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Electronic Tattoos: A Promising Approach to Real-time Theragnostics

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Abstract

Real-time monitoring of relevant biological signals, in combination with the timely delivery of target drugs, would be ideal for treating most medical conditions. However, access to biological fluids without a bulky, costly, and cumbersome apparatus remains challenging, as does the ability to deliver drugs of controlled dosage in a similarly unobtrusive fashion. The skin provides a promising medium for access and dosing using biomedical electronics, colloquially dubbed electronic tattoos. Recent developments in biologically compatible, flexible materials and devices have brought electronic tattoos closer to reality for sensing biomarkers extracted from the skin and delivering target drugs through the dermis. In this review, the materials and engineering requirements, fabrication developments, and sensing and therapeutic advancements of electronic tattoos are presented. Three components are required for a complete theragnostic electronic tattoo system: 1) supporting electronics for control and data transmission; 2) diagnostic sensors, categorized as mechanical (measure an internal stimulus) and chemical (measure a chemical change); and 3) therapeutics for drug delivery. The leading approaches for fabrication are summarized, including the transfer of flexible devices to the skin and the direct printing of devices onto the epidermis. Altogether, while significant obstacles remain, the advancements in this field show great promise for realizing electronic tattoo theragnostics to revolutionize point-of-care medicine.

Introduction and Background

One of the greatest shortcomings in modern medicine is the infrequent measurement of key biomarkers, particularly those within the blood, combined with the regimented dosing of drugs. Continuous monitoring of relevant analytes in tandem with the precise dosing of medication would have profound implications on treatment and health. From early diagnosis to improved long-term prognosis, low delay between the onset of symptoms and detection of an aberrant signal has the potential to revolutionize medicine[1,2]. This is readily apparent for chronic diseases, such as diabetes, where it has long been understood that frequent collection of data on current blood sugar levels is pivotal to proper management of symptoms[3]. Countless other chronic and acute diseases, such as Crohn's disease and complications due to heart failure, could be transformed with similar capabilities; yet, the closest we have come to widespread continuous health monitoring is the recent proliferation of wearables, such as smartwatches, which allow for facile, non-invasive monitoring of limited *ex vivo* patient data, such as heart rate, daily movement, and sleep[4,5]. Thanks to advancements in biocompatible materials and sensors, the scope of devices for continuous monitoring and chronic symptom regulation is expanding rapidly. As numerous biological signals (including both

chemical and physical signals) become more accessible to measurement, the capability for targeted and timely drug delivery upon detection of a specific biological trigger progresses closer to reality.

There are numerous modalities that support continuous monitoring and dosing, including wearables (such as a smart watch or smart clothing), ingestibles or implantables, and on-skin electronics (also referred to as electronic tattoos, epidermal electronics, and e-tattoos). While wearables are currently the most ubiquitous option, their utility is somewhat limited by their form factor. To maintain comfort during use, minimal direct contact with the skin is made, thus detection of chemical (e.g., biomarkers in blood) and physical (e.g., strain) biological signals may be limited[6,7]. Ingestible electronic biomonitoring technology is unsurpassed in its ability to detect chemical signals within the native biological environment, but is intrinsically transient and difficult to control location post ingestion[8,9]. Further, any *in vivo* technology, including implantable electronics, will be wrought with challenges of biofouling due to an immunogenic foreign body response, which can lead to discomfort, signal drift, and the rejection of the device[10].

Electronic tattoos are nonpermanent electrical devices or systems placed in intimate contact with the skin and intended for relatively short-term use (upwards of 1-2 weeks). Their name is derived from their similarity to temporary, decal-style tattoos rather than an ink embedded into the dermis to change local pigmentation. While there may be some minimally invasive penetration into the skin, the vast majority of the device, including all electronics, are on top of the skin. Electronic tattoos combine the comfort and less transient nature of wearables with much of the precision of ingestibles; an on-the-skin technology with the promise of advancing the current diagnosis-only model to one that combines therapy and diagnostics for a complete "theragnostic" system. Electronic tattoos have intimate contact with the skin, and thus the ability to directly monitor biological signals through the epidermal layer in addition to transferring a therapeutic drug via the dermis. Their relative thinness would allow these tattoo-like biomedical devices to be comfortable to wear, with semi-permanence in that they have been demonstrated to be stable in performance for over a week of continuous usage[11]. Their lifetime is frequently considered to be a few days at the shortest[12] to the cycle length of desquamation of the outermost layer of the dermis, which is about 20-30 days[13].

To facilitate the development of electronic tattoos for continuous monitoring and therapy, three separate components must work in concert with one another: biological sensing / diagnostics; drug delivery / therapeutics; and a support system to facilitate the functioning of all components (Figure 1). While sensing and dosing frequently retain focal eminence, the support system (including electrodes, processing, encapsulation, and filtering) is no less pivotal to the functionality. Herein, we describe the recent progress across these three areas in the field of electronic tattoos for theragnostics.

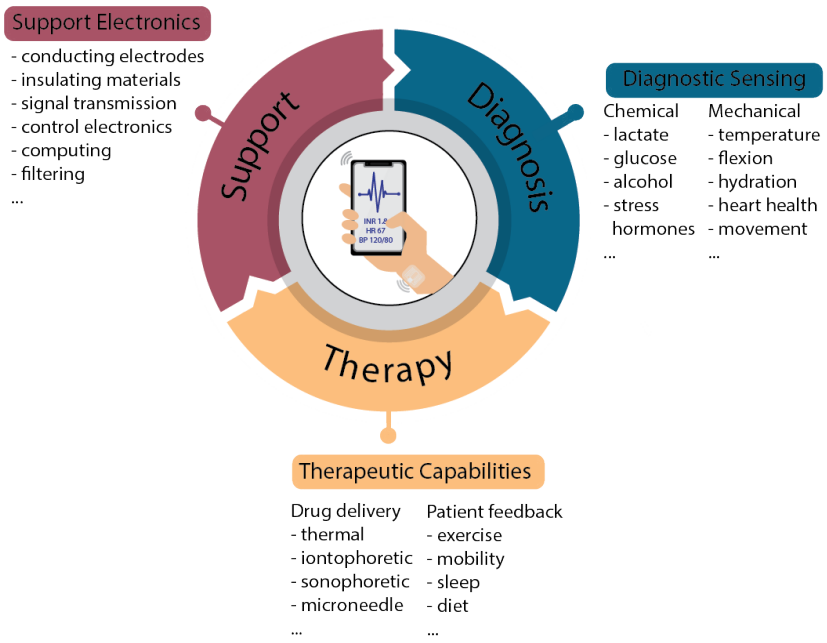

Figure 1. Schematic of modules required for on-skin, electronic tattoos for theragnostics. For each module, an example list of biomarkers (diagnostics), approaches (therapeutics), or components (supporting system) is provided. Some degree of unified functionality across these modules is critical to realizing biomedical electronic tattoos.

Support Electronics

Without a system to support and facilitate transduction and communication, the implementation of on-skin sensing and therapy would be all but impossible. Numerous considerations must be made to ensure accuracy, comfort, and durability. Human skin can stretch by up to 25% before incurring damage[14]. Given this, to maintain comfort, an epidermal tattoo must be thin enough and have a sufficiently low modulus (< 1.5 mm thick and < 600 kilopascals (kPa)) to retain comfort and must maintain performance metrics when strained[15].

One major concern is loss of electrical conductivity due to strain; to alleviate this failure mechanism, numerous methods have been proposed, starting with material selection. Recently, significant work has been performed on liquid metals for stretchable conductive electronics[16,17]. At room temperature, metals such as eutectic indium-gallium maintain a liquid form, which allows conductive channels containing these materials to be stressed over 300% without any noticeable degradation[18]. This, however, has the drawback of requiring encapsulation, which greatly reduces utility and versatility**.** Another materials category, that perhaps is more directly suited to electronic tattoos, are high aspect ratio materials, such as silver nanowires. Their high aspect ratio allows for only a small increase in electrical resistance with applied bending and tensile strain[19,20], and makes them an ideal candidate for electrodes and contacts in an electronic tattoo[21].

In addition to materials choice, significant improvements to lifetime and resistance to degradation from cyclic strain can be achieved via engineering design of electrodes through the incorporation of a serpentine path. This approach can increase ultimate strain from as little as 1% for some materials to upwards of 300%[22]. This design alleviates stress from tensile strain as it allows for the coiled electrodes to straighten before considerable stress is placed upon the conductive trace itself. To further resist degradation, encapsulation can also work to sustain performance by upwards of 6x after numerous cyclic strain episodes typical of quotidian movement[23].

Finally, in addition to conductive traces that are the backbone of electronics, signal processing and transmission are required. Most conventional electronic medical devices separate on- or in-body measurement from amplification, signal filtering, processing, and interpretation; however, in some cases for fully on-skin devices, these processes must be miniaturized and incorporated into the electronic tattoo package. While the vast majority of demonstrated electronic tattoos use conventional silicon-based integrated circuits (ICs)[19,24], there is a growing body of research developing stretchable transistors and other stretchable electrical components for incorporation into flexible electronics[25,26]. Currently, the performance of conventional electronics is orders of magnitude greater and the scale is substantially smaller than achievable with flexible components. Thus the incorporation of flexible circuit boards may require an increase in footprint as compared to a silicon IC[27]. However, if conformity to the skin is a requirement, a device fabricated from all flexible components may be desired, in which case, the larger area could be less of a concern.

The most likely path for the support electronics will be to first implement only the needed control circuitry and signal transmission to an external device (e.g., smartphone, as depicted in Figure 1), keeping the complexity on-skin to a minimum; then, in the longer term, implement other support electronics into the tattoo when the feasibility of doing so is realized. Even in the near-term, obstacles remain for realizing all needed diagnostic and therapeutic control along with signal transmission in an on-skin electronic tattoo, including in the performance and stability of the electronic devices, electrical interconnections and interfaces, and scalability in cost and size.

Diagnostic Sensing

There are numerous cases where continuous monitoring can be advantageous as compared to discrete point monitoring, not least of which is the removal of required human interfacing, which can be hindered by exhaustion, misuse of tools, and/or access to a clinic. With new technological advancements propelling both consumer electronics and medical devices towards an internet-of-everything (IOE) ideal of connectivity, research into electronic biomedical sensors has proliferated. Much of the development focus is in on-skin sensors. From its birth in 1999 with the continuous detection of blood glucose[28], the field has expanded to include sensing of strain[29,30] (Figure 2A-B), temperature[31] (Figure 2C) and several other biological markers related to the exponential increase in sweat sensors[32,33] in the past several years. These on-skin electrical sensors can be divided into two equally necessary categories: physical and chemical sensors.

Physical and chemical sensors can be distinguished by the sensing mechanism. Physical sensors measure an attribute via a change to the sensor itself, whereas chemical sensors measure a reaction between the target analyte and the sensor. As an example, physical sensors include temperature sensors and strain sensors. For a temperature sensor, the sensing mechanism is derived from a change in resistance of the active sensing component in response to a modification in skin temperature. A strain sensor, likewise, transduces the strain experienced by the skin (through compression, extension, or torsion) via a proportional change in the resistance caused by some physical change to the sensor. Depending on the sensor itself, this could

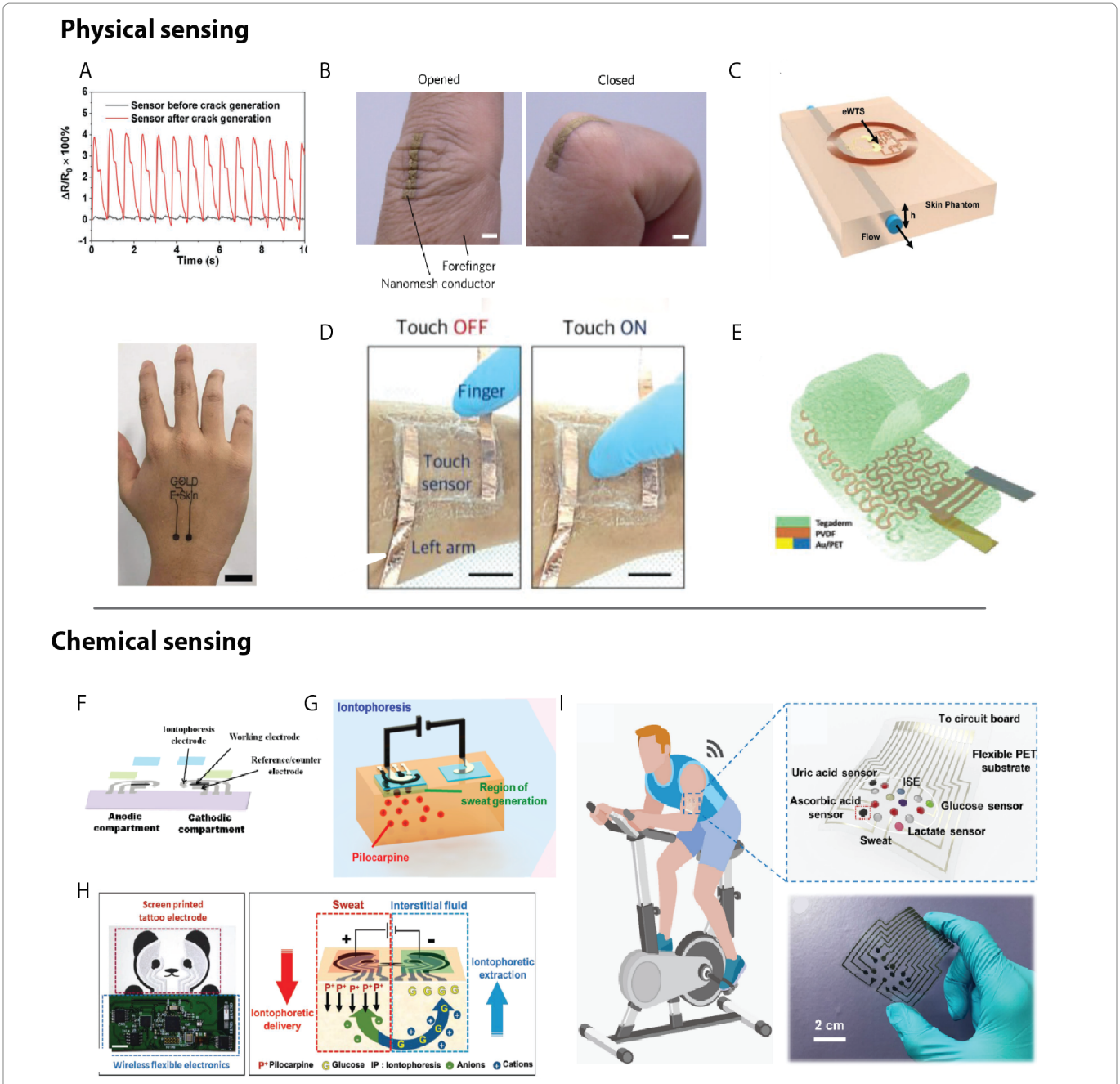

Figure 2. Types of electronic tattoo diagnostic sensors. Physical sensors, which use a physical change in the sensor to measure a biological signal, including (A, B) strain sensors and (C) thermal sensors, (D) touch sensors, and (E) electrocardiograms. Chemical sensors measure the response of chemical reactions such as (F) blood glucose and (G) alcohol. Multiplexed sensors to measure both (H) alcohol & blood glucose and (I) sweat analytes. Reprinted with permission from: (A) ref. 29, copyright 2019, Advanced Materials; B) ref. 30, copyright 2017, Nature Nanotechnology; C) ref. 31, copyright 2019, Advanced Science; D) ref. 12, copyright 2018, Advanced Functional Materials; E) ref. 22, copyright 2019, Advanced Science; F) ref. 34, copyright 2015, Analytical Chemistry; G) ref. 35, copyright 2016, ACS sensors; H) ref. 36, copyright 2018, Advanced Science; I) ref 37, copyright 2019, Science Advances).

be a capacitive change as in a touch sensor[12] (Figure 2D), an increase or decrease to the junction density between electrically conductive components (such as silver nanowires)[30], or modulation to energy band gap in the channel region of a transistor[34], among others. The commonality between these transduction mechanisms is an internal change to a structure or property of the sensor itself. Hence, an electrocardiogram (ECG), would likewise be categorized as a physical sensor as the electrical signal is generally measured via a capacitive change[22] (Figure 2E).

Chemical sensors, on the other hand, transduce information (most often, electrically) via the response to a chemical shift. This may be with an oxidoreductase

enzymatic reaction (such as glucose oxidation facilitated by glucose oxidase, as seen in Figure 2F-H)[35–37] or via the binding event of a protein-protein pair (such as the immunogenic antibody-antigen binding of an immunoassay)[38–40]. While physical sensors can measure signals transdermally, chemical sensors require a solute, and hence a bodily fluid. This can be achieved *ex vivo* via sweat[41] (Figure 2I) or interstitial fluid[42,43].

For interstitial fluid – the fluid between cells within the body – cultivation requires microneedles to puncture the epidermis, while sweat sensing can be achieved without any poration of the skin. As with blood, interstitial fluid is easily probed with an implantable device; however, it is difficult to access non-invasively[44], whereas sweat can be easily generated and measured transdermally. There are two methods for generation of sweat: natural production[33] and the more common induction via the iontophoretic delivery of a drug, such as Pilocarpine[45]. While natural methods may be ideal for monitoring sweat during exercise, stimulated perspiration allows for greater control over sweat timing and volume. Sweat generation remains an issue for long-term use as natural techniques cannot be maintained due to physical exertion requirements and induced perspiration uses a limited drug resource on a localized device. Furthermore, due to degradation of the sensing mechanism, much of the testing focuses on rapid detection on the order of seconds[29,35,36,41,46,47], minutes[24,37,48,49], and hours[50], rather than stability over days of use. To propel chemical sensing development into a commercializable stratum, more focus is needed on extending the lifetime of sensors from hours to days.

Given the relative novelty of this field, many of the reports are proof-of-concept and thus require further testing to directly compare to commercial sensors. To overcome this barrier, significant efforts are currently underway to increase the sensitivity, selectivity, and reproducibility of chemical biosensors[51]. Simultaneous delivery of all three of these metrics is required and will reduce anguish caused by false positives and delayed treatment caused by false negatives[52]. One significant hurdle, as of yet not entirely overcome, is lack of reproducibility in electronic biosensors at least partially caused by drift during storage or intrinsic device-to-device variations[53]. Furthermore, as the field advances, validation studies comparing electronic tattoos to the gold standards of clinic-based detection to ensure the correct and accurate measurement of analytes will become imperative. The field is new enough that this morass has not yet affected development because much of the work to date focuses on initial, singular demonstrations[54]; however, more detailed and long-term studies should become a more expected element of future studies. Recent efforts have seen success in on-chip calibration, which compares the response from a blank to that of a functionalized device on a single chip[55], yet more research and validation are required to extend this development to more devices.

In contrast to chemical sensors, much of the limitations of current physical sensors are largely related to degradation due to repetitive sensing and to cyclic bending/stretching[56–58]. As previously stated, human skin can be strained significantly before damage[14]. Recent studies indicate that a 90° wrist flexion can strain the epidermal surface of the forearm by upwards of 25%[59,60]. Given that these are minor movements that occur continually throughout daily motion, cyclic strain reliability is a major issue. While numerous reports include some cyclic strain data, the majority fall short of truly substantive findings, given that most perform tests to below 1000 cycles[58,61–66] or perform cyclic tests to low strain rates[64]. As the field progresses, cycle number in cyclic degradation testing must also increase if these epidermal electronics are to be used for the entire lifecycle of the epidermis. While there are still significant impediments to overcome, non-invasive, continuous monitoring has the potential to bring a momentous leap in disease control when combined with a feedback loop-based therapy system.

Therapeutic Capabilities

In conjunction with a diagnostic sensing and support system, transdermal drug delivery via an epidermal tattoo has the potential for non-invasive therapy as well as patient-specific regulation of drug delivery[67]. The skin is constituted by three layers: the waterproof epidermis, which is made up of keratinocytes, melanocytes, merkel and Langerhans cells; the middle layer or dermis, consisting of hair follicles, sweat and sebaceous glands, nerves, collagen, lymph vessels, and blood vessels; and the last layer, the hypodermis, which consists of the subcutaneous fat layer. The outermost layer of the epidermis, the stratum corneum (SC), acts as an efficacious barrier membrane, limiting diffusion of large molecules to the dermis[67].

Multiple methods, both physical and chemical, have been developed to increase diffusion of a target drug through the SC, the most prominent of which are thermal enhancement[68] (Figure 3A), which uses localized vasodilation from directly applied heat that can increase blood flow to a specified area by upwards of 9x, causing a 13x increase in uptake of a drug, such as nicotine[69]. The elevated heat can lead to some discomfort for the user and it is also difficult to predict delivery rates, which could lead to the delivery of potentially fatal drug concentrations[70]. A more controlled method is iontophoretic delivery (Figure 3B)[71,72], which uses an applied voltage to transport charged drugs across the SC via electrophoresis and electroosmosis, allowing for upwards of a 10x improvement in drug diffusion over thermal delivery[68]; however, this method does require large, possibly dangerous voltages to achieve

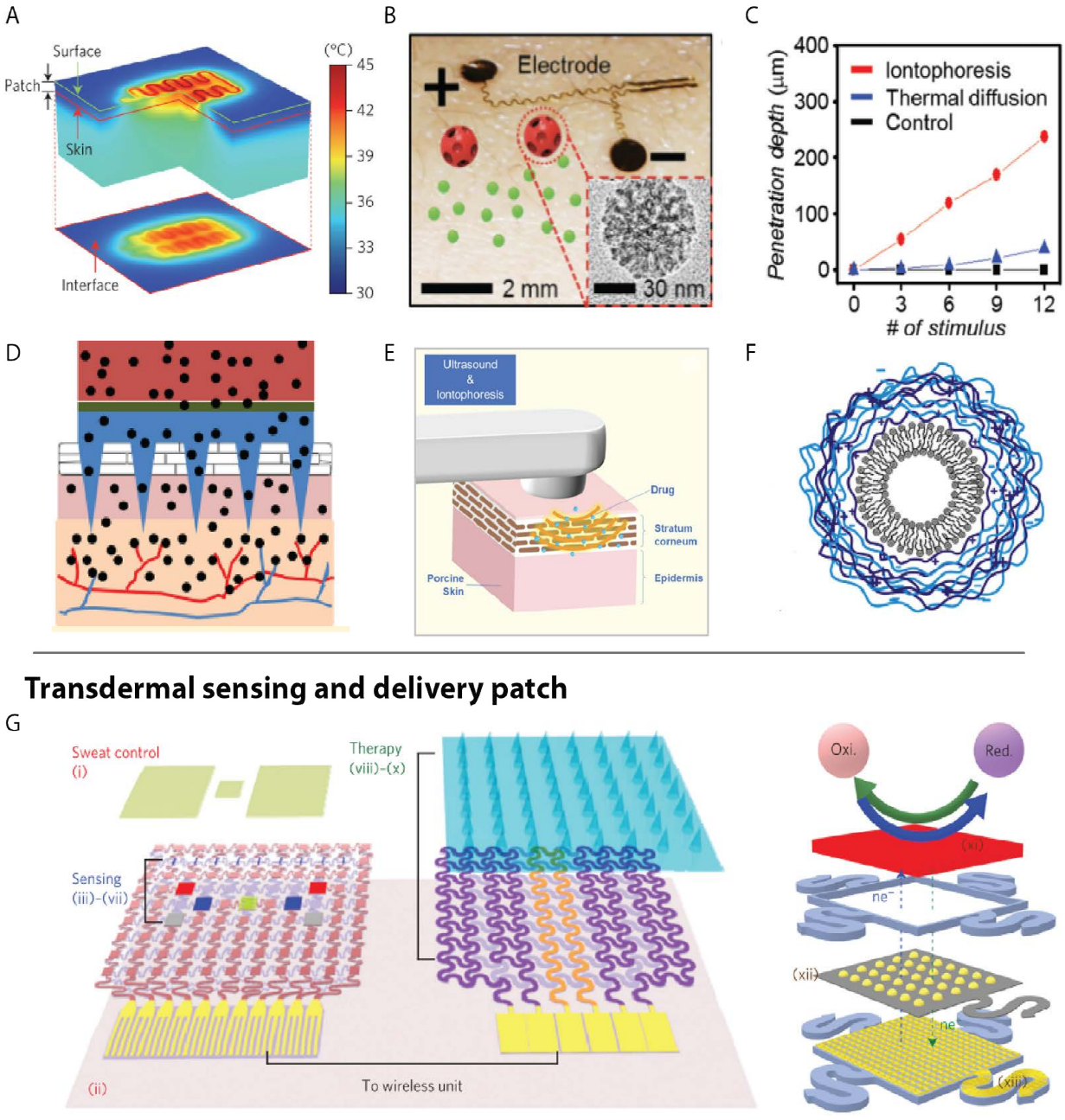

Figure 3. Electronic tattoo-based transdermal drug delivery. Delivery methods for diffusion of drugs through the SC layer of the epidermis include (A) thermal (using heat to increase diffusion), (B-C) iontophoresis (using an electro-repulsive force), (D) microneedle (puncturing the SC layer), (E) sonophoresis (using ultrasonic enhancement), and (F) chemical/ encapsulation (coating the desired drug to increase diffusion). (G) A schematic of a complete patch demonstrates the incorporation of a diagnostic sensing component and a therapeutic component that contains one or more of the delivery enhancement strategies. Reprinted with permission from: (A) ref. 80, copyright 2014, Nature Nanotechnology; B-C) ref. 68, copyright 2016, Advanced Healthcare Materials; D) ref. 73, copyright 2013, Molecular Pharmaceutics; E) ref. 77, copyright 2018, Advanced Drug Delivery Reviews; F) ref. 79, copyright 2015, Colloids Surfaces B: Biointerfaces; G) ref. 46, copyright 2016, Nature Nanotechnology).

desirable delivery rates. Another method is microneedle delivery (Figure 3D)[73,74], which uses small needles to penetrate through the SC; this poration allows for a desired drug to bypass the SC and migrate directly to the dermis. Microneedle is frequently used with another method to further enhance performance. In addition, another technique is sonophoresis[75-77] (Figure 3E), which uses ultrasound to either heat the skin or increase permittivity

via acoustic cavitation and generally requires a large ultrasonic transducer incompatible with electronic tattoos, and finally chemically enhanced diffusion (Figure 3F)[78], which increases permittivity of the desired drug through encapsulation and thus is difficult to accurately dose in timed increments[79]. Regardless of the delivery mechanism, transdermal drug delivery requires a sensing component to take the requisite readings, (as seen in Figure 3G). Of all these options for skin-based drug delivery that can be electronically controlled, iontophoresis shows the greatest promise for electronic tattoos.

Iontophoretic drug delivery offers a promising method for incorporation into an electronic tattoo system due to its electronic operation, especially when combined with poration of the epidermis using microneedles[80,81], and elimination of the discomfort associated with elevated temperatures incident to thermal diffusion enhancement[82]. Iontophoresis enhances drug diffusion through the skin with an induced electric field. This method functions via electrophoresis and electroosmosis, which allows for transportation of larger molecules (>500 Da) previously blocked by the SC[83]. The strength of the electric field directly controls diffusion, and thus iontophoretic delivery can fully control dosage and dosing intervals. However, many embodiments of iontophoretic delivery require non-ideal conditions to enhance drug dosing. Given that the resistivity of human skin is between 1,000 to 100,000 Ω[84], frequently high voltages are required for even modest currents required for diffusion enhancement. While numerous publications solely report currents, the publications that do report voltages use staggeringly high voltages of between 30-90V. These voltages are of such a magnitude to lyse red blood cells[84,85] and would be difficult to implement in standalone electronics; hence, further research is required to decrease the electric field strength required to increase diffusion. One possible route to accomplish this is by decreasing the electrode gap, thus decreasing the electrical resistance of the system. While the remaining challenges are significant, motivation for complete electronic theragnostic epidermal tattoo systems is high and thus warrants further research into solutions for an on-skin therapeutic drug delivery system.

Fabrication and Scalability

One main differentiator distinguishing epidermal electronics from conventional wearables is the application method. While wearables are generally incorporated into a rigid electrical device, such as a wristwatch, epidermal electronics necessitate intimate contact to the skin, and thus must be flexible and stretchable. These limitations enforce constraints on materials and design selection, both of which limit processing options. There are two subsets of fabrication: transfer method, where the tattoo is fabricated onto a disposable substrate and transferred to the desired location on the skin in a similar manner to placing a decal-style tattoo or a sticker[37,86,87]; and direct printing, wherein the device is printed directly onto the epidermis[21,88]. For a directly printed device, this can be achieved either via a 3D printing technique, such as an extrusion method like FDM, or via a tradition printing technique using an inkjet or aerosol jet printer to print the temporary tattoo directly onto the skin. The transfer method offers a large array of fabrication approaches that include conventional cleanroom techniques, which allow for high performing devices through well-established processing technologies[29,41,47,89] (Figure 4A-B); however, these processing technologies are costly and compromise the needed scalability in cost for bespoke electronic biomedical tattoos. Whereas printed electronics[30,90–92] (Figure 4C-D) allow for the custom fabrication of low-cost components[93] with challenges related more to the performance of the printed devices.

Direct printing allows for customization to the patient's needs and rapid prototyping because there is no delay between fabrication and utilization. Direct printing also eliminates the potential for errors in transferring, which plague alternate methods. Yet, direct printing is not yet a drop-in replacement for traditional fabrication methods and their transfer to skin, as deposition of electronically active materials and inks directly onto biological tissue of nearly all printed electronics requires caustic or otherwise damaging post-processing to achieve the desired electrical properties[94]. Recently, research interest has grown in the area of printable electrically conductive inks that can be cured at low temperatures[95], with a subset that allow for desired performance at biologically compatible temperatures[96]. Yet, even so, the conductivity of these is often orders of magnitude below that of their bulk equivalents[21]. The growing interest in in-place-printed electronics also provides promising developments for the incorporation of more complex components into direct printed epidermal tattoos[21,88] (Figure 4E-F).

Further development is still required to eliminate biologically incompatible temperatures and toxic chemicals and a substantial amount of progress is needed for other electronic materials and, ultimately, devices to be printed onto skin. Hence, direct printed electronic tattoos are currently limited to only a few uses that focus on electrically conductive inks for the fabrication of both sensing and supportive components[21,88]. Even so, both demonstrations have used silver nanomaterials, which are known to be cytotoxic and, as with other metal nanoparticles, may alter immune responses[97] and might thus eventually cause cancer[98,99]. While silver nanowires are less cytotoxic than silver nanoparticles, frequent use still remains a concern, especially with the incorporation of heating and microneedles to increase penetration into the dermis as the reduction of elemental silver (Ag^0) to ionic silver (Ag^+) is at

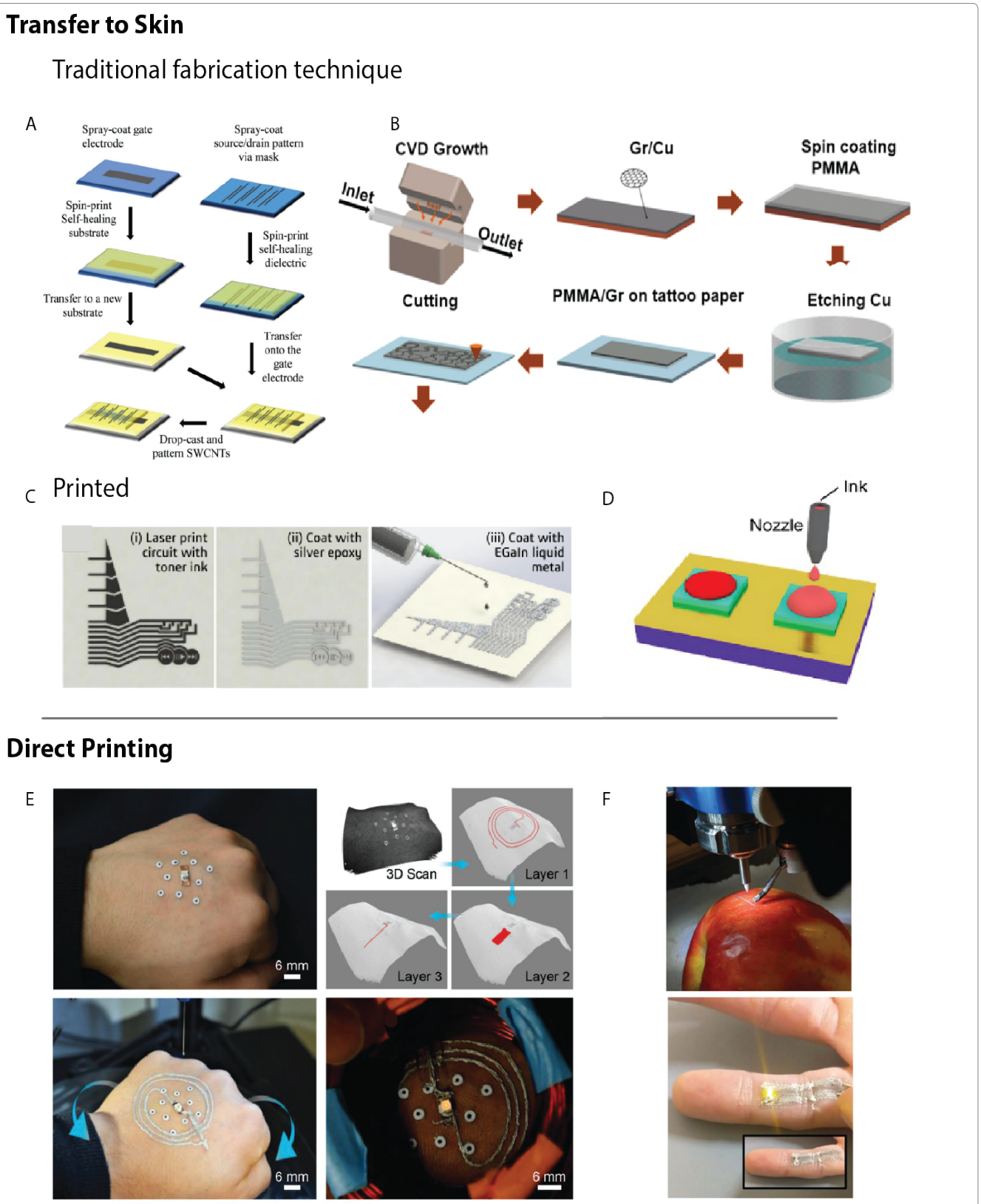

Figure 4. Fabrication techniques for electronic tattoos. The transfer method involves fabrication onto a disposable substrate either via (A-B) traditional, cleanroom fabrication technique schematic process flow or (C-D) via a printing method where the material is deposited in a solution form onto the transfer substrate. (E-F) The direct printing technique involves deposition of the electrically active inks directly onto the desired biological tissue. Reprinted with permission from: (A) ref. 90, copyright 2018, Small; B) ref. 89, copyright 2017, ACS Nano; C) ref. 92, copyright 2018, ACS Applied Materials & Interfaces; D) ref. 91, copyright 2018, Nature; E) ref. 88, copyright 2018, Advanced Materials; F) ref. 21, copyright 2019, Nanoscale).

least a contributing factor to its toxicity and heating may increase the reaction rate while poration of the skin will increase exposure to the dermis[100]. As research progresses, a greater focus must be placed on the development of biocompatible inks, both in terms of ink constituents and long-term effects of the resultant printed films. Direct printing could be a powerful tool for expanding the utility of electronic tattoos beyond the one-size-fits-all model that prevails with transferred on-skin electronics. It's likely that the first implementation of biomedical electronic tattoos would include some combination of transferred and directly printed components.

Even with completely biocompatible materials, further complications such as allergic contact dermatitis (ACD) may arise from frequent use of a patch in intimate contact with the skin. Along with increased discomfort from skin irritation, frequent exposure to a specific allergen could lead to skin sensitization, which is an immunological response[101]. The T cell mediated inflammatory response could potentially skew the results, or cause complete failure, of the intended sensing capabilities that prompted the use of the electronic tattoo in the first place due to biofouling, as occurs with implantable glucose sensors for diabetes patients[102]. Thus, considerable research must be performed on large populations to assess the viability and general safety of the extended use of electronic tattoos for theragnostic purposes.

Conclusion and Outlook

Significant work has recently been performed to develop the three systems required for transdermal theragnostics – supporting electronics, diagnostic systems, and therapeutic delivery. Advancements in support electronics allow for comfortable use through stretchable electronic materials and engineering design developments; yet, more work is required to enhance the performance of stretchable support electronics to a level commensurate with the rigid silicon-based devices currently on the market. Diagnostic systems, especially the monitoring of analytes in sweat, have garnered significant interest recently, and monumental advancements in detection breadth and sensitivity have been achieved in both chemical and physical sensing. However, improvements in reproducibility and degradation resistance still require focused development to improve accuracy and duration, two metrics that must be improved in future transdermal sensing devices. Finally, therapeutic delivery, when used in tandem with diagnostic systems and facilitated by support electronics, can seamlessly maintain homeostasis through targeted and automated transdermal, iontophoretic drug delivery; however, to realize these advancements, the power requirements of iontophoresis must be reduced to increase the safety of these devices.

In order to fabricate these on-skin devices, two separate methods can be used: the devices can be fabricated on a disposable substrate and transferred to the skin or the devices can be printed directly onto the skin. Transfer deposition allows for a broader range of fabrication methods, including traditional, cleanroom fabrication techniques; this could allow for high-performance devices given the materials choices available. However, transferring has the potential to introduce errors and cleanroom fabrication is costly, particularly for custom electronics. Direct printing alleviates this potential for error and offers a scalable, low-cost approach, but currently is limited in scope due to the small number of inks that are compatible with low-temperature deposition. In order to move towards direct printing, significant focus must be spent on the development of a wide array of inks compatible with direct deposition onto the skin.

Electronic tattoos have the potential to shift the paradigm of medical testing towards continuous monitoring, allowing for more rapid, potentially lifesaving, treatment in addition to a simplified cycle of care that eliminates much of the complexities involved with discrete point monitoring systems. This type of real-time monitoring is required for the incorporation of fast-acting and customized therapeutic systems that can, for instance, deliver a customized dose of target drugs in response to biological signals. While more developments are necessary, electronic tattoos have the potential to revolutionize the point-of-care landscape by incorporating a continuous and non-invasive feedback loop into theragnostics, decreasing the time to care and transforming long-term prognosis.

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