



Smartphone-Based and Point-of-Care Green Analytical Devices: Engineering Design for Resource-Limited Settings

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Abstract: Green analytical chemistry (GAC) aims to minimise the environmental impact of analytical methods, such as the amount of toxic chemicals, energy consumption and waste produced, while maintaining the analytical quality of the methods. The smartphone is a ubiquitous device that is carried by billions of users and has become a versatile and intuitive tool that naturally fits in with these goals, combining both illumination and detection capabilities, computation and connectivity within a single device, which the user already owns. This review covers engineering design of green analytical devices for resource-limited environments that are reliant on the smartphone for detection or analysis and are lacking in centralised laboratories, stable electrical power, cold-chain supply chains, trained operators, etc. We place these platforms into the context of the 12 principles of GAC, the family of greenness and applicability metrics (Analytical Eco-Scale, Green Analytical Procedure Index, Analytical GREENness calculator, Blue Applicability Grade Index) and link them to the ASSURED and REASSURED criteria for ideal diagnostics. Then, we explore the hardware and software architecture of the smartphone reader, substrate and fabrication selection affecting cost and “greenness”, principal detection modalities and controlling equations, and a calibration and validation framework that is required for credible field results. A structured survey of clinical, environmental, food and agricultural applications is given, and device attributes are explicitly mapped onto each GAC principle and REASSURED criterion. Finally, we speak about standardisation, reproducibility, validation and the electronic-waste paradox, and propose future trends in machine learning, connectivity and sustainable materials. Smartphone POC devices are demonstrated to be one of the most reliable practical applications of green analytical chemistry in low-resource areas.

Keywords: Green Analytical Chemistry, Smartphone Sensing, Point-of-Care Testing, Microfluidic Paper-Based Analytical Devices, Colourimetric Detection, Greenness Metrics

INTRODUCTION

Measurement is important to healthcare, environmental protection, food safety and industrial quality control, yet no one ever thinks about the environmental cost of the act of measurement. Organic solvents, corrosive digestion reagents, energy-consuming instruments and central facilities are the basis of the classical workflow. A typical dedicated liquid chromatography laboratory with routine determinations will use thousands of litres of organic solvent a year and produce the same quantity of hazardous waste, which will need special disposal. The demands do not easily dovetail into the broader development objectives of sustainable development and are especially hard to meet in areas of weak infrastructure. The green analytical chemistry approach was developed to meet this challenge and to decrease toxic substances, energy consumption and waste produced during analysis while maintaining the reliability of the results (Gałaszka *et al.*, 2013). Anastas and Warner (1998) developed 12 principles of green chemistry for designing green products and green processes. Only a few of these rules can be

readily translated into measurement, and Gałuszka *et al.*, (2013) chose four of the original principles and combined them with eight additional rules, creating a mnemonic of 12 principles of green analytical chemistry: SIGNIFICANCE. These principles include: Direct measurement, minimisation of sample size and number, on-site analysis, integration and automation of steps, miniaturisation, avoidance of derivatisation, minimisation of waste, multi-analyte methods, lower energy demand, use of renewable reagents, elimination of toxic substances, and improved operator safety. Above all, these are goals of design, not a specific method, and call out the analyst to look for the "least green" step in any procedure and make it better. Hence, such a small, low-power, reagent-sparing and field-deployable measurement platform is a well-engineered smartphone device, and vice versa.

Point-of-care testing brings the testing closer to the patient or to the point of sampling, shortens the turnaround time, and eliminates the need to send samples to a remote lab. This convenience is a good thing in a high-income country, while in a low-resource country, this may be a gaping void that could go to waste. The World Health Organisation (WHO) Special Programme for Research and Training in Tropical Diseases (TDR) alluded to the attributes an ideal test should possess: it should be Affordable, it should be Sensitive, Specific, User-friendly, it should be Rapid, it should be robust, it should be Equipment-free, and it should be Deliverable to those who need it. With the evolution of digital technology, Land *et al.*, (2019) updated this benchmark to REASSURED, which includes Real-time connectivity and Ease of specimen collection, a new trend within mobile health. These ideas were translated into engineering programmes by Yager *et al.*, (2006) which set out the vision for microfluidic diagnostic technologies for global public health and the microfluidic paper-based analytic devices developed by Martinez *et al.*, (2007) which introduced patterned paper as a platform for low-volume bioassays. The goal of green analytical chemistry and of point-of-care design is essentially the same goal, just from two perspectives. Reagent frugality, low energy use, miniaturisation and waste reduction are principles of GACs. Affordability, equipment-light operation, portability, and robustness in the field are REASSURED criteria. A cellulase assay, glucose oxidase or Griess nitrite assay which is performed in a tiny volume of fluid (a microlitre) on a substrate and read by a phone that the user already has, reduces the amount of consumables and power needed to run the assay and is easily usable in a clinic without access to mains electricity. The convergence is captured in this case as a single signal pipeline where a sample is fed into a recognition/reaction zone, which is then transformed into an optical or electrochemical response that is picked up by the smartphone camera or interface, processed within the device, and reported with optional connectivity (Fig. 1).

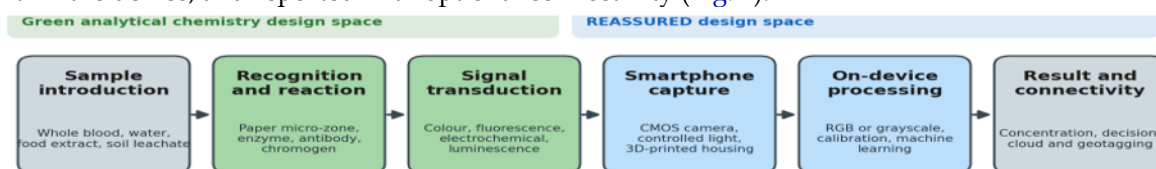


Fig. 1. Conceptual signal pipeline of a smartphone-based green point-of-care analytical device. The same field-deployable transduction routes, optical and electrochemical, converge on one ubiquitous reader, and the workflow sits simultaneously within the green analytical chemistry and REASSURED design spaces.

This present review focuses on the development of the engineering design of green analytical devices, with applications of a smartphone or a point-of-care device, for environmental applications in resource-limited environments. It is organised as follows. In Section 2, the principles and metrics are outlined where greenness and practicality can be measured. How the smartphone can be used as an analytical instrument is described in Section 3. Section 4 covers engineering of substrate, fabrication, illumination, power and reagent storage. The detection modalities, as well as the equations used to convert raw signals to concentrations, are presented in Section 5 along with the calibration and validation framework. The applications of Section 6 cover the health, environment, food and agriculture fields. A list of device attributes is now mapped to each GAC principle and REASSURED criterion in section 7. Section 8 addresses these challenges, such as the electronic-waste paradox, while Section 9 conclusion and presents future directions.

MATERIALS AND METHODS

The greenness is not intrinsic to the description of a method, so the community has created tools to be able to move from a description of the method to a comparable score or pictogram. These tools can be divided into three categories. The principles set (e.g. the twelve principles of GAC) give qualitative design rules. Scoring and pictogram metrics (like Analytical Eco-Scale, Analytical GREENness calculator or Green Analytical Procedure Index) will provide a score and/or a picture representing the impact on the environment. There are various applicability and criteria frameworks, such as the Blue Applicability Grade Index and the REASSURED criteria, that describe whether a method is applicable and deployable. A platform can be very green but not very applicable, and very applicable but not very green; therefore, it is important to have a greenness and applicability metric for the platform. Table-1 documents the most pertinent frameworks and metrics to smartphone and point-of-care design.

Table-1 Principles, metrics, and frameworks that underpin the design and appraisal of green smartphones and point-of-care analytical devices. Years for criteria frameworks refer to the cited source that defines or revises them.

Framework or metric	Category	Assessment focus and output form	References
Green chemistry, 12 principles	Principle set	Foundational rules for benign synthesis and processes; qualitative checklist	Anastas & Warner (1998)
Green analytical chemistry, 12 principles (SIGNIFICANCE)	Principle set	Twelve design rules for benign analytical procedures; qualitative	Gałuszka <i>et al.</i> , (2013)
Ten principles of green sample preparation	Principle set	Benign sample-preparation guidance; qualitative	López-Lorente <i>et al.</i> , (2022)
National Environmental Methods Index (NEMI)	Pictogram metric	Four-field pictogram for hazard, corrosivity, persistence, waste; qualitative	Sajid & Plotka-Wasyłka (2022)
Analytical Eco-Scale	Scoring metric	Penalty-point score out of 100 for reagents, energy, hazard, waste; semi-quantitative	Gałuszka <i>et al.</i> , (2012)
Green Analytical Procedure Index (GAPI)	Pictogram metric	Five-pentagram colour pictogram across the full workflow; qualitative to semi-quantitative	Plotka-Wasyłka (2018)
ComplexGAPI	Pictogram metric	GAPI extended with a hexagon for pre-analysis and reagent synthesis	Sajid & Plotka-Wasyłka (2022)
AGREE (Analytical GREENness)	Scoring and pictogram	Score from 0 to 1 from the twelve SIGNIFICANCE inputs; clock-style pictogram	Pena-Pereira <i>et al.</i> , (2020)
AGREEprep	Scoring and pictogram	Score from 0 to 1 for sample preparation across ten criteria	Wojnowski <i>et al.</i> , (2022)
Blue Applicability Grade Index (BAGI)	Scoring and pictogram	Practicality score from 0 to 100; blue asteroid pictogram	Manousi <i>et al.</i> , (2023)
RGB model and White Analytical Chemistry	Composite model	Combines greenness, analytical performance, and practicality into a colour space	Nowak & Kościelniak (2019)
Green analytical chemistry metrics review	Review	Comparative appraisal of greenness metrics, merits and limitations	Sajid & Plotka-Wasyłka (2022)
ASSURED criteria	Criteria framework	Affordable, Sensitive, Specific, User-friendly, Rapid, Equipment-free, Deliverable	Land <i>et al.</i> , (2019)
REASSURED criteria	Criteria framework	ASSURED plus Real-time connectivity and Ease of specimen collection	Land <i>et al.</i> , (2019)
Microfluidic diagnostics for global health	Design vision	Requirements for low-resource diagnostic platforms: conceptual	Yager <i>et al.</i> , (2006)
Paper-based device design for the developing world	Design vision	Capillary-driven, equipment-light device design; conceptual	Martinez <i>et al.</i> , (2010)
Optical smartphone sensing in low-resource settings	Design framework	Design considerations for optical smartphone sensing where infrastructure is scarce	McCracken & Yoon (2016)
Smartphone biosensor taxonomy	Design framework	Smartphone as detector versus interface: review classification	Roda <i>et al.</i> , (2016)
Smartphone analytical biosensor categories	Design framework	Optical and electrochemical smartphone biosensing taxonomy	Huang <i>et al.</i> , (2018)
Smartphone electrochemical POC framework	Design framework	Connectivity routes and electrochemical technique integration	Sun & Hall (2019)

Emerging point-of-care technology landscape	Review framework	Next-generation POC platforms and commercialisation pathways	Vashist <i>et al.</i> , (2015)
Mobile phone biosensing as diagnostic and communication technology	Design framework	Dual diagnostic and data-transmission role of the mobile phone	Quesada-González & Merkoçi (2017)

The Analytical Eco-Scale of [Gałuszka *et al.*, \(2012\)](#) starts with a perfect score of 100 and subtracts penalty points for the amount and hazard of reagents, the energy consumed, the occupational hazards, and the waste produced, with a higher score indicating a "greener" procedure. The whole procedure, from sampling to final determination, is depicted as a pentagram with its fields marked green, yellow or red, depending on the low, medium or high impact of the procedure. The Analytical GREENness calculator of [Pena-Pereira *et al.*, \(2020\)](#) allows each of the twelve principles from the SIGNIFICANCE list to be represented on a common (zero to one) scale, and the weighted result is expressed as a pictogram in a clock-like fashion, with unity being the greenest. These tools are complementary, and many of the recent studies report two or three of the above, along with the Blue Applicability Grade Index of [Manousi *et al.*, \(2023\)](#), for the purposes of evaluating environmental impact and applicability in tandem. A field-ready smartphone colourimetric method can thus be supported not only from the standpoint of greenness, but of practicality as well. If an analytical performance and cost are not taken into consideration, the pure green score can be misleading. The analytical, environmental and safety friendliness, and practical and economic features are represented by the red, green, and blue components of the [Nowak and Kościelniak \(2019\)](#) concept of the White Analytical Chemistry model, respectively. A good balancing technique is white, as it has a good balance on all three axes. This framing is useful for those who have limited resources, as a device that is extremely sensitive will not be affordable, and a very inexpensive device will not be reliable. When designed carefully, smartphone-based point-of-care devices can be appealing because they can achieve a high score on all three of these axes.

RESULTS AND DISCUSSION

3.1 The Smartphone as an Analytical Instrument

The smartphone is an amazingly complete measurement platform. It's equipped with a complementary metal-oxide-semiconductor (CMOS) camera, which is a tightly packed array of light-sensitive elements covered by a mosaic of red, green and blue colour filters, and as such, the camera is inherently able to resolve colour. It offers a light with controllable flash, a processor that analyses image curves and performs analysis locally, a screen that guides the operator and a radio that uploads the results. [Roda *et al.*, \(2016\)](#) categorise the smartphone biosensors into a phone as a detector or an instrumental interface type, while [Huang *et al.*, \(2018\)](#) expand this to optical and Electrochemical.

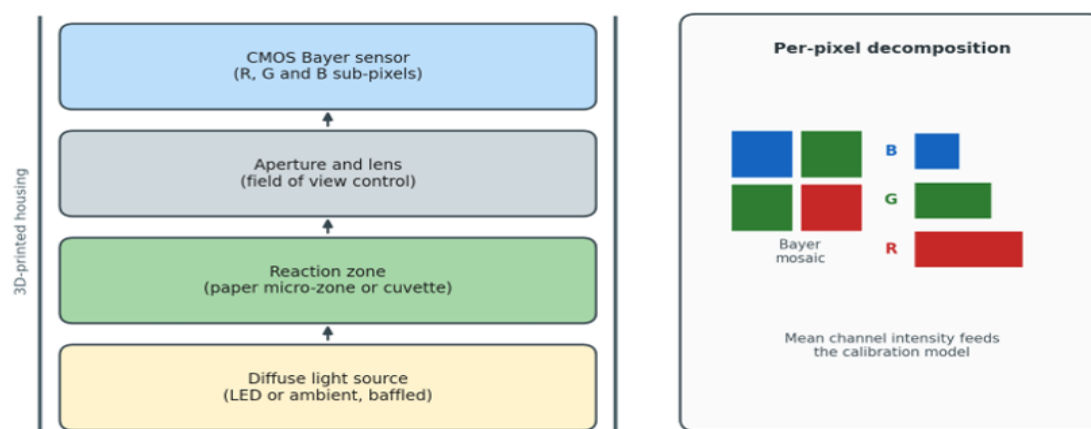


Fig. 8 Anatomy of the smartphone optical readout. A baffled light source, the reaction zone, the aperture and lens, and the CMOS Bayer sensor form the acquisition chain; each captured pixel is decomposed into red, green, and blue components whose mean intensity feeds the calibration model.

The same hardware that helps the platform in photography is also helping in the analytical sensing with hardly any additional instrumentation; that is the structural reason the platform is so green. In optical mode, the phone catches the light that is reflected from a reaction zone. The light source is diffuse and stable, the reaction changes the concentration of the analytes with a change in colour or luminescence of the sample, the lens creates an image of the analytes, and the CMOS sensor breaks the scene down into per-pixel red, green, and blue values. The analytical signal is the mean intensity of a selected channel in a specified region of interest. This chain is represented in Fig. 2 in conjunction with the per-pixel decomposition that gives channel intensities. The environmental light and viewing geometry have a strong effect on the intensity measured; a short optical path is provided within a controlled enclosure, which is why the 3D printed housings are repeated throughout the field (Wilkes *et al.*, 2017). In the electrochemical mode, the phone does not actually detect the analyte but instead activates and reads a transducer via a wired or wireless connection. Sun & Hall (2019) describe how the miniature potentiostat is wired to the proprietary ports or audio jack, or gets connected to a short-range radio (SRR) and that the phone performs amperometric, potentiometric, voltammetric or impedance measurements and reports the results. The screen-printed carbon or silver and silver-chloride electrodes are an inexpensive, disposable transducer that is easily compatible with a paper substrate. The low detection limit and the small sample volume allow electrochemical detection to meet the greenness objective; moreover, the ability to detect in turbid and coloured matrices in which optical measurements are difficult makes it very attractive. The application layer is as crucial as the optics. A dedicated application sets the region of interest, corrects the illumination from the on-card reference, solves the calibration model, and provides a concentration and simple language explanation. More and more machine learning models are built into the app to classify or quantify colours that are hard for a human to read consistently, making it more robust to lighting variation. The Real-time connectivity element sets REASSURED apart from ASSURED diagnostics (Land *et al.*, 2019) and uploads geotagged results into a central dashboard. Hernández-Neuta *et al.*, (2019) contend that this blend of local intelligence and global connectivity is what enables smartphone diagnostics to help facilitate evidence-based care at scale.

3.2 Engineering Design for Resource-Limited Settings

Constraints in low-resource environments impact the design of each layer of the device. There may be intermittent power, high ambient temperatures and humidity, frequent dust and vibration, little operator training, and unreliable supply chains. The engineering solution is to add complexity to the smartphone, which the consumer operates, maintains, and charges, and to make the throwaway part as simple, strong, and inexpensive as possible. The most basic substrate for low-resource devices is cellulose paper. Martinez *et al.* demonstrated the ability of paper to create microfluidic channels which transport the fluid by capillary action without the need for pumping or power (Martinez *et al.*, 2007), and later described the potential of these microfluidic paper-based analytical devices in developing countries (Martinez *et al.*, 2010). The concept has been extended to multi-step assays (Martinez *et al.*, 2008) and a wide design space has emerged, as described by Yang *et al.*, (2017) and Cate *et al.*, (2015). Paper is low-cost, renewable, biodegradable, lightweight and can be burned for elimination, which satisfies several of the principles of GAC. For higher mechanical strength and defined channel geometry, alternatives are available, such as thread, polymer films or three-dimensional printed chips (Yetisen *et al.*, 2013). The resolution, cost and equipment burden on the manufacturer are all determined by fabrication and often compete against each other. However, the smallest features are achieved through photolithography, but it requires a cleanroom, UV-exposure and organic developers, which reduces the green or makes it more expensive. But they are much simpler and less expensive: wax printing, wax dipping, screen-printing and inkjet printing are much more common in the field. Roll-to-roll flexographic printing is an alternative to mass production and low unit cost. Table-2 shows a comparison of the main methods in terms of barrier principle, achievable resolution, burden of equipment and relative cost, and citations are provided for each.

Table-2 Fabrication and platform-engineering methods for paper-based and point-of-care green analytical devices, compared by barrier principle, resolution, equipment burden, and relative cost. Resolution and cost are indicative and depend on materials and scale.

Method	Barrier or structuring principle	Typical resolution	Equipment burden	Relative cost	References
Photolithography	Photoresist barrier	Sub-millimetre, high	High (cleanroom, UV)	High	Martinez <i>et al.</i> , (2007)
Wax printing	Solid-ink wax melted into paper	About 1 mm	Low to moderate	Low	Yang <i>et al.</i> , (2017)
Wax dipping	Patterned wax via a mould	About 1 mm	Low	Low	Cate <i>et al.</i> , (2015)
Wax screen-printing	Wax pushed through a screen	About 1 mm	Low	Low	Cate <i>et al.</i> , (2015)
Inkjet printing	Printed hydrophobic ink	Sub-millimetre	Moderate	Low to moderate	Yang <i>et al.</i> , (2017)

Flexographic printing	Roll-to-roll polymer barrier	About 1 mm	Moderate, scalable	Low at scale	Yang <i>et al.</i> , (2017)
Screen-printed electrodes	Carbon or Ag/ AgCl ink	Hundreds of micrometres	Low to moderate	Low	Sun & Hall (2019)
Laser cutting and engraving	Ablated channels or zones	Tens to hundreds of micrometres	Moderate	Moderate	Cate <i>et al.</i> , (2015)
Craft (xurography) cutting	Mechanically cut paper or vinyl	About 0.5 mm	Low	Very low	Cate <i>et al.</i> , (2015)
Stamping	Hydrophobic ink stamp	About 1 mm	Very low	Very low	Cate <i>et al.</i> , (2015)
Plasma treatment	Selective hydrophilic patterning	Sub-millimetre	High	Moderate	Yang <i>et al.</i> , (2017)
Polymer (PDMS, polystyrene) barrier	Solvent-cast polymer wall	Sub-millimetre	Low to moderate	Low	Cate <i>et al.</i> , (2015)
Alkyl ketene dimer patterning	Sizing-agent hydrophobisation	Sub-millimetre	Moderate	Low	Yang <i>et al.</i> , (2017)
Vapour-phase silanisation	Hydrophobic silane barrier	Sub-millimetre	Moderate	Moderate	Yang <i>et al.</i> , (2017)
Origami paper folding (3D)	Folded multilayer fluidics	Layer-defined	Very low	Very low	Martinez <i>et al.</i> , (2008)
Toner or laser-printer patterning	Fused toner barrier	About 1 mm	Low	Very low	Cate <i>et al.</i> , (2015)
Thread-based fabrication	Hydrophilic thread channels	Thread diameter	Very low	Very low	McCracken & Yoon (2016)
3D-printed device housing	Additive manufacture of optics box	Device scale	Moderate	Low to moderate	Wilkes <i>et al.</i> , (2017)
3D-printed microfluidic chip	Printed channels and wells	Hundreds of micrometres	Moderate	Moderate	McGonigle <i>et al.</i> , (2018)
3D-printed smartphone spectrometer	Printed slit and grating mount	Optical grade	Moderate	Low	Wilkes <i>et al.</i> , (2017)
Drop-casting or dip-coating of sensing film	Deposited recognition layer	Film scale	Low	Low	Roda <i>et al.</i> , (2016)

Without control of ambient light, the largest cause of irreproducibility in smartphone colourimetry is uncontrolled ambient light. The mitigation here is to have a small reaction space in a small chamber whose geometry and the light are fixed, often fabricated three-dimensionally from polylactic acid, which can be produced locally from a renewable, inexpensive filament. These enclosures, along with an on-card colour reference for white balancing, ensure different cell phones yield similar white balancing results. The same additive-manufacturing technique also makes it possible to create low-cost diffraction-based smartphone spectrometers, which report a resolution of ~1 nanometre, that transform the phone into a real "smartphone spectrophotometer" for only a small fraction of the cost of a benchtop spectrophotometer (Wilkes *et al.*, 2017; McGonigle *et al.*, 2018). Paper colourimetry is a special feature: the assay itself requires no power; capillary flow and a spontaneous colour reaction are enough, and the phone provides illumination and computation based on its own battery. Electrochemical assays take in a small current, which the phone can supply through its port. If there is no signal at the time of testing, connectivity will rely on the cellular network or store-and-forward synchronisation is possible, so a result will never be lost just because a signal is not present. The operation is usually very simple: add a drop of sample, wait a given period, then photograph the zone under App guidance, and is suitable for users who are minimally trained and pushes the criterion of User-friendly. As to reagents required to be kept cold, this is a serious disadvantage in case of unreliable refrigeration. The engineering solution is to immobilise the reagent in dry form inside the device, such as by coating the substrate with the enzyme, chromogen, antibody, or aptamer and encapsulating them with sugars or polymers that will keep them alive for a long time at ambient temperature. The Dry-reagent storage avoids the cold chain, the amount and weight of the reagent to be transported, and operator handling of hazardous substances, which comply with the Deliverable criterion and the waste and safety principles of green analytical chemistry (Vashist *et al.*, 2015).

3.3 Detection Modalities and Quantification

The quality of the device and its ability to transform the raw signal into a reliable focus are only as good as its ability. The main transduction strategies, the relation between signal and concentration and the calibration and validation scheme that safeguards the user of the instrument against misleading results

are described in this section. Optical transduction is based on the Beer-Lambert law: absorbance of a sample is directly proportional to the path length and the concentration of the absorbing species (Equation 1),

$$A = \log_{10} \left(\frac{I_0}{I} \right) = \varepsilon b c \quad (1)$$

where A is the absorbance, I_0 and I are the incident and transmitted intensities respectively, ε is the molar absorptivity, b is the path length, and c is the concentration. The intensity of the transmitted or reflected light is read as an average channel value in the case of a smartphone, and an effective absorbance is calculated for each colour channel, comparing a blank area to a sample area

$$A_k = \log_{10} \left(\frac{I_{\text{blank } k}}{I_{\text{sample } k}} \right), \quad k \in \{R, G, B\} \quad (2)$$

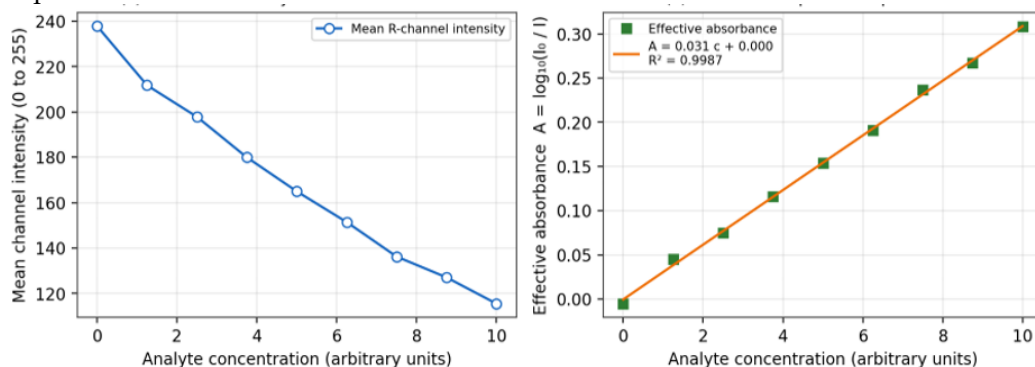
The channel which yields the steepest and most linear response to the analyte is chosen for quantification. Simpler readouts utilise the difference between the mean grayscale intensity of blank and sample (Equation 3),

$$\Delta I = I_{\text{blank}} - I_{\text{sample}} \quad (3)$$

Colour-shift assays are best reflected using the Euclidean distance between blank and sample locations in the red, green, and blue colour space,

$$\Delta E = \sqrt{(\Delta R)^2 + (\Delta G)^2 + (\Delta B)^2} \quad (4)$$

Hue, which maps red, green, and blue to a hue space and saturation, value is sometimes more preferred because its hue angle is correlated with the dominant wavelength and is relatively insensitive to the brightness, which makes it more robust to lighting (McCracken & Yoon, 2016). Reflected intensity decreases as the concentration increases, with the linearised response shown in the plot as the solid line. Increasing the concentration decreases the reflected intensity (shown as the dashed line), whereas the linearised response increases linearly with the concentration for this quantity (shown as the solid line) for quantitation.



(a) Reflected intensity falls with concentration (b) Linearised response for quantification

Fig. 3 Illustrative smartphone colourimetric calibration (schematic data for demonstration). Panel (a) shows the fall of mean channel intensity with concentration; panel (b) shows the corresponding effective absorbance, which is linear and suitable for quantification.

Fluorescence is more sensitive than absorbance due to the fact that there is a dark background against which an emission is measured. In the dilute limit, the intensity emitted is directly proportional to the fluorophore concentration and quantum yield, and a ratiometric design, in which the comparison of two emission channels yields a self-referenced signal which is not affected by drift. Chemiluminescence and electrochemiluminescence do not require an excitation source because light is generated by the reaction itself, making the optics simpler and reducing the power requirement: the camera (long exposure) detects the light inside a dark enclosure. These glow paths are suitable for enzyme/immunoassay-based detection and have been shown to work for glucose and lactate detection on paper devices using a phone (Sun & Hall, 2019; Roda *et al.*, 2016). Amperometric detection is based on the Cottrell equation, which relates the diffusion-limited current to the concentration,

$$i(t) = n F A C \sqrt{(D / \pi t)} \quad (5)$$

Where i is the current at time t , n is the number of electrons transferred, F is the Faraday constant, A is the electrode area, C is the bulk concentration, and D is the diffusion coefficient. Potentiometric detection with an ion-selective electrode follows the Nernst relation,

$$E = E^0 + (R T / z F) \ln a \quad (6)$$

where E is the measured potential, E^0 is the standard potential, R is the gas constant, T is the temperature, z is the ion charge, F is the Faraday constant, and a is the ion activity. where I is the current at time t , n is the number of electrons transferred, F is the Faraday constant, a is the ion activity. Voltammetric techniques, including cyclic, square-wave, and differential-pulse voltammetry, relate a peak current to concentration and are widely used for heavy metals by anodic stripping, while impedance spectroscopy reports the change in charge-transfer resistance on affinity binding (Sun & Hall, 2019). Several modalities even eliminate the need for colour intensity to be interpreted. Distance-based detection is the conversion of concentration into the length of a coloured bar which moves along a channel; the concentration is then read as if it were a thermometer,

$$L = k c + L_0 \quad (7)$$

Where L is the bar length, c is the concentration, and k and L_0 are calibration constants. Counting, text-based devices report the number of zones that change colour, and time-based devices relate the time to a visible change to concentration, which can be checked with the phone stopwatch or by analysing a short video (Cate *et al.*, 2015; McCracken & Yoon, 2016). These formats are quite simple and less precise, but in a field environment, they may be beneficial. The modalities are summarised in Table 3 along with the relation in which they are covered, the typical outcome of the modality, and several examples of classes for which they are relevant.

Table-3 Detection modalities for smartphone and point-of-care green analytical devices, with their governing relations, typical readouts, and representative target classes.

Detection modality	Governing relation or descriptor	Typical smartphone readout	Representative target classes	References
Transmission colourimetry	Beer-Lambert, $A = \log_{10}(I_0/I)$	Channel intensity through a cuvette	Metal ions, nutrients	Wilkes <i>et al.</i> , (2017)
Reflectance colourimetry on paper	Effective absorbance from reflected light	Mean R, G, B of the reaction zone	Glucose, pH, nitrite	Yang <i>et al.</i> , (2017)
Grayscale intensity	$\Delta I = I(\text{blank}) - I(\text{sample})$	8-bit gray value	Enzymatic assays	Roda <i>et al.</i> (2016)
RGB channel ratios	Ratio of channel means	Ratiometric colour index	Dyes, pH	Ozdemir <i>et al.</i> , (2017)
Hue (HSV) analysis	Hue angle in HSV space	Dominant-wavelength proxy	Colour-shift assays	McCracken & Yoon (2016)
Euclidean colour distance	ΔE in RGB space	Composite colour change	Multi-analyte panels	Huang <i>et al.</i> , (2018)
Distance-based detection	$L = k c + L_0$	Length of a colour bar	Metals, glucose	Cate <i>et al.</i> , (2015)
Counting or text-based	Number of coloured bars or digits	Discrete count	Semi-quantitative screening	Yang <i>et al.</i> , (2017)
Time-based detection	Time to visible change vs $1/c$	Stopwatch or video	Hypochlorite, oxidants	McCracken & Yoon (2016)
Fluorescence intensity	Emission proportional to yield and c	Intensity under excitation	Pathogens, ions	Roda <i>et al.</i> , (2016)
Ratiometric fluorescence	Ratio of two emission channels	Self-referenced signal	Heavy metals	Huang <i>et al.</i> , (2018)
Chemiluminescence	Photon flux from the reaction	Long-exposure capture	ATP, glucose, and immunoassays	Roda <i>et al.</i> , (2016)
Electrochemiluminescence	Emission at the electrode	Camera-captured glow	Glucose, lactate	Sun & Hall (2019)
Amperometry	Cottrell, $i = nFAC\sqrt{(D/\pi t)}$	Current via port or radio	Glucose, lactate	Sun & Hall (2019)
Potentiometry	Nernst, $E = E^0 + (RT/zF) \ln a$	Potential of an ISE	Ions, pH	Sun & Hall (2019)
Voltammetry (CV, SWV, DPV)	Peak current vs concentration	Plug-in potentiostat	Heavy metals, drugs	Sun & Hall (2019)
Impedance spectroscopy	Charge-transfer resistance shift	Impedance via add-on	Affinity binding	Sun & Hall (2019)
Lateral-flow line intensity	Test-line darkness vs concentration	Line grayscale	Antigens, hormones	Quesada-González & Merkoçi (2017)

Plasmonic (LSPR) colour	Plasmon shift to visible colour	Colour of a nanoparticle zone	Aptamer assays	Quesada-González & Merkoçi (2017)
Turbidimetry scattering	Attenuation by scattering	Intensity drop	Microbial load	Roda <i>et al.</i> , (2016)
Microscopy-coupled imaging	Spatial features in a magnified image	Magnified image analysis	Cells, parasites	Hernández-Neuta <i>et al.</i> , (2019)

To quantify, there needs to be a relationship with calibration; usually, the linear model is used

$$y = m c + b \quad (8)$$

Here, y is the analytical signal, m is the sensitivity, and b is the intercept. Limit of detection and the limit of quantification are obtained from the standard deviation of the blank or of the intercept, σ , and the sensitivity, S,

$$\text{LOD} = 3.3 \sigma / S, \quad \text{LOQ} = 10 \sigma / S \quad (9)$$

In addition, smartphone methods need to be able to account for the image response variations that occur between different devices, the effects of ambient light, and the variation in sample positioning. Best practice is to use a fixed enclosure, an on-card reference for white balancing, for replica(s) and validate against an accepted reference method like inductively coupled plasma mass spectrometry (ICP-MS) for metals, or an enzymatic analyser for clinical markers. As evidenced in the smartphone literature (Roda *et al.*, 2016; Hernández-Neuta *et al.*, 2019), close to 100 per cent recoveries and agreement between the reported and reference methods are the basis for the trustworthiness of a field result.

3.4 Applications Across Health, Environment, Food, and Agriculture

There has been proof-of-concept of the use of smartphones and point-of-care green analytical devices for a growing number of analytes and matrices. The clinical domain has the longest history, due to glucose and infectious disease testing, and the environmental water quality, food safety and agriculture soil testing domains are growing rapidly due to the need for decentralised, low-cost measurement. Examples are collected in Table-4 in each of these domains, with an indication of the platform, of the detection modality used, of a typical sensitivity and/or working range, of relevance to resource-limited settings, and a citation. Sensitivities quoted are typical from the cited reviews and the primary sources and are not fixed values as performance is very dependent on the particular chemistry, substrate and particular reader used.

Table-4 Representative applications of smartphone and point-of-care green analytical devices across clinical, environmental, food, and agricultural domains. Sensitivities and ranges are representative values synthesised from the cited reviews and primary sources, not single-study claims.

Target analyte	Matrix	Platform or substrate	Detection	Representative sensitivity or range	Setting	References
Glucose	Blood, plasma	Paper μ PAD with 3D-printed cassette	Reflectance colorimetry	Clinically relevant mM range	Diabetes screening	Cai <i>et al.</i> , (2024)
Glucose	Serum, urine	Paper bipolar electrode	Electrochemiluminescence	About 10^{-5} M	Metabolic testing	Sun & Hall (2019)
Multi-parameter blood panel	Plasma	Microwell colourimetric kit	RGB colourimetry via app	Wide clinical ranges, minutes per test	Primary-care check-up	Roda <i>et al.</i> , (2016)
Hematocrit	Whole blood	Paper μ PAD	Colourimetric and distance	Clinical packed-cell range	Anaemia screening	Cai <i>et al.</i> , (2024)
Total cholesterol	Blood	Paper μ PAD	Colorimetry	mg/dL clinical range	Cardiovascular risk	Yang <i>et al.</i> , (2017)
Infectious disease antigen	Serum, nasal	Lateral-flow strip	Test-line grayscale	Visual to semi-quantitative	Infection triage	Quesada-González & Merkoçi (2017)
Pathogen nucleic acids	Swab, lysate	Paper with isothermal amplification	Fluorescence or colour	Low copy numbers	Field molecular diagnosis	Hernández-Neuta <i>et al.</i> , (2019)
Malaria parasite	Blood smear	Smartphone microscope	Magnified imaging	Parasite-stage detection	Rural malaria diagnosis	Hernández-Neuta <i>et al.</i> , (2019)

Lactate	Serum	3D-printed electrode	Electrochemiluminescence	Sub-mM to mM	Metabolic monitoring	Sun & Hall (2019)
Arsenic	Drinking, pond water	Colourimetric assay with a phone	Reflectance colorimetry	Near the WHO 0.01 mg/L guideline	Safe-water screening	McCracken & Yoon (2016)
Hexavalent chromium	Water	Paper μ PAD with 3D light box	Colourimetry, image analysis	Sub-mg/L water-quality range	Effluent screening	McCracken & Yoon (2016)
Nitrite and nitrate	Surface water	Paper μ PAD	Griess colorimetry	Environmental range μ M	Eutrophication monitoring	Yang <i>et al.</i> , (2017)
pH	Water, soil leachate	Indicator paper	Hue (HSV) colourimetry	pH units	Field soil and water testing	McCracken & Yoon (2016)
Synthetic dyes	Wastewater	Smartphone optical cell	RGB ratiometric	Visible-range concentrations	Textile effluent monitoring	Ozdemir <i>et al.</i> , (2017)
Heavy metals (Pb, Cd)	Water	Screen-printed electrode	Anodic stripping voltammetry	μ g/L to mg/L	Contaminated-water screening	Sun & Hall (2019)
Free chlorine	Drinking water	3D-printed smartphone spectrometer	Time-based, colourimetry	Disinfection-relevant mg/L	Treatment verification	McGonigle <i>et al.</i> , (2018)
Fluoride	Groundwater	Paper μ PAD	Colorimetry	Near mg/L guideline	Endemic-fluorosis screening	Yang <i>et al.</i> , (2017)
Pesticide residue	Produce extract	Enzyme-inhibition paper	Colorimetry	Trace residue range	Food-safety field testing	Roda <i>et al.</i> , (2016)
Food pathogen (Salmonella)	Food rinse	Immuno paper device	Colourimetry fluorescence or	Low cell counts	Supply-chain screening	Yang <i>et al.</i> , (2017)
Milk adulterant	Milk	Paper μ PAD	Colorimetry	Adulteration-relevant range	Dairy quality control	Cate <i>et al.</i> , (2015)
Aflatoxin	Grain extract	Lateral-flow aptasensor or	Line intensity or LSPR	Regulatory range μ g/kg	Post-harvest screening	Quesada-González & Merkoçi (2017)
Soil phosphate	Soil leachate	Paper μ PAD	Colorimetry	Agronomic range	Precision-agriculture support	McCracken & Yoon (2016)

Glucose continues to be the major application due to the highest incidence of diabetes in low and middle-income countries, where laboratory capacity is the lowest. Combined with 3-D printed smartphone cassettes, paper devices have been used to measure blood glucose and hematocrit simultaneously at the point of care (Poc) (Cai *et al.*, 2024), and multi-parameter colourimetric kits have sent back panels of clinical markers in mere minutes after a single image. Molecular diagnosis can be performed by infectious-disease testing, such as lateral-flow antigen testing or paper devices that use isothermal nucleic-acid amplification, in locations that lack thermal cyclers, and smartphone microscopy can aid the diagnosis of malaria and other parasitic diseases using a stained smear (Hernández-Neuta *et al.*, 2019). Safe water is one of the major challenges of resource-limited areas, and smartphone colourimetry has been used in arsenic, chromium, nitrite, fluoride, free chlorine, and synthetic dyes, with many tests approaching regulatory guideline values (McCracken & Yoon, 2016; Mutlu *et al.*, 2017; Ozdemir *et al.*, 2017). The technology of anodic stripping voltammetry (ASV) is useful

when optical techniques are limited by turbid and coloured samples, as it can be used to detect heavy metals, including lead and cadmium (Sun & Hall, 2019). These measurements can also be geotagged and uploaded, so they can be used to help with distributed monitoring of contamination that would otherwise not have been possible with centralised testing. Along the whole food chain, food-safety screening for pesticide residues, microbial pathogens, mycotoxins and adulterants is important both for consumers and producers; and paper and lateral-flow formats, read by a phone, offer a first line of defence before confirmatory laboratory testing, and are thus very important (Yang *et al.*, 2017; Quesada-González & Merkoçi, 2017). With colourimetric soil nutrient testing, farmers in agriculture can make decisions based on the nutrient level of their soil and avoid over-fertilising or under-fertilising, which helps to improve yields and prevent nutrient run-off.

3.5 Mapping Device Design onto Green and Point-of-Care Criteria

To illustrate the possibility of the smartphone as a POC device being a representative example of green analytical chemistry, the design considerations of the device can be directly correlated with the twelve principles of GAC and REASSURED criteria. Table-5 identifies each principle/criterion and the typical lab practice it supplants, and the specific design response that is provided by a well-designed smartphone device. The design is uniform. The conventional approach is big, powered or low current, solvent-based, centralised, while the smartphone response is small, ambient powered or low current, aqueous, and decentralised. Fig. 4 is the same comparison as above, but presented as a conceptual profile of greenness and practicability.

Table-5 Mapping of smartphone point-of-care design choices onto the twelve principles of green analytical chemistry and the REASSURED criteria, contrasted with the conventional laboratory practice each replaces.

Principle or criterion	Conventional laboratory practice	Smartphone point-of-care design response	References
GAC 1. Direct, in situ measurement	Offline extraction and digestion	Direct on-zone reaction with minimal preparation	Gałuszka <i>et al.</i> , (2013)
GAC 2. Minimal sample number and size	Large aliquots and many replicates	Microlitre volumes wicked onto paper	Martinez <i>et al.</i> , (2010)
GAC 3. On-site measurement	Transport of specimens to a central laboratory	Reading at the point of need	McCracken & Yoon (2016)
GAC 4. Integrate steps and automate	Multi-step manual workflow	Reaction, capture, and computation in one app	Huang <i>et al.</i> , (2018)
GAC 5. Miniaturise	Bench-scale instruments	Pocket-scale device and reader	Yager <i>et al.</i> (2006)
GAC 6. Avoid derivatisation	Added derivatising reagents	Native colour or label-free transduction, where possible	Gałuszka <i>et al.</i> , (2013)
GAC 7. Minimise waste	Litres of solvent waste	Microlitre reagents and disposable paper	Martinez <i>et al.</i> , (2010)
GAC 8. Prefer multi-analyte methods	One analyte per run	Multiplexed zones on one device	Yang <i>et al.</i> , (2017)
GAC 9. Minimise energy	Mains-powered instruments	Capillary-driven or low-current, ambient light	McCracken & Yoon (2016)
GAC 10. Use renewable reagents and materials	Petrochemical consumables	Cellulose substrate and bio-derived reagents	Martinez <i>et al.</i> , (2010)
GAC 11. Eliminate toxic reagents	Hazardous organic solvents	Aqueous chemistries and benign chromogens	Gałuszka <i>et al.</i> , (2013)
GAC 12. Operator safety	Exposure to hazardous substances	Closed, low-volume, low-hazard format	Gałuszka <i>et al.</i> , (2013)
REASSURED. Real-time connectivity	Paper records and manual reporting	Cloud upload, geotagging, and surveillance	Land <i>et al.</i> , (2019)
REASSURED. Ease of specimen collection	Venous draw by trained staff	Finger-prick or swab with minimal skill	Land <i>et al.</i> , (2019)
REASSURED. Affordable	Costly capital instruments	Low device and per-test cost	Land <i>et al.</i> , (2019)
REASSURED. Sensitive	Laboratory-grade detection	Adequate via amplification and controlled optics	Land <i>et al.</i> , (2019)
REASSURED. Specific	Confirmatory reference methods	Antibody, aptamer, or enzyme selectivity	Land <i>et al.</i> , (2019)
REASSURED. User-friendly	Expert operation	Guided app workflow	Land <i>et al.</i> , (2019)
REASSURED. Rapid and robust	Hours of turnaround	Minutes, tolerant of field conditions	Land <i>et al.</i> , (2019)
REASSURED. Equipment-free or minimal	Dedicated powered hardware	The smartphone is the only instrument	Land <i>et al.</i> , (2019)

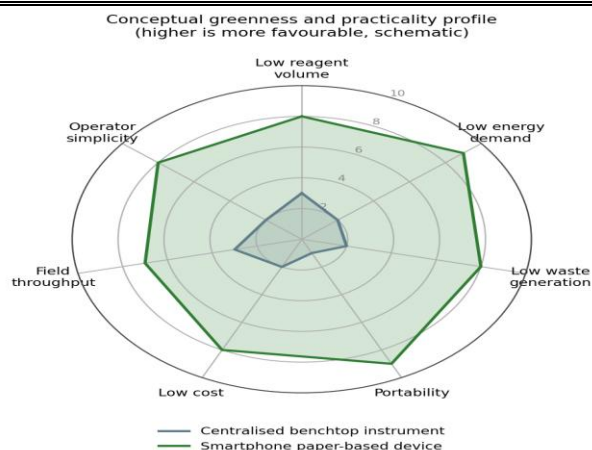


Fig.4 Conceptual greenness and practicality profile contrasting a centralised benchtop instrument with a smartphone paper-based device across seven design-relevant axes. Higher values are more favourable; the chart is schematic and intended to convey relative tendencies rather than measured data.

3.6 Challenges and Limitations

The most challenging technical problem is the ability to reproduce the same results across devices, operators and lighting conditions. Raw values will vary from phone to phone because of different colour processing, exposure and white balancing. This variability has been reduced but not eliminated by the mitigations described above, such as the fixed enclosures, on-card colour references, locked camera settings and machine learning correction, and a shared validation protocol is still lacking. Until there is consensus on such protocols, the results should not be assumed to be interchangeable among platforms. The sensitivity of camera-based colourimetry is intrinsically lower than that of dedicated photodetectors, and real matrices like whole blood, turbid water and food extracts cause interferences and background colour. Sample preparation, internal standard, and selective recognition elements help, but add steps that can erode the greenness and simplicity that inspire the platform. Additional hardware or reagents are required for electrochemical and luminescent modalities to regain sensitivity, and the designer must weigh the performance against the principles that the device is to serve.

Many of the smartphones reported as proofs of concept do not have the multi-site validation, quality control and regulatory clearance necessary for routine use, whereas validated, traceable methods are required for clinical and environmental decisions. The challenge here is to compare with the reference method in all relevant matrices, to field-test stability assessment, and to engage with the regulators in a time-consuming and resource-intensive process, especially when considering the speed at which devices are published (Vashist *et al.*, 2015). There is a conflict of tension in the field. The disposable paper element is truly green, but the smartphone is a complex electronic product that requires a lot of energy and materials to produce and will end up contributing to an increasing electronic-waste problem that is particularly heavy on low-income areas (Baldé *et al.*, 2024). The best answer is that the device is already owned and used for a lot of other things, and that the analytical functionality imposes minimal additional “marginal footprint”; and that the elimination of “solvent-intensive central laboratories” represents a true net savings. Nevertheless, an honest assessment of the greenness of a smartphone method should recognise the life-cycle effects of the reader and give credit to the method not just for the frugality of the paper strip.

CONTRIBUTION TO KNOWLEDGE

This review proposes a common engineering approach that aligns the green analytical chemistry principles with the REASSURED point-of-care criteria and establishes a mapping between the attributes of the smartphone devices. It explains the calibration/validation procedure to provide trustworthy field measurement, and addresses the electronic-waste paradox, where smartphone platforms appear as useful green analysis in resource-poor environments.

CONCLUSION

There are many examples of green analytical chemistry that are most likely to be realised in a practical way for resource-limited environments, such as sensitive analytical devices based on smartphones and point-of-care analytical devices. These platforms address several of the 12 principles of green analytical chemistry and the REASSURED criteria with one device that billions of people already have, and coupled with the recognition element (which is often paper-based) that uses minimal resources. The engineering challenge is to maintain analytical quality while being frugal, to be controlled in illumination, be mindful of substrate and fabrication, be careful about calibration validation and be honest with the life-cycle impacts of the reader. If that discipline is used, the consequence is a measurement that is small, low power, low waste, inexpensive and available to those who need it the most. The development of greenness metrics, embedded intelligence, connectivity and sustainable materials implies continued growth of the role of these devices in equitable and sustainable measurement. The next step in development will be characterised by several trends. Embedded machine learning will further enhance the accuracy of colour and image interpretation, enabling accurate quantification with poor lighting and eliminating the need for large enclosures. The vision of REASSURED is the real-time connectivity achieved by tighter integration with the Internet of Things and cloud analytics, thereby making individual measurements into distributed surveillance networks for disease and pollution. Point-of-care testing that has been used as a single event will be transformed into continuous; also, the electrochemical and luminescent transductions will be expanded to wearable formats. From materials, the need for renewable substrates, bio-derived reagents and recyclable or biodegradable electronic materials will help to solve the paradox of electronic waste and increase the real greenness of the whole system. This would professionalise the field and drive towards fast and reliable deployment together with the established greenness metrics, so that every new device added to the market comes with a report of its Analytical Figures of Merit together with its AGREE or BAGI evaluation.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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