to use a particular tool. Due to the cognitive boundaries of deterministic design, it is not possible to for a training tool or machine learning routine to educate an agent to deliver support in non-deterministic scenarios. The latter makes it mandatory to recognize the boundaries of "artificial" systems and consider maintaining provisions for humans-in-the-loop, by design, for non-deterministic cases (exception management).

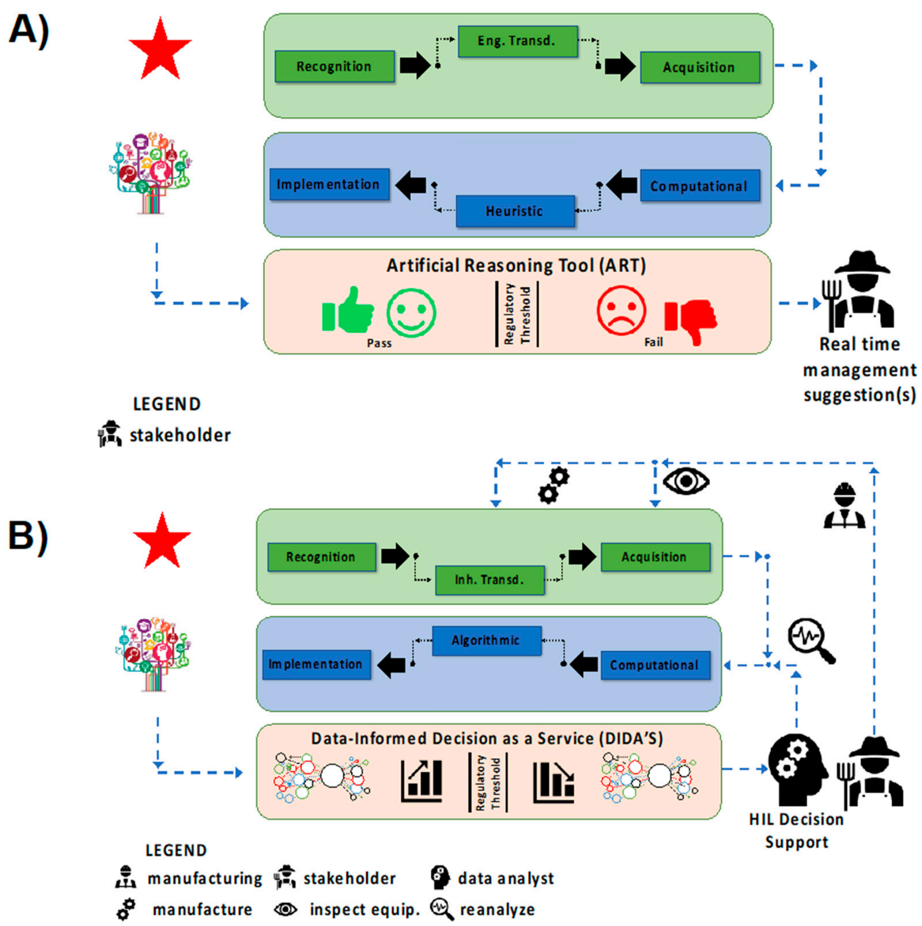

Figure 6. Classification of two major types of SNAPS based on user/stakeholder expectations. (**A**) SNAPS-ART produces qualitative, or semi-quantitative sensor data based on engineered transduction for analysis using heuristic analysis tools to provide management suggestions. (**B**) SNAPS-DIDA'S produces quantitative, streaming data for algorithmic analysis to be implemented in a variety of decision support paradigms, which may include human-in-the loop and/or agent-based systems. The diagram provides a basic map for avoiding mismatch (i.e., loss of quality of service) between sensor chemistry and application needs but are not intended to be dogmatic.

The theoretical boundary between ART and DIDA'S is blurry, at best. The classification of the two systems into discrete boxes in Figure 6 is by no means intended to be reductionist, rather this strategy is merely an attempt to introduce SNAPS and suggest future improvements and innovations. The distinction between ART and DIDA'S may be made in terms of the data that must converge or the degree to which data fusion may be necessary when rendering the decision or recommendation. ART is expected to be a rapid-response system which aims to solve low risk problems with only a few data sources and data dependencies using either qualitative or quantitative sensors matched with heuristic analysis. To contrast the two, qualitative SNAPS-ART may provide the instruction to turn off the irrigation water pump if [a] the rate of change of 80% of the soil moisture sensor readings fall above/below a given range of values or [b] if the data from the sensor(s) indicates that the rainfall rate is above a certain value. For quantitative SNAPS-ART, the instruction may be to monitor and turn up/down the rate of irrigation water flow, by grids/zones, depending on the soil moisture sensor readings, if the sensor data falls above/below a range of values. The tool may refer to the logic instructions in a look-up table which recommends water flow rates versus soil moisture. DIDA'S may be viewed as a mutiny of multiple ART units, each vying to contribute data. At each gateway or node in the DIDA'S platform, there are agents which are queueing, to be triggered by a specific data strand/stream, to initiate a search and discovery process for identifying what tools must be used. This represents dynamic composability of tools triggered by data in a manner similar to application-dependent-networking, which connects two mobile phone users in diverse environments. In addition, agents are triggered to discover which databases or data resources must be accessed, to satisfy the context of dependencies, and when/how to feed the results from the search and discovery to a higher-level agent.

In the context of SNAPS-DIDAS, agent-based systems begin to function upon receiving input from SNAPS. Using logic capabilities (learned, trained, reinforced), agent(s) determine which tool, or sets of tools, may be necessary to execute the action or automation that the SNAPS output expects to trigger. Agents are limited by the tools contained within MAT and MAP, unless embedded logic provides the option to place a remote function call (RESTful API) to a cloud repository to source other tools or algorithms. If this feature is included, agent(s) can "discover" which are contextually relevant for the use case, providing higher levels of automation. Search and knowledge discovery functions of machine-assisted systems are key performance indicators (KPI) which are inextricably linked with quality of service (QoS). Synergistic integration with external tools and modules is subject to interoperability among platforms, which are influenced by standards and architecture. As is apparent from this brief discussion, automation of SNAPS-DIDA'S is far from trivial, and we are only beginning to scratch the surface in terms of the confluence of ideas necessary to transform this vision into reality. In the following section we provide tangible examples of SNAPS, with a specific focus on SNAPS-ART (tangible examples of SNAPS-DIDA'S is beyond the scope of this review).

6. Proof of Concept SNAPS

In this section we show two proof of concept SNAPS-ART tools to demonstrate the application of the concept to environmental and agricultural problems related to safe drinking water and food. These two examples were selected based on the global significance of the problem, as well as the transdisciplinary nature of the question at hand for ensuring planetary health (i.e., the health of the planet and the humans that inhabit the space) [97–99]. In each case the analytics are embedded into the mobile device and the tool supports manual data entry as well as auto-upload of sensor data.

Figure 7 demonstrates an example of SNAPS-ART for heavy metal analysis coupled with hazard analysis risk assessment. In this design, a sensor with engineered transduction (qualitative data) is coupled with a heuristic risk analysis tool (hazard quotient indicator) for monitoring and assessing risk of mercury exposure in drinking water applied to locations lacking adequate water management infrastructure. The tool was designed for use in rural settlements located near artisanal and small-scale gold mines [100]. In this example, a nanosensor was developed based on LSG electrodes decorated with anchored nanocopper for measuring ionic mercury (Hg^{2+}) via stripping voltammetry [101] (Figure 7A). Rapid screening of water samples for mercury contamination is highly useful, but the value of sensor data is inconsequential without information on how compounded factors, such as body weight, ingestion rate, and length of exposure contribute to overall public health risk for an individual. A mobile app was developed in R language (see supplemental section for code) using the heuristic hazard quotient (HQ) methodology used by regulatory agencies across the globe [102]. MIT App Inventor was used to create the smartphone app, which is rooted in drag and drop techniques using the Blockly modular tool for functionality. Figure 7B displays the graphic user interface and an example output for the SNAPS-ART tool, where users input drinking water ingestion rate, body weight, length of exposure, and age. The app captures Hg^{2+} levels (ppm) obtained from the sensor, and uses the framework established by the US Environmental Protection Agency (EPA) and the World Bank to calculate a HQ score [103–105]. Using the standard HQ threshold set by the EPA [106], HQ scores greater than 1.0 indicates higher risk of potential adverse health effects increases, while a score less than 1.0 indicates low risk. SNAPS-ART provides a real time management suggestion to the user based on international standards for mercury contamination of drinking water. In addition, ART provides a suggestion to seek additional screening at a verified laboratory if the sample is positive, which is a critical feature for secondary validation. The HQ output significantly increases the end-user value of the sensor by combining the raw sensor data in the context of human-specific factors and micro-environment, to provide actionable information relevant to precision public health.

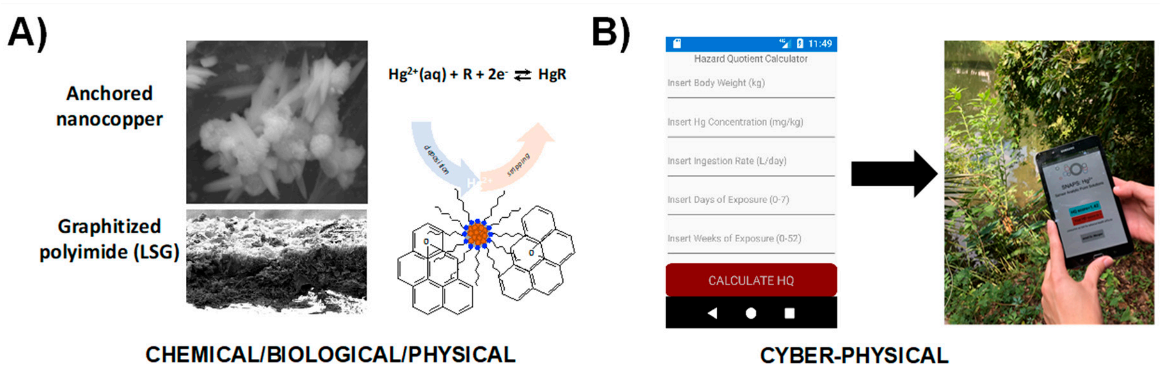

Figure 7. Proof of concept demonstration for SNAPS-ART in heavy metal analysis (drinking water). (**A**) Hg^{2+}-selective nanosensor based on LSG and nanocopper developed by Abdelbasir et al [101]. (**B**) Screenshot and photograph of heuristic analysis tool for calculating risk of mercury exposure (hazard quotient calculator).

Figure 8 shows another application of the SNAPS-ART platform applied to impedimetric sensors for detection of pathogenic bacteria in food samples. The *Listeria monocytogenes* biosensor developed by Hills et al [107] is used as a demonstration (Figure 8A), and an ART tool was developed using machine learning (code written in R programming language, see supplemental section for code). The ART tool for *L. monocytogenes* detection is grounded in binary classification using bagged random forest, and the smartphone app was created using MIT App Inventor. The program reads a raw impedance data file from the biosensor, converts the data to the necessary form for machine learning classification, optimizes hyperparameter values, and then uses machine learning techniques to compare the sample to a training library; other methods are feasible as described by Rong et al [53]. The tool is used for predicting whether the food sample may be contaminated or is safe according to thresholds set by guidelines established in the Food Safety Modernization Act (FSMA), and how the user may seek secondary validation if the sample is positive (Figure 8B). The major benefit of this tool is the avoidance of computationally expensive (and time intensive) analytical methods such as equivalent circuit analysis. While some equivalent circuit models, such as the Randles-Ershler circuit, provide some description of the physical meaning for each circuit element related to an impedimetric biosensor, in most cases more complex models are used and parameters are tuned with Chi^2 fitting. If not used with expert guidance, equivalent circuit analysis leads to significant errors in both interpretation and accuracy and may be cost prohibitive for many labs. In field analyses, equivalent circuit analysis is computationally and energy intensive, limiting the practicality for monitoring rural regions or dense urban areas where network connectivity and power are limited. For pathogens such as *L. monocytogenes*, the threshold for contamination is one live cell in a food sample, and thus speed and accuracy of the tool are paramount, particularly for rapid screening. Delays in data analysis lead to food waste, increased risk of contamination, and a significant reduction in quality of service [108]. Use of machine learning tools and other similar algorithms to rapidly perform screening on site with SNAPS significantly increases the value of the sensor and provides actionable information in the hands of the user, regardless of location or access to a formal laboratory.

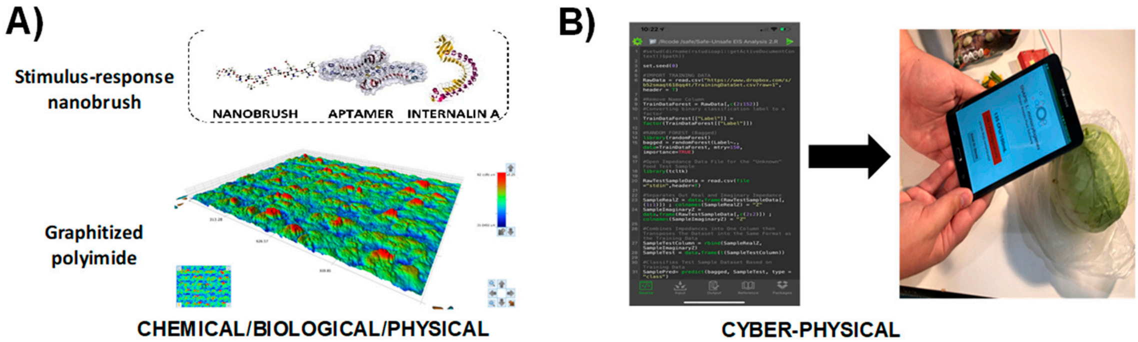

Figure 8. Proof of concept demonstration for SNAPS-ART in food safety analysis (vegetable broth). (**A**) *Listeria monocytogenes* biosensor developed with stimulus-response polymers and DNA aptamers by Hills et al [69]. (**B**) Screenshot and photograph of machine learning analysis tool for determining whether sample is contaminated based on an index score derived from machine learning analysis.

The benefits of the approach in Figures 7 and 8 may be vastly extended by adapting the sensor RTA scheme to allow the tool to detect and alert users about other targets. For example, development of a sensor array to simultaneously target other heavy metal contaminants including lead, cadmium, and arsenic or other biomolecule targets such as viruses. SNAPS-ART may be used for detection and diagnostics for a plethora of contaminating agents not only in liquid or food (as shown here), but in any other medium as long as the analyte is presented in a form that binds with the sensor material. The immense value of this approach when combined with mobility (smartphones) is the ability to source sensor data for a myriad of analytes in different environments where humans or drones may reach to interact with the sample. In our approach, we have eschewed the use of high cost sensors, to highlight the potential for diffusion of low-cost tools to enable democratization of data and distributed decisions to serve community-specific needs. To acquire, curate, analyze and extract useful information from sensor and other data, we advocate synergistic integration with MAT and MAP. SNAPS is a preliminary step in that direction, and there are a many challenges and opportunities as discussed in the following section.

7. Challenges and Opportunities

From SNAPS to PEAS

There are many challenges and opportunities for SNAPS (see Table 1). As SNAPS evolves, sensor engineering for controlling or modulating hysteresis is an absolute requirement if the user expectation is rooted in real time, in situ, sensor data connected to data analytics (see Figure S5). Rudimentary control over system performance through the use of SARA-driven smart SNAPS to auto-actuate select system components is applicable to the agro-ecosystem, environmental health, as well as public health. While no specific example is shown here, SNAPS is the first step toward DIDA'S, which may rely on tools such as drag and drop analytics and models using agent based systems. DIDA'S is a tangible goal on the horizon, but current progress is rather slow. In agricultural and environmental systems, connectivity is often assumed, but rarely functional at the level required for a complex system [109–111] such as SNAPS-DIDA'S. As SNAPS and similar tools mature, the true value may be realized through the interaction of agents which embrace the collective optimization of performance in the context of the environment. This futuristic concept is captured by the convergence of performance metrics (precepts, environment, actuators, sensors) or PEAS, a mnemonic borrowed from the literature on agent-based systems (ABS) to address "whole" system performance [112].

Table 1. Challenges and Opportunities for SNAPS.

Challenge	Opportunities
Extraction of information from sensor data for real time decision support	• Development of SNAPS-ART tools using established regulatory standards as a guide
Controlling or modulating sensor hysteresis in situ	• Integration of smart materials on sensor surface (e.g., stimulus-response polymers) • Rudimentary control over system performance through the use of sense-analyze-respond-actuate (SARA) systems
Mobility and connectivity in agricultural and environmental systems	• Deploy high bandwith, low latency, systems • Develop low power sensor data management
Integrating SNAPS into a standardized platform	• Establishment of data management systems based on lessons learned from other systems such as integrated clinical environment (ICE) • Establishment of standard architectures for real time sensing (interoperable with other standards)
Development of data informed decision as a service (DIDA'S)	• Establishment of SNAPS-ART as a common tool • Integration of drag and drop analytics (DADA) and agent based systems (ABS) • Dynamic/reiterative analysis of streaming data from sensors (captured in time series databases) • Demonstration of feedback logic that interfaces with processed data • Dynamic composability of tools triggered by data (application-dependent-networking) • Database discovery or data resource discovery by agents using embedded logic (e.g., remote function call, RESTful APIs) • Use of logic capabilities (learned, trained, reinforced) and agent(s) to determine which tool, or sets of tools, are required for the given problem

There is an enormous opportunity to develop decision support systems using the PEAS as a platform. PEAS are pillars on which we may build "machines that work for us" versus "cogs" in the wheel as envisioned by Ellul a half century ago [113]. SNAPS, ART, and DIDA'S are examples of tools with which we are working and represent short-term opportunities for Pareto-like solutions. Beyond SNAPS, PEAS represent goal-dependent strategic perspectives for systems-level synergy. Each platform contains an array of dynamic push-pull elements and user-directed levers, which may be used in any combination, to accomplish short term tasks (SNAPS) for establishing the foundation of long-term attempts to orchestrate systems performance (PEAS). This interrelationship may be analogous to components of the engine (SNAPS, ART, DIDA'S) which are essential and dependent for the function and performance of the "whole" vehicle (PEAS).

Aggregating data and information for systems performance using the PEAS concept is the Holy Grail and, in some instances, the "whole" picture is the only relevant picture. This concept may seem far reaching, but related attempts in biomedical engineering have already proven viable, such as the integrated clinical environment (ICE) effort [114]. ICE drives data interoperability between all sub-systems to focus on the "whole patient" rather than isolated parts. These two concepts (PEAS, ICE) may serve as a guiding light for innovations applicable to agriculture, environment, or other verticals areas, where a tapestry of solutions may be more valuable than point solutions. Regardless of the application domain, convergence of solutions to create systems level performance is the key challenge going forward (i.e., avoidance of isolated solutions). Isolated solutions in the medical systems lead to errors in medical device interoperability. The latter is often fatal, claiming as many as 250,000 lives per year, in the US alone, and is the third leading cause of death in the US [115]. In the coming decade(s), there is a major opportunity to develop platforms such as PEAS based on the lessons learned from ICE. Integrating such platforms will both improve knowledge gain, as well as contribute to transformational convergent thinking such as the planetary health concept [98,116]. One of the underlying themes in all use cases is the use of mobility and low latency signal transmission (for example, future potential for use of 5G) as key enablers for facilitating various levels of partial autonomy within system of systems, which responds to remote instructions and other relevant secure signals. However, often, very small amounts of data and/or information, at the right time, can be far more critical and helpful, rather than a deluge of data (erroneously referred to as big data).

The excruciating struggle to extract information from sensor data (if there is information in the data) is an indication that unleashing knowledge from information is an enormous challenge, at present. The much-anticipated evolution of data-science to knowledge-science is the central thrust of knowledge-informed decision as a service (KIDS), an aspirational idea which may not be addressed by current tools and contemporary thinking. The broad spectrum of "data-informed" approaches will vary by use cases, from simpler instances where SNAPS-ART may be the first step, to more complex expectations where DIDA'S will be necessary as a foundation. The first step in resolving this immense challenge is to identify which tool is needed, when it is pertinent, and where to apply the tool.

8. Concluding Remarks

The pivotal role of sensors, data, and information in decision support and partial automation or auto-actuation is of critical importance in any field. SNAPS represent a confluence of ideas and is the foundation for making sense of data and adding value to sensor data. Basic sensor design choices, described in this review, dictate the value and quality of service for SNAPS, and this fundamental concept cannot be overlooked without inducing a fatal flaw that limits the usefulness of downstream cyber-physical systems. At the most basic level, matching the type of sensor transduction (engineered or inherent) together with the appropriate analytical approach (heuristic or algorithmic) to meet the needs of the end user ensures a baseline quality of service. SNAPS and ART offer a glimpse of a few elements of the machine-assisted tools and machine-assisted programs in terms of the quest to deliver value from data analytics. Drawing on these trends, we suggest how SNAPS may evolve to inform knowledge gain as the system complexity increases.

Knowledge discovery cannot be treated as a separate topic when discussing sensors and sensor data. Without discovering the context and relevance of data to the bigger picture, the outcome will remain narrow. Sensors will be impotent without tools to extract value from sensor data. This discussion, therefore, is not peripheral to sensors, it is central to all sensors. The growing ubiquity of sensors which are increasingly woven into almost every facet of our daily lives makes it imperative that sensor scientists and sensor engineers consider the data science impact of their work. Data scientists must take a closer look at sensor data and sensor engineering, to ask the correct questions. Each group must ensure that the tools are designed with the end user in mind for ensuring quality of service. Tools for knowledge discovery are not in short supply, but the rate limiting factor preventing the diffusion of these tools are rooted in their complexity, lack of standards and common open platforms that users can easily access. When and if these "open platforms" emerge, the race to adapt and adopt will not be determined by its success due to technological strength or computational excellence. Rather the economics of technology may be the single most important criteria which will influence and determine feasibility of mass adoption, the latter, in turn, will reduce cost of adoption due to economies of scale.

We are on the brink of change, albeit slowly, with the advances in search and discovery of data and information, using tools based on graph theoretic approach, to establish relationships and dependencies between data, objects, and subjects. New research at the nexus of natural language processing, linguistics, and semantics may be the trans-disciplinary convergence necessary to advance knowledge discovery from sensor data. Broad spectrum dissemination of this knowledge using simple and tangible user interfaces (TUI) will be crucial. Knowledge discovery is at the heart of sensor research and sensor engineering, if we wish to extract value from sensors and aspire to deploy sensors as global public goods.

Supplementary Materials: The following are available online at http://www.mdpi.com/1424-8220/19/22/4935/s1, Figure S1: Overview of Review, Figure S2: Recognition-Transduction-Acquisition (RTA) triad, Figure S3: Design of SNAPS must use a retrosynthetic approach, beginning with the intended application in mind. This allows proper selection of materials, transduction techniques, and analytics for ensuring quality of service. (A) Correct matching of engineered transduction with heuristic analytics. (B) Incorrect matching of engineered transduction with algorithmic analytics leads to overdesign of the tool, consuming unnecessary energy and computational power. (C) Incorrect matching of inherent transduction with heuristic analytics leads to excessive data collection, which causes systematic negative effects unless the data. This approach is valid for long term monitoring programs, but is not relevant for rapid, point of need SNAPS. (D) Correct matching of engineered transduction with algorithmic analytics, Figure S4: Traditional autonomy may not be the dogma for development of SNAPS, Figure S5: (A) Information hierarchy depicting the evolution of sensor data towards knowledge. Higher levels (wisdom, understanding) may be beyond the scope of sensor data, but here we describe a platform for evolution of sensor data to information (SNAPS-ART and SNAPS-DIDA'S) and suggest a path forward for evolution to knowledge via the KIDS platform. (B) When KIDS is applied to the agro-ecosystem, the convergence of performance metrics, environment, actuators, and sensors (PEAS) encompass the platform through agent-based systems, Table S1: Recognition-Transduction-Acquisition (RTA) triad.

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diagnostics

MDPI

Review

Sensor-as-a-Service: Convergence of Sensor Analytic Point Solutions (SNAPS) and Pay-A-Penny-Per-Use (PAPPU) Paradigm as a Catalyst for Democratization of Healthcare in Underserved Communities

Victoria Morgan [1], Lisseth Casso-Hartmann [2,3], David Bahamon-Pinzon [4], Kelli McCourt [4], Robert G. Hjort [5], Sahar Bahramzadeh [6], Irene Velez-Torres [2,3], Eric McLamore [1], Carmen Gomes [5], Evangelyn C. Alocilja [7,8], Nirajan Bhusal [7,9,10], Sunaina Shrestha [10], Nisha Pote [10], Ruben Kenny Briceno [11,12,13,7], Shoumen Palit Austin Datta [1,14,15,16] and Diana C. Vanegas [3,4,*]

1. Agricultural and Biological Engineering, Institute of Food and Agricultural Sciences, University of Florida, Gainesville, FL 32611, USA; tvlmorgan@ufl.edu (V.M.); emclamore@ufl.edu (E.M.); shoumen@mit.edu (S.P.A.D.)
2. Natural Resources and Environmental Engineering, Universidad del Valle, Cali 760026, Colombia; lisseth.casso@correounivalle.edu.co (L.C.-H.); irene.velez@correounivalle.edu.co (I.V.-T.)
3. Interdisciplinary Group for Biotechnological Innovation and Ecosocial Change BioNovo, Universidad del Valle, Cali 760026, Colombia
4. Biosystems Engineering, Department of Environmental Engineering and Earth Sciences, Clemson University, Clemson, SC 29631, USA; dbahamo@g.clemson.edu (D.B.-P.); mccourt923@aol.com (K.M.)
5. Mechanical Engineering, Iowa State University, Ames, IA 50011, USA; ghjort@iastate.edu (R.G.H.); carmen@iastate.edu (C.G.)
6. School of Computer Engineering, Azad University, Science and Research Branch, Saveh 11369, Iran; sahar.bahramzade@gmail.com
7. Global Alliance for Rapid Diagnostics, Michigan State University, East Lansing, MI 48824, USA; alocilja@msu.edu (E.C.A.); nirajanbhusal@gmail.com (N.B.)
8. Biosystems and Agricultural Engineering, Michigan State University, East Lansing, MI 48824, USA
9. School of Medical Sciences, Kathmandu University, Kathmandu 44600, Nepal
10. Dhulikhel Hospital, Kathmandu University, Kavrepalanchok 45200, Nepal; stha.sunaina@gmail.com (S.S.); potenisha@gmail.com (N.P.)
11. Instituto de Investigacion en Ciencia y Tecnologia, Universidad Cesar Vallejo, Trujillo 13100, Peru; rubskenny@gmail.com
12. Hospital Victor Lazarte Echegaray, Trujillo 13100, Peru
13. Institute for Global Health, Michigan State University, East Lansing, MI 48824, USA
14. MIT Auto-ID Labs, Department of Mechanical Engineering, Massachusetts Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA
15. MDPnP Interoperability and Cybersecurity Labs, Biomedical Engineering Program, Department of Anesthesiology, Massachusetts General Hospital, Harvard Medical School, 65 Landsdowne Street, Cambridge, MA 02139, USA
16. NSF Center for Robots and Sensors for Human Well-Being, Purdue University, 156 Knoy Hall, Purdue Polytechnic, West Lafayette, IN 47907, USA

* Correspondence: dvanega@clemson.edu; Tel.: +1-864-656-1001

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Abstract: In this manuscript, we discuss relevant socioeconomic factors for developing and implementing sensor analytic point solutions (SNAPS) as point-of-care tools to serve impoverished communities. The distinct economic, environmental, cultural, and ethical paradigms that affect economically disadvantaged users add complexity to the process of technology development and deployment beyond the science and engineering issues. We begin by contextualizing the environmental burden of disease in select low-income regions around the world, including environmental hazards at work, home, and the broader community environment, where SNAPS may be helpful in the prevention and mitigation of human exposure to harmful biological vectors and chemical agents. We offer examples of SNAPS designed for economically disadvantaged users, specifically for supporting decision-making in cases of tuberculosis (TB) infection and mercury exposure. We follow-up by discussing the economic challenges that are involved in the phased implementation of diagnostic tools in low-income markets and describe a micropayment-based systems-as-a-service approach (pay-a-penny-per-use—PAPPU), which may be catalytic for the adoption of low-end, low-margin, low-research, and the development SNAPS. Finally, we provide some insights into the social and ethical considerations for the assimilation of SNAPS to improve health outcomes in marginalized communities.

Keywords: sensor analytic point solutions (SNAPS); environmental health; poverty; pay-a-penny-per-use (PAPPU); public health

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1. Environmental Burden of Disease

According to the World Health Organization (WHO), environmental factors including unsafe water, poor sanitation, air pollution, and unintentional exposure to hazardous chemical and biological agents are root causes for the burden of disease, disability, and death in the developing world [1,2] Impoverished communities living in polluted and crowded environments are much more susceptible to the double burden of infective and non-communicable diseases, and this situation is often compounded by a lack of adequate infrastructure, weak environmental policy, and deficient or inequitable healthcare systems that disfavor economically challenged users [3–8]. Despite the global efforts to reduce poverty, indicators of health disparities between disadvantaged and affluent populations continue to persist. For instance, the 2018 World Bank estimates showed that, on average, there is a 12-fold difference in the mortality rate of infants between low- and high-income populations [9], but in countries experiencing extreme deprivation such as Somalia and Sierra Leone, this rate is nearly 20-fold higher than the average rate in wealthy nations. In 2016, diarrheal diseases linked to poor sanitation and the consumption of contaminated food and water were responsible for 1.6 million deaths, 90% of which occurred in South Asia and sub-Saharan Africa [10,11] The per capita burden of disease from inhalation exposure to airborne polycyclic aromatic hydrocarbons (by-products of fuel combustion) has been found to be nearly 33-fold higher in India compared to the USA [12,13].

Nonetheless, it is important to note that due to the myriad ways in which socioeconomic and environmental factors interact, it is very difficult to establish highly detailed associations of single environmental risk factors with epidemiological outcomes [14–17]. Moreover, environmental factors rarely occur in isolation; for example, a population can be exposed to a combination of pollutants from different sources, which could result in additive or synergistic effects and symptoms, making medical diagnostic processes extremely cumbersome [1]. In addition to limited access to healthcare systems, the problem is compounded by the relatively high cost of clinical testing, which may cause many illnesses to go under-reported or mis-diagnosed in economically challenged populations [18]. Despite the complexities involved in linking environmental and socioeconomic factors to epidemiological outcomes, there is no question that such factors can result in serious public health problems, particularly in low-income communities that bear the largest proportion of the burden of environmentally-related diseases [19,20].

Undoubtedly, much of the economic strain from both infectious and non-communicable diseases associated with unhealthy environments could be effectively diminished through preventive strategies that tackle associated risk factors [18,21]. One promising approach for addressing health risk factors in low-income communities is the deployment of integrated technologies for data-informed decision support such as sensor analytic point solutions (SNAPS). The concept of SNAPS was recently introduced as part of a platform approach to converge sensor data and analytics to deliver data-informed decision support for a number of applications, including healthcare [22]. Even though thousands of sensors and point-of-care diagnostic tools have been developed in research labs around the world in the past few decades, the large majority of these technologies have not yet translated into implementable solutions due to different obstacles including the unsuitability of operation under real-world conditions, high fabrication and operation costs (which limits market penetration and profitability), and a lack of convergence with other technologies to yield actionable information for the user [23].

Consider, for instance, the case of diarrheal diseases associated with *Escherichia coli* infection from the ingestion of contaminated food or water, which significantly contributes to the mortality and morbidity of children under five years of age in African and Eastern Mediterranean countries [24]. By conducting a literature search on the Web of Science, we found that, in the past 10 years, 303 research articles have been published in peer-reviewed journals that have portrayed the development of *E. coli* biosensors. However, only a small fraction of these papers has included claims such as real-sample testing (~29%), low-cost fabrication (~10%), portability (~9%), and user-friendly operation (~2%) (the complete report from this search is available in the Supplemental Section S1, Tables S1–S3).

In this manuscript, we provide examples of SNAPS that have been tested in field conditions, within the context of low-income communities. The first example was developed for assisting the early diagnosis of infectious disease and the prevention of public health outbreaks, and the second example supports decision making in cases of human exposure to an environmental pollutant. We also propose the concept of pay-a-penny-per-use (PAPPU) as a potential paradigm to reduce economic barriers to implement SNAPS in economically-deprived regions. The two examples of field-tested SNAPS are at different stages of maturity, providing insight into the design process and logic flow. Finally, we provide some insights on the social and ethical considerations for the effective use of SNAPS in assisting users and improving health outcomes in underserved communities.

2. Examples of SNAPS-ART

Near real-time qualitative decisions are often key for rapid response. SNAPS make up a tool that uses sensor data to provide a response at the point of use with minimal analytics. If two or more factors must be considered by the human-in-the-loop to take a decision, artificial reasoning tools (ARTs) are implemented. ARTs make up a data fusion layer that combines sensor data and displays suggestions or information on the user's mobile device. In principle, SNAPS are designed to offer "point solutions," which implies a rapid binary output (yes/no) based on the data captured from the sensor signal (for example, sensor binds to an analyte). However, even in rudimentary scenarios, a single source of binary data may fail to provide basic information. Hence, the need for artificial reasoning tools (ARTs), which are light-weight middleware (software that sits in the "middle") embedded with preliminary logic to decide what is the meaning of the data and what information may be conveyed (displayed) for the end-user. By introducing a modular ART, the user takes advantage of a combinatorial variant configuration menu to change, adapt, or introduce new reasoning/logic in the middleware by re-programming the logic "buckets" by simply re-shuffling and inserting the user's preferred choices from a repertoire of pre-programmed logic [22].

There are many complex layers to a system-level solution to ease the environmental burden on impoverished communities. Velez-Torres et al. [25] recently developed a circular system framework for integrating analytic tools (such as SNAPS) with social action research (Closed-loop integration of social action and analytical science research, CLISAR). The CLISAR framework is a transdisciplinary approach that involves analytical tools such as sensors for informing community action that is related to, for example, public health, environmental issues, or food security. Beyond simple commercial colorimetric detection strips that are used in development of CLISAR, information derived from SNAPS can transform this system by supporting decision-making processes that are aimed at improving the health outcomes of marginalized communities.

Herein, we suggest a conceptual approach for selecting and implementing the type of diagnostic tools for implementation of SNAPS (see Figure 1). The examples that follow in the subsequent section used a five-step process that followed a closed-loop approach similar to CLISAR and other circular economic models [25,26]. The first step is to understand the specific problem as well as the social and economic context where decision-support technology may be needed. The next step is to identify readily available resources and then design diagnostic tools for creating a technology portfolio (sensors, analytics software, portable hardware, etc.). The third step involves the selection of the most appropriate tools to create SNAPS based on technical capabilities as well as interactive feedback from stakeholders. In step four, scientists and end-users test technology prototypes in field conditions by using established participatory methodologies. Finally, the results from the proof-of-concept testing are used to evaluate and refine the technology. This process is repeated until a solution meets user expectations and desired performance characteristics. The concept is based on principles of circular systems and convergent thinking [25,26], where technology refinement may occur by using reductionist or parallel approaches. Below, we present two examples of how this conceptual model is applied in real-world settings. The first example is in advanced stage field-testing (refinement and technology improvement, with some elements in the second circular phase), while the second example is in the early phase of development (tool selection and technology transfer).

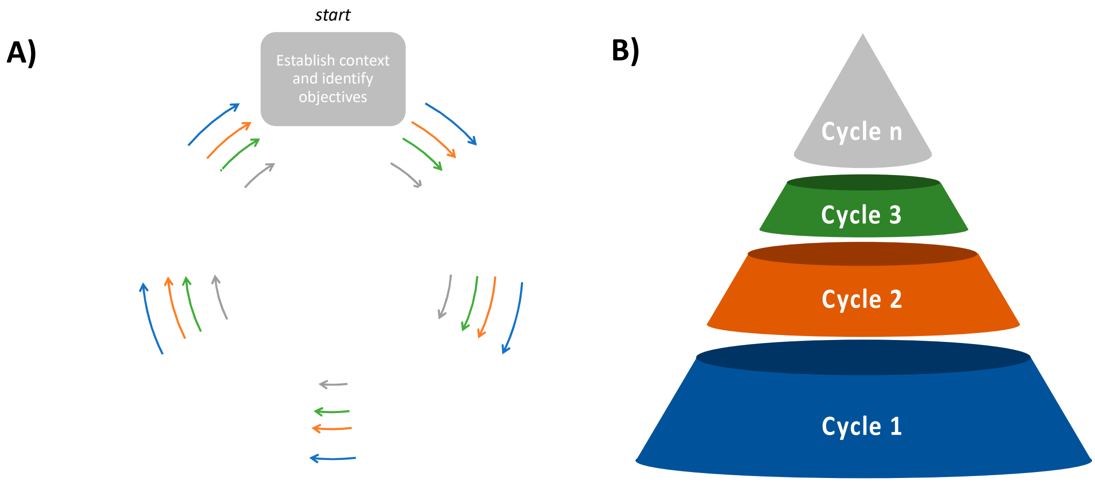

Figure 1. Overview of process in development of sensor analytic point solutions (SNAPS) for the examples shown below. (**A**) The process begins with establishing context, and each cycle concludes with technology refinement based on user feedback. The blue, orange, and green arrows indicate technology evolution by using established principles of circular feedback systems. (**B**) A conical representation of the blue, orange, and green cycles shown in Panel (**A**) indicate convergence toward a systems-level solution through feedback/refinement pathways. The total number of cycles is context-specific and proceeds from cycle 1 to cycle n.

2.1. *Early Assessment of Tuberculosis in Vulnerable Populations*

In 2017, 1.6 million people died from tuberculosis (TB) globally, and there were 10 million new TB cases that occurred in the same year [27]. TB has surpassed HIV as the leading infectious disease killer worldwide since 2014 [28]. Furthermore, multidrug-resistant and extensively drug-resistant TB (MDR/XDR-TB) are current global public health threats. The 2017 Moscow Ministerial Declaration on ending TB, involving 120 countries and over 800 partners, identified "to advance research and development of new tools to diagnose, treat and prevent TB" as one of four action items [29]. This meeting was followed in 2018 by a United Nations (UN) General Assembly first-ever high-level meeting to accelerate efforts to end TB [30].

The care of TB patients starts with accessible and affordable diagnosis. The majority of TB patients live in poor conditions and in geographically remote areas. Culture-based techniques are the gold standard for diagnosis, but this is relatively expensive and results take six-to-eight weeks [31]. For decades, TB diagnosis has relied on direct sputum smear microscopy (SSM) in many countries [31]. SSM is fast, inexpensive, facile, and specific for detecting *Mycobacterium tuberculosis* (Mtb) in high incidence areas [31–34]. SSM does not require a highly specialized apparatus and is therefore very suitable for low-resource settings [31,33]. However, the accuracy of SSM is only 25–65%, which is considerably lower than the standard culture technique, and its limit of detection is about 10,000 colony forming units per milliliter (CFU/mL) [34,35]. In a recent study involving hundreds of specimens tested with culture, SSM, and the Xpert MTB/RIF system, the SSM method exhibited an average accuracy of 54% for respiratory samples and 50% for non-respiratory samples [36]. Furthermore, the overall performance of SSM depends on different variables including the type of lesion, the type and number of specimens, the specific *Mycobacterial* species, the staining technique, and the competence of the microscopist [35]. In a 2014 survey, 22 high-burden countries conducted 78 million sputum smears valued at 137 million USD in 43,000 microscopy centers; about 61% of the analyses were conducted in the BRICS countries (Brazil, Russian Federation, India, China and South Africa) [37]. About 79% of the smears performed in the BRICS countries were used for initial diagnosis. On average, the unit cost for a smear was 1.77 USD, including materials, labor, and overhead expenses [35]. Several studies had shown that the accuracy of SSM improved when specimens were subjected to liquefaction, followed by the concentration of the *Mycobacteria* through overnight sedimentation or centrifugation [34,38–42]. However, the enhanced SSM performance provided by these pretreatment steps may not be sufficient to offset their increased cost, the complexity of their process, and potential biohazards.

Recent advances in bacteria preconcentration and the diagnosis of TB and multi-drug resistant tuberculosis (MDR-TB) include sophisticated techniques such as Xpert MTB/RIF, TB beads, liquid culture, centrifugation, filtration, and line probe assays [43–47]. However, these techniques are not necessarily accessible or affordable for those who need them the most [48]. Considering the high accuracy (~97%) and specificity (~99%) of the Xpert system relative to the culture standard [36], the World Health Organization issued a recommendation in 2010 to use Xpert MTB/RIF for the diagnosis of all persons with signs and symptoms of TB. However, the Xpert MTB/RIF assay entails a price of US$10 per cartridge. Thus, if this method was to be implemented for all people with presumed TB, the cost would exceed 80% of the total TB spending in low-income countries such as India, Bangladesh, Indonesia and Pakistan [49]. In 2014 and 2015, there were 33 and nine SSMs for every Xpert MTB/RIF test procured, respectively [50]. While high-end diagnostic methods are more accurate and/or specific than SSM, these techniques remain cost-prohibiting and inaccessible for people living in low-income countries where Mtb has a high prevalence.

An essential aspect of TB is the substantial financial burden placed on patients and their families due to treatment and associated costs. For example, TB patients are often required to take absence leave from work, which, is unpaid in some cases, leading to a higher risk of financial struggle in the household [51]. Tanimura et al. reported the distribution of financial burden for the TB patient as 20% due to direct medical costs, 20% due to direct non-medical costs, and 60% due to income loss [52]. On average, the total cost was equivalent to 58% of reported annual individual income and 39% of reported household income [52].

In this context, accurate, rapid, and cost-effective diagnostic tests are paramount for reducing TB infection and its unacceptably high mortality rates, especially for an easily treatable disease [53]. The ambitious goal of the global "End TB Strategy" to diminish TB incidence by 90% and reduce TB mortality by 95% by the year 2035 is unlikely achievable without highly accurate yet low-cost tools to address epidemics in settings of poverty [54]. New tools must include improved point-of-care diagnostic tests that are delivered to low-income communities and at the first point-of-contact by patients in the healthcare system. Ideally, TB tests should be performed with the use of non-invasive sampling procedures, and results should be promptly delivered to the patients, allowing for a quick turnaround time for treatment in a single clinical encounter and hence avoiding the loss of patient follow up [54].

Thus, our strategy was to develop low-cost biosensing assay for rapid TB detection by employing modern advances in nanoparticle science and glyco-chemistry, thus resulting in an accuracy matching the performance of Xpert MTB/RIF [55,56] and standard culture. The nanoparticle-based colorimetric biosensing assay (NCBA) is based on the concept of the magnetically activated cell enrichment (MACE) technique using glycan-coated magnetic nanoparticles (GMNP). In this technique, the Mtb cells are isolated and enriched by applying a magnetic field to activate nanoparticle-bound Mtb cells without using any expensive antibodies or energy-consuming centrifuge instruments, thus eliminating the need for time-consuming growth of Mtb. The NCBA test involves the utilization of iron oxide nanoparticles with superparamagnetic properties. The incorporation of magnetic nanoparticles (MNPs) allows for significant improvements over other pre-concentration techniques due to their high surface-area-to-volume ratio and physicochemical properties. The MNP solution is colloidal in nature, providing stability, low sedimentation rates, and minimal precipitation due to gravitation forces. The MNPs are coated with glycan to facilitate their attachment to the bacterial cell wall through carbohydrate-binding protein sites, providing selectivity to the biosensing mechanism. There are three stages of specificity involved in this method: First, glycan–cell interaction is specific to the bacteria cell membrane through carbohydrate–protein binding. Second, the Ziehl–Neelsen staining used in the NCBA test is specific to acid-fast bacilli *Mycobacteria*. Third: the *Mycobacteria* present in sputum due to respiratory hemoptysis (i.e., intense coughing) is likely TB-causing bacteria.

The NCBA has been used to test sputum samples in Nepal (500 samples), Peru (1108 samples), and Mexico (24 samples) [55–57]. In the case of Nepal, all sputum samples were tested for TB by using three different methods: SSM, Xpert MTB/RIF, and the NCBA. In this study, SSM detected only 40% of the true-positive specimens, while Xpert and the NCBA successfully detected 100% of the true-positive samples. Neither one of the methods yielded false-positive results. Table 1 presents the results from the SSM (left panel) and the NCBA tests (right panel), using Xpert MTB/RIF as the standard for defining the number of true-positive and true-negative TB cases. Table 2 presents the performance characteristics for both SSM and the NCBA, including sensitivity, specificity positive predictive value (PPV), negative predictive value (NPV), and accuracy. As shown in Table 2, at a 95% confidence interval, SSM had a relatively low sensitivity of only 40% (29−52%), while the NCBA exhibited high sensitivity comparable to the Xpert system (95−100%). The accuracy of SSM was 90% (87–93%), while the accuracy of the NCBA was 100% (99–100%). Given the sample size and nature of the collected samples, the calculated prevalence for this cohort of patients was 16% (80 out of 500).

Table 1. Results found by using Xpert MTB/RIF as the gold standard for true tuberculosis (TB) cases and non-TB cases [55].

SSM Test	True TB Cases	Non-TB Cases	NCBA Test	True TB Cases	Non-TB Cases
Positive test	32	0	Positive test	80	0
Negative test	48	420	Negative test	0	420

Table 2. Comparison of diagnostic performance [55].

Technique	Xpert MTB/RIF as the Gold Standard, % (95% CI)				
	Sensitivity	Specificity	PPV	NPV	Accuracy
SSM Test	40 (29–52)	100 (99–100)	100	90 (88–91)	90 (87–93)
NCBA Test	100 (95–100)	100 (99–100)	100	100	100 (99–100)

When samples were positive, the Xpert MTB/RIF system reported the bacterial load set by the manufacturer as very low, low, medium, and high. These four categories were used to estimate the equivalent load in SSM and the NCBA by matching the corresponding samples with Xpert results. Table 3 shows a comparison of the detection limit and dynamic range of the detection of the two techniques with respect to the Xpert system. As seen in the table, the NCBA yielded the same results as Xpert MTB/RIF at all levels of bacterial load. Conversely, SSM was unable to detect positive samples at the very low level and detected only 14% of true-positives at the low level, 48% at the medium level, and 79% at the high level. TB positive samples are normally distributed around the medium level, at which SSM exhibited a poor detection rate of less than 50%.

Table 3. Detection limit and dynamic range of detection of the two techniques with respect to the Xpert MTB/RIF categories [55].

Xpert MTB/RIF Categories **	Very Low	Low	Medium	High	Total
Xpert MTB/RIF	10	22	29	19	80
NCBA	10	22	29	19	80
SSM	0	3	14	15	32
% Detection (NCBA/Xpert)	100%	100%	100%	100%	
% Detection (SSM/Xpert)	0%	14%	48%	79%	

** The Xpert MTB/RIF assay provides semiquantitative readouts based on the cycle threshold (C_t): very low = C_t > *28*, low = C_t *22–28*, medium = C_t *16–22*, high = C_t < *16*.

The NCBA method significantly outperformed SSM with a lower detection limit for acid fast bacilli (AFB) of 10^2 CFU/mL and a fast analysis time of 10–20 min. This diagnostic tool is facile (Figure 2), easily scalable, and inexpensive (0.10 USD/test). According to the Ministry of Health of Nepal, a low-cost TB diagnostic test with 70% accuracy could potentially save 300,000 lives just in Nepal over the next five years [58]. The NCBA technique shows promising potential for improving the TB control program in Nepal and other high-prevalence low-income countries. The deployment of the NCBA in remote rural areas would help increase case finding and case notification, thus supporting public health programs for fighting drug-resistant TB. There are nearly 600 microscopy centers distributed throughout Nepal in which the immediate implementation of the NCBA is possible. Similarly, this technique is applicable in many of the high TB-burden countries. In 2013, Desikan hypothesized that a universally accessible and rapid detection method with a sensitivity of 85% and specificity of 97% could save about 392,000 lives every year worldwide [33]. Thus, the developed NCBA technology may enable the "End TB Strategy" and lead towards a TB-free world.

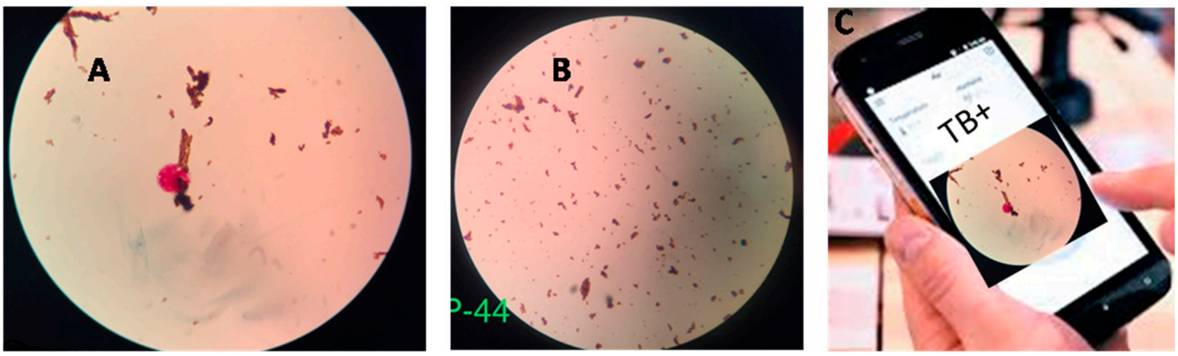

Figure 2. Typical nanoparticle-based colorimetric biosensing assay (NCBA) results for TB+ and TB− sputum samples, as viewed through the eyepiece of the bright field microscope. (**A**) The TB-positive sample (clumped red GMNP-AFB complex surrounded by brown GMNPs). (**B**) TB negative sample (dispersed brown GMNP). (**C**) Schematic of smartphone app for image processing and display of test results [55].

2.2. *Alerting Mercury Exposure in Artisanal Gold Mining Communities*

In South America, Africa, and Asia, millions of individuals are exposed to dangerous levels of mercury concentrations as a result of artisanal small-scale gold mining (ASGM) [59]. ASGM is a rudimentary gold mining approach that is performed by individuals or groups with little or no mechanization, often in informal (illegal) operational settings with toxic chemicals [60]. ASGM is composed of three main steps: crushing the ore into fines, mixing the fines with liquid mercury, and separating the mercury from gold by evaporating the mercury [61]. Often in unregulated occupational conditions, workers perform mercury evaporation by using open pits, which not only have severe adverse health effects for the workers that inhale the mercury vapor but also release the toxic vapor into the environment. ASGM recently exceeded combustion of coal as the leading anthropogenic source for mercury emissions globally [62]. The risk of exposure to mercury can lead to detrimental effects on the nervous, immune, reproductive, and digestive systems, induce infertility, reduce mental function, and induce kidney failure [63–67].

The global responsibility for reducing mercury emissions was recognized by the Minamata Convention in Switzerland in 2013. At the convention, over 140 countries signed a treaty committing to protect human health from mercury exposure [62]. The signatory countries pledged to "ban new mercury mines, phase-out existing mines, ensure the phase out and phase down of mercury use in a number of products and processes, develop control measures for emissions, and regulate the informal sector of ASGM" [62]. In order to mitigate mercury exposure and regulate mining operations, it is prudent for marginalized communities to monitor the presence of mercury in their water through low-cost, rapid, and facile devices.

Several analytical methods have been developed for mercury determination in water. Standard laboratory techniques include cold vapor atomic absorption spectroscopy (CV-AAS) [68,69], cold vapor-atomic fluorescence spectrometry (CV-AFS) [70,71] and inductively coupled plasma mass spectrometry (ICP-MS) [72,73]. These spectroscopic techniques are highly sensitive and accurate but are often impractical for environmental applications due to the high cost of analysis. In addition, these standard methods require extensive user training, and the results often require days or even weeks to produce results, making them less suitable for rural communities [74–76]. Some field capable units are commercially available, namely based on direct mercury analysis (DMA) and handheld nanosensors/biosensors [77,78]. DMA is based on the principle of thermal decomposition (vaporization), followed by amalgamation and subsequent atomic absorption spectroscopy. While extremely accurate, DMA is cost prohibitive for low-income communities because commercial prices of US-manufactured equipment range between 13k and $30k USD. Perhaps inexpensive nanosensors/biosensors that are coupled with low-cost electrochemical techniques on portable devices are likely to be more suitable as tools for the on-site analysis of mercury, especially where ASGM is in practice.

While there are many types of transduction methods for the low-cost determination of mercury, electrochemical methods are sensitive, quantitative, and may be the mechanism of choice for cost-effective rapid detection in the field [79]. The most common electrochemical method for ionic mercury detection is that of the anodic linear stripping voltammetry (ASV) techniques [74,80]. ASV is a two-step method of deposition/accumulation during the reduction of mercury ions and stripping during the oxidation of mercury ions along the surface of the electrode. As the mass transfer limit is reached in the reaction, the oxidative current forms a well-defined peak that can be used to calculate the concentration of mercury in the sample [81]. The efficiency of any electrochemical stripping test can be determined by calculating the percent change in oxidative current relative to baseline.

Carbon-based nanomaterials are a popular choice for improving the electrochemical detection of mercury, as this type of material exhibits a high surface area, strong mechanical strength, excellent thermal conductivity, and high conductivity [82–84]. Some of the carbon nanomaterials in recent literature include glassy carbon [85,86], carbon nanotubes [87], graphene [88], and reduced graphene oxide [89]. While each of these nanocarbon materials is efficient for mercury detection via stripping voltammetry, some of the materials are complicated to fabricate and exhibit poor water solubility [90]. Among carbon nanomaterials, graphene and reduced graphene oxide (rGO) have the highest water solubility and one of the lowest fabrication costs. For these reasons, there is a growing trend to develop disposable, low-cost, graphene-based electrodes for field applications.

Examples of low-cost graphene electrodes include screen-printed electrodes and conductive paper and plastic [74,91]. In 2014, Lin et al. (2014) [92] discovered a low-cost, one-step, conductive material when reducing graphene on a commercial polymer with a carbon dioxide infrared laser. Since then, multiple researchers have shown that laser scribing could be used to design electrodes to sense biomolecules by using infrared and ultra-violet light lasers [93–96]. While graphene is indeed a useful material in sensing, one of its problems is the tendency of graphene and graphene oxide to bind to a variety of materials in aqueous phase [97]. For this reason, sensor labs typically metallize graphene electrodes with a noble metal that has a specific interaction with mercury ions. These metals can be deposited by using simple electrodeposition methods or advanced techniques such as pulsed sono-electrodeposition [98]. Recently, Abdelbasir et al. 2018 [99] showed that copper nanoparticles recovered from waste cables can be used to detect ionic mercury by using linear sweep stripping voltammetry (LSSV).

Low-cost, portable, mobile phone-based acquisition systems have been developed for mercury analysis in the field [100]. While this is significant for deploying sensors in low-income regions, the inexpensive-portable sensor-systems lack data analytics capability to transform the data into meaningful information that could be useful for the user. For example, the maximum concentration level for inorganic mercury in drinking water is 6 ppb [101]. However, bodyweight, ingestion rate, length of exposure, form and pathway of the contaminant, health of the individual, and concentration of mercury influences the degree of mercury toxicity [102–104]. Thus, a SNAPS tool may assist communities in acquiring data and extracting actionable information for decision support.

Our group is currently working on developing the SNAPS platform for estimating the toxicity risk associated with the ingestion of mercury-contaminated water. This SNAPS platform is composed of a disposable graphene–nanocopper sensor that is coupled with a low-cost handheld potentiostat and a smartphone. The working mechanism of the platform starts with the detection of mercury present in the sample by using the graphene–nanocopper sensor. Next, selective electrochemical interactions between mercury and the electrode generate an electrical signal. The electrical signal is acquired and processed by the potentiostat to produce a current output. Then, computer software records the current output and transforms it into concentration data via calibration curves. Finally, a smartphone app is used by the user to enter the data for the following parameters: mercury concentration in water (from the sensor), bodyweight of the user, water ingestion rate, and length of exposure. Based on these parameters, the app runs an algorithm that includes a hazard quotient formula to generate an estimation of the risk of toxicity for the user [105–108].

We recently conducted a proof-of-concept demonstration of this SNAPS platform in a rural area that has been dramatically impacted by ASGM known as La Toma in Cauca, Colombia. Even though this SNAPS platform is in an early stage of development, it represents an example of how rural communities in developing countries may use sensors as a service to access data on mobile devices and extract actionable information to help make informed decisions. Figure 3 shows the progression of the proof-of-concept demonstration of the technology.

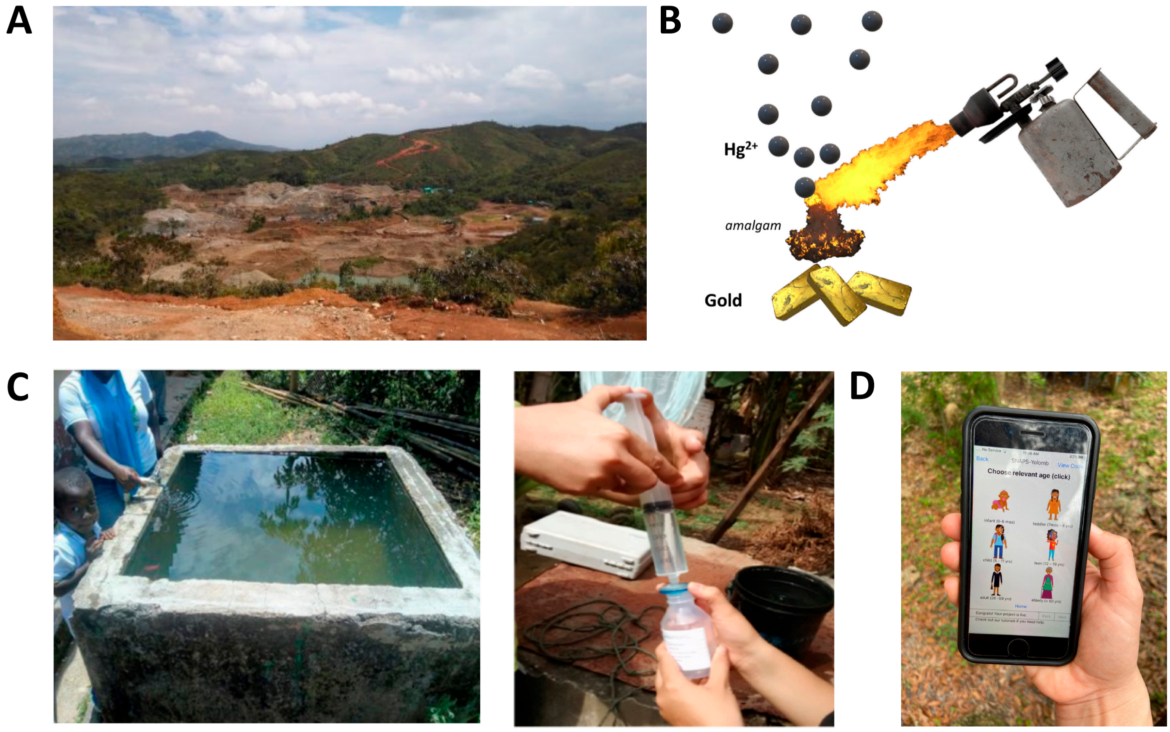

Figure 3. Demonstration of a SNAPS tool for assessing risk due to the inadvertent consumption of mercury in drinking water for gold mining communities in Colombia. The first step was to (**A**) characterize the local socioeconomic dynamics and (**B**) identify related routes of mercury exposure (in this case from smelting of amalgam). (**C**) Together with community members, we collected samples from local water sources. (**D**) These samples were tested with nanomaterial-enabled sensors. (**D**) Concentration data derived from sensors were transformed into customized information about the toxicity risk for specific user groups who were using a mobile app.

Mercury enters natural aquatic systems primarily due to the burning of mercury amalgam during the extraction of gold from raw ore.

3. Can We Overcome the Economic Barriers for Distributing Diagnostic Tools in Low-Income Settings?

Framing the issue of diagnostic tools in the context of technology leads us to recognize a vast spectrum. On one hand, ideas about telemedicine were proposed about 100 years ago [109], and on the other hand, milestones in computational speed occurred about 100 days ago [110]. It may be justifiable to suggest that technological barriers may not be the primary reason why many diagnostic tools are still absent from communities under economic constraint. The powerful incentive of lucrative profitability, in the short term, may not be realized by serving impoverished regions.

Transaction cost [111] may be the over-arching factor that has multiple interpretations [112] but appears to be the economic barrier with respect to the reasons why accelerating the rate of diffusion of diagnostic tools in distressed communities continues to pose difficult challenges [113–115]. We must focus on value to the user or the extent of the benefit to the beneficiary's environment and/or ecosystem (for example, the early diagnosis of tuberculosis in a patient may save the entire village from infection and epidemic). However, delivery of value is inextricably linked to cost, unless it is aimed to deliver philosophical or mythical messages [116].

In over-simplified terms, the convergence of the cost of the product and the cost to deliver the service contributes to transaction cost [117]. A plethora of costs and cost-incurring processes are involved, but we shall bypass the details. The physical product (in this case is the sensor) and the service is the solution delivery (SNAPS). Academics cannot control cost, but their contribution can impact implementation and use. A low-cost sensor from a lab must be manufactured, calibrated, evaluated, and sufficiently scaled if the outcome can still be claimed as a "low-cost" sensor that is capable of delivering value with respect to maintaining a certain pre-agreed quality of service (QoS) in keeping with the key performance indicators (KPI) that the users desire, demand, or deem necessary.

In addition, a working sensor that is delivered to a user is useless without a visualization system to capture the data from the sensor. Stand-alone visualization devices (for example, blood glucose home monitors with dedicated devices to read the blood glucose strip and deliver data readout) add inordinate costs to the system. The alternative is to use a mobile phone as a platform to visualize the data from the sensor. The signal transduction from the sensor to the mobile phone calls for multiple layers of tools, technologies, and software (middleware), in addition to the functional use of a mobile phone. The presence of a mobile phone in any environment is contingent upon available cellular and/or wireless infrastructure to support its use. It may not be prudent to assume the presence of a telecommunications infrastructure despite the global penetration of such services [118–121]. Thus, even if a working sensor is at hand, the obvious process of signal to data transition and the visualization of the data involves multiple layers of capital expenses (infrastructure cost), as well as associated technologies and software.

Assuming that the above layers are in working order, the sensor data meets a "dead end" upon data visualization. A number (with units) is only meaningful if there is a relevant framework for interpreting such data, e.g., the combination of sensor data from mercury contamination expressed in terms of a hazard quotient score, which uses other vital pieces of information to assess health risk. It is the delivery of information based on sensor data that drives value. Taken together, the physical product is no longer the focal point of value. Information pertaining to the health of the user is the service that delivers value to the user. Transaction cost, therefore, is no longer a product-based entity; rather, it is the cost of service that must be feasible for the service to be delivered, disseminated, and adopted by a community.

Overcoming the economic barriers to deliver SNAPS will be virtually impossible if the chasm between product and service continues to overshadow the concept of value delivery to the user. The economic principle, which may work in impoverished nations, is rooted in micro-finance and micro-payments with low transaction costs [122,123]. The paradigm shift from "product sales" to delivery of "service" involves combining the product with resources (including retail mobile banking, infrastructure, telecommunications, cybersecurity, and customer service). Users pay only when they use the service. The latter lowers the transaction cost and hence the barrier to entry into vast markets of low-income users. It is not the product but the user experience that is the pivotal fulcrum for the inversion of traditional business models in the era of the Internet of Things (IoT) [124].

The PAPPU model was epitomized by the plain old telephone system (POTS), where the user paid only the "charge per call" which was reasonably affordable even if the per capita income was low. In this paper, we advocate for PAPPU as a metaphor for ethical profitability through social business models. In principle, the user may pay a penny for each use of a SNAP (suggested but not restricted to one penny). The "penny" is a placeholder for the financial design of an ultra low-cost nano-payment model, which, in the real world, may represent one Rupee (INR), one Yuan (CNY, RMB) or one Peso (COP). The PAPPU metaphor may evolve to become the generalized monetization mantra that signifies pay-a-price-per-unit wherever the principles of IoT may be deployed or embedded as a digital by design metaphor including ubiquitous sensing. The diffusion of connectivity may serve as a tool and IoT may be catalytic as a platform to better facilitate the practice of equality, equity and égalité. PAPPU offers an economic instrument for businesses to build a profit model based on economies of scale to serve low-income communities and abide by ethical profitability. PAPPU offers an alternative strategy for enterprises and businesses who are seeking to engage with the next billion users, albeit profitably, but within the realms of ethical profitability that can be sustained by the per capita income of these communities.

The concomitant growth of infrastructure (e.g., affordable access to low latency, reduced jitter, high bandwidth wireless telecommunications, 5G, and trusted mobile banking) may be necessary to pave the road for the pursuit of PAPPU. The ability to escape the dead weight of old technology in the developing world may accelerate the implementation of PAPPU as an integral part of the socio-economic fabric of a product-less, service-based economy where payment per unit of service (one liter of municipal water, one kilo-watt hour of energy, or one gallon of sanitation waste) may become the new normal.

Implementing PAPPU may require alliances, public–private partnerships, or global consortia with an altruistic fervor to pay and pave for the synergistic integration that is necessary to promote SNAPS as services in low-income communities. The challenge is to bring to the table global organizations, benevolent individuals, and thoughtful governments who may choose to lead this effort to channel science to serve society for the less fortunate. We need new eyes, unbridled imagination, and the moral fabric of synergistic solutions that can wrap around—not to isolate—and protect, provide and promote acceptable solutions for remediable injustices.

4. Social and Ethical Considerations for the Development and Implementation of SNAPS

Social and ethical considerations are inextricably linked with the transformation of SNAPS from an academic vision to real-world implementations that may actually help people. Academics must remain cognizant of their ethical responsibility to discourage the misapplication and dissemination of misinformation about their inventions. In this section, we attempt to analyze some potential interactions between the social and technological domains, as well as how democratic approaches for technology creation and diffusion could favor the improvement of health outcomes for disadvantaged communities.

Since the introduction of the technology acceptance model (TAM) decades ago, several extended versions of this archetype have been proposed to elaborate a more comprehensive framework for predicting people's intention to use a particular product or service [125–127]. The TAM and its variants have served as the guiding rationale behind R&D for a variety of commercial technologies that are mass-produced, including healthcare devices [128]. However, this model may be inadequate in the context of technology development for low-income communities [129]. It is worth noting that the ultimate goal of the TAM and related models is to forecast user behavior across a broad range of consumer populations, which means that the model focuses on highly generic predictors of technology acceptance. For instance, the TAM does not explicitly include any cultural or social variables, which is a significant limitation because social differences may contribute significantly to the variance in users' attitudes towards technology [127,130]. However, the goal of SNAPS with the PAPPU concept is to provide an affordable sensor-analytics service platform to support decision-making and the enhancement of health outcomes for economically challenged groups. Thus, a useful model to guide the development of SNAPS should include bi-directional communication between researchers and users, and it should perhaps motivate researchers and users to change or adapt or better inform their behavior [131].

Trust in the technology [132] is quintessential for adoption and continued use, because technology is equally seen as a double-edged sword [133,134]. Driving positive impacts from the introduction of SNAPS in low-income regions may involve not only the transfer of fully functional technology but also the empowerment of the beneficiary communities by enabling the local mastery of the technology along with the possibility to re produce and even adapt the technology to local conditions. We believe this open-source approach to technology adoption is auspicious for supporting marginalized communities, especially when trying to avoid the known failures of the charitable approach of technology leapfrogging. For example, the WHO estimates that only 10%–30% of the medical devices that are donated to developing countries are used as intended; the remaining 70–90% end-up being dumped in landfills, thus contributing to more pollution problems and environmental health risks [135]. This situation is explained not only by the incompatibility of the technology with the locally available infrastructure but also to the lack of local capacity to adapt or fix the donated devices once they break [136]. Additionally, dependence on foreign technologies could lead to an imbalance of power in which the users have no option other than relying on the willingness of external entities to continue to deliver much-needed technology in their regions. Thus, if the goal is to make technology work effectively on behalf of society, we must divert from the mainstream handed-down from the top approach and enable society to create and transform technology in meaningful ways, in dispersed regions, and from the bottom-up.

Engaging the community through operational transparency may prevent public anxiety and may also facilitate the proper implementation of technology. Users' understanding of the limitations and potential risks associated with SNAPS could be vital for setting clear expectations about SNAPS-assisted testing while avoiding misapplications of the technology. As Wallace et al. pointed out, the misuse of many direct-to-consumer screening tests could have caused an unnecessary increase in healthcare costs due to people's overreaction to inaccurate readings from direct-to-consumer screening tests, as well as their subsequent demand for further testing with advanced clinical technology [132]. However, this concern is mostly relevant for developed countries in which people have access to healthcare systems where clinical testing is readily available for patients. In low-income settings, such as remote rural areas in developing countries, health care services are often dysfunctional or completely inaccessible. For marginalized communities, information from SNAPS could instead drive actions that are aimed at limiting the exposure to harmful biological vectors and chemical agents. Thus, communities in territories that suffer from prolonged government abandonment could greatly benefit from the democratic adoption of SNAPS to make informed decisions and solve their problems with more autonomy. Nonetheless, we agree that transparency and accountability from everyone involved in the process of technology deployment are paramount for protecting the users' rights and integrity.

5. Conclusions

Monitoring environmental contamination is essential to protect the public from diseases and other health issues. This monitoring requires accurate and cost-accessible sensor technologies to enable early warning capabilities for users to minimize negative impacts (Figure 4). The framework of SNAPS with PAPUU has the potential to pave the way for economically viable systems that can potentially be applied as tools to reduce local environmental risks and mitigate health problems that are derived from them. We envision that the use of SNAPS will increase low-income communities' participation in the public/government planning process by providing data that they can use to fight for their right to public health care, clean water and adequate sanitation. By bridging smart technology with basic needs and public health, SNAPS will advance our understanding of how information can change public participation, having low-income communities' representatives as 'change agents' that influence public policies and planning. These communities' representatives benefit from rights-based arguments, evidence-based research, and effective data analyses. SNAPS have the potential to serve as an illustration of how empowering impoverished communities in their local context can strengthen democratic practice in their region. Grounded on an integrated perspective that takes social and ethical considerations into account, we foresee that SNAPS will shed some light to improve implementation of public health plans in underserved communities by increasing public participation in planning. Moreover, SNAPS could potentially become a new approach to achieve the United Nations Sustainable Development Goals 3 and 6: ensure healthy lives while promoting well-being at all ages and ensure access to water and sanitation for all, respectively. Furthermore, it could also help empower impoverished communities to obtain the rights they have been promised such as basic sanitation, clean water, and adequate health care services.

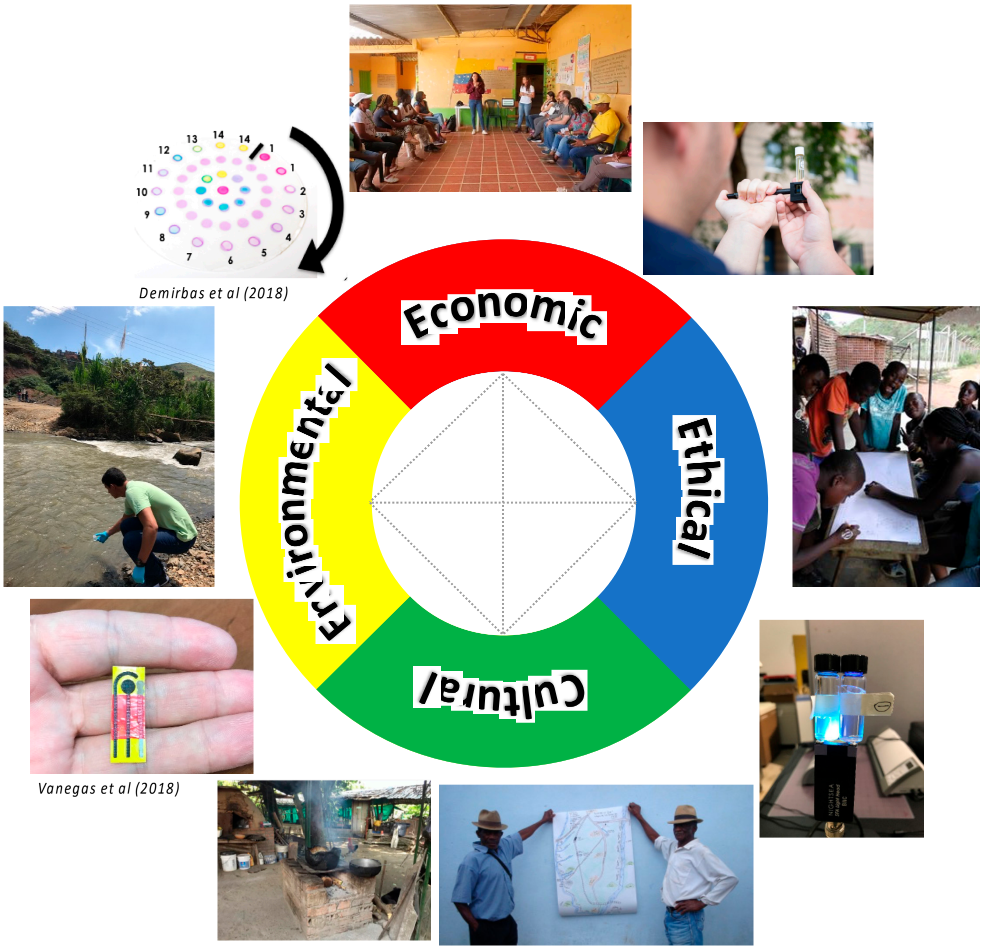

Figure 4. SNAPS converges with pay-a-penny-per-use (PAPPU) to establish a framework for sensor-as-a-service. The paradigm is rooted in economic, ethical, cultural, and environmental core values that synergistically act as a catalyst for the democratization of healthcare in underserved communities. Where noted, photos credited to Demirbas et al. [137] and Vanegas et al. [95].

Supplementary Materials: The following are available online at http://www.mdpi.com/2075-4418/10/1/22/s1, Table S1: Number of research articles published every year for the past ten years in peer-reviewed journals on the topic of *E. coli* biosensors, Table S2: Top five agencies that provide funding for research on *E. coli* biosensors, Table S3: Depiction of research articles on *E. coli* biosensors that contain claims related to real-world applicability.

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