Supplementary Materials for

**Reliable, low-cost, fully integrated hydration sensors for monitoring and diagnosis of inflammatory skin diseases in any environment**

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**Fig. S1. Encapsulation Procedure.** Schematic diagram of (A) a bare glass slide. The same glass slide coated with (B) a poly(methyl)methacrylate (PMMA) release layer followed by (C) silicone gel, (D) A piece of pre-cut fabric adhered to the silicone gel via Van der Waals forces, and (E) an additional layer of tacky silicone gel. (F) UV treatment of the resulting structure formed from steps A-E. (G) Schematic image of the SHS flexible printed circuit board coated on the bottom side with SiO$_2$ being placed onto the bottom layer structure. (H) An aluminum mold with silicone poured inside that forms (I) the silicone top shell when cured. (J) The resulting bottom layer structure with uncured silicone screen printed around the edges of the f-PCB. (K) The top shell adhered to the bottom layer by way of the uncured, screen-printed silicone. (L) The finished skin hydration sensor after curing the screen-printed silicone, cutting out the final structure out using a custom-made die, and peeling it off the glass slide. Photo Credit: Surabhi R. Madhvapathy, Northwestern University.
Fig. S2. Individual antenna performance and interference characteristics. (A) Schematic illustration of the NFC system. The magnetic field distributions around the Ant. 2 (B) with Ant. 1 and (C) without Ant. 1. (D) The inductance and Q factor versus frequency (top) and the S11 parameter of the matched ant. 1 (bottom). (E) The inductance and Q factor versus frequency (top) and the S11 parameter of the matched Ant. 2 (bottom). (F) The magnitude (top) and phase (bottom) of the impedance for the ant. 2 with and without Ant. 1. (G) Comparison of a fully wired data acquisition system (with a current source and digital multimeter) and the wireless SHS platform on two standard materials with known $k$ (Sylgard 184, $k = 0.2$ W/m-K, Sylgard 170, $k = 0.4$ W/m-K). In this case, the width of copper interconnects was 25 µm instead of the 60 µm width used throughout the rest of this work, leading to larger sensitivity relative to the other sensors. The difference in width (25 µm) resulted from in-house fabrication capabilities compared to all other devices (60 µm) which were outsourced to an external vendor. (H) Variation in temperature vs, ADC result of the SHS resulting in variations from the thermistor resistance. The minimum, maximum, and typical resistance tolerances are derived from the thermistor datasheet. (I) Variations in the temperature vs. ADC result of the SHS resulting in small variations in the rectified voltage output from the microcontroller.
Fig. S3. Measurements of ΔT on curved surfaces. (A) Schematic diagram of a hemisphere of Sylgard 184 with radius of curvature ρ. (B) Measurements of ΔT as a function of time on flat Sylgard 184, followed by curved (ρ = 1 cm) Sylgard 184, followed by flat Sylgard 184 once again.
Fig. S4. Factors that influence device sensitivity. (A) Influence of measurement power on $\Delta T$ at $t = 13$ s of measurement time for different $q$ on two samples of PDMS with different $k$ (Sylgard 184 ($k = 0.2$ W/m-K) and Sylgard 170 ($k = 0.4$ W/m-K)). The dotted line indicates a linear fit for the measured points shown as symbols. $R^2$ is provided in the figure. (B) $\Delta T$ measured at $t = 13$ s and inversely determined water content (blue) from a mixture of different volume percentages of water in vegetable glycerin (measured $k_{\text{glycerin}} = 0.285$ W/m-K and $\alpha_{\text{glycerin}} = 0.093$ mm$^2$/s). The mixture of vegetable glycerin and water served as a benchtop model for the micromechanics model to determine $\varphi$. (C) Influence of copper trace width on the transient temperature response of $\Delta T$ for a mixture of water ($k = 0.6$ W/m-K) and vegetable glycerin ($k = 0.285$ W/m-K) as a function of water content ($\varphi$) at a measurement time of $t = 13$ s and thermal power $q = 10$ mW/mm$^2$. 
through the heater. (D) $\Delta T$ at $t = 13$ s as a function of $\varphi$ for the water-glycerin mixture with varying silicone gel adhesive thickness.
Fig. S5. Difference in sensitivity between a separated heater – sensor design and single heater/sensor structure. (A) Analytical solution for a simplified model. (B) FEA based on the actual designs.
Fig. S6. Measurement Depth. (A) $\Delta T$ vs. $t$ for bilayer structures of Sylgard 184 ($k = 0.2$ W/m-K) of different thickness $h$ on 12 mm thick (bulk) Sylgard 170 ($k = 0.4$ W/m-K). (B) $\Delta T$ at $t = 13$ s for different $h$ of S184. (C) Heat profile in skin generated by the heater at different time $t$ for $\alpha = 0.15$ mm$^2$/s.
Fig. S7. Skin thermal properties vs. water content as determined from the micromechanics model.

(A) thermal conductivity. (B) thermal diffusivity.

\[ k_w = 0.60 \text{ W/(m-K)}, \quad \sigma_w = 0.14 \text{ mm}^2/\text{s}, \]
\[ k_{dry} = 0.20 \text{ W/(m-K)}, \quad \sigma_{dry} = 0.15 \text{ mm}^2/\text{s} \]
Fig. S8. Relationship of $\Delta T$ vs. $\varphi_E$ and $\varphi_D$ for a thick epidermis. (A) short time ($t = 2$ s). (B) long time ($t = 13$ s).
Fig. S9. Error in the determined water content due to error in measurements of \( \Delta T \). (A), (B) error in \( \varphi_E \) and \( \varphi_D \) vs. relative error in temperature for two water contents. (C) The maximum and average error for \( \varphi_E \) and \( \varphi_D \) in the range 5\%–95\% with 3\% relative error in temperature.
Fig. S10. FEA curve fits of experimental $\Delta T$ vs. $t$ data for healthy/normal subjects. (A–F) Subject 1 (female). (G–L) Subject 14 (male). RMS error appears above each graph.
Fig. S11. $T_0$ and ScH data corresponding to the data in Fig. 4. (A-H) respectively.
Fig. S12. Remaining lesions. (A-E) Photographs, $\varphi$, $T_0$, and ScH for the remaining atopic dermatitis lesions not displayed in Fig. 4. (F-H) Photographs, $\varphi$, $T_0$, and ScH for the remaining psoriasis lesions not displayed in Fig. 5. (I-J) Photographs, $\varphi$, $T_0$, and ScH for two lesions on a patient diagnosed with rosacea on both cheeks. ScH and $T_0$ data appear as black circles and red squares, respectively. Photo Credit: Michael Zhang, Vanderbilt University, and Surabhi R. Madhvapathy, Northwestern University.
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Fig. S15. $T_0$ and ScH data corresponding to the data in Fig. 5. (A-D) Correspond to the data in Fig 5A-D and (E-F) correspond to Fig. 5H-K. ScH and $T_0$ data appear as black circles and red squares, respectively.
Fig. S16. TEWL data for all lesions and non-lesional areas. (A-H) correspond to the data in Fig. 4A-H, respectively. (I-P) correspond to the data in Fig. 5A-H, respectively, and (Q-Z) correspond to the data in Fig. S12A-J respectively.
Fig. S17. Moisturizer treatment for an additional atopic dermatitis patient.
Fig. S18. Schematic illustration of the FEA model.
Fig. S19. Influence of Environmental Temperature on Sensor Response. Before heating, the steady-state temperature, T of the device is 35 °C, which is close to body temperature. The convective heat transfer coefficient between the outer surface of the encapsulation and the environment is 10 W/(m²-K). Air has a very narrow range of thermal conductivity (~0.024 – 0.027 W/m-K) for a wide range of outdoor temperature conditions (0 – 40 °C) and the relative humidity levels (0 – 100%) (32).
| COMPONENT  | QUANTITY PER SENSOR | DESCRIPTION                  | MANUFACTURER PART NUMBER |
|------------|---------------------|-------------------------------|--------------------------|
| C1         | 2                   | CAP CER 10000PF 10V X7R 0201  | GRM033R71A103KA01D       |
| C2         | 5                   | CAP CER 0.1UF 16V X75 0201    | GRM033C71C104KE14D       |
| C3         | 2                   | CAP CER 2.2UF 10V X5R 0201    | GRM033R61A225ME47D       |
| C4         | 1                   | CAP CER 5.1PF 50V COG/NPO 0201| GRM033SC1H5R18A01D       |
| C5         | 1                   | CAP CER 4.7UF 6.3V X5R 0201   | GRM035R60J475ME15D       |
| C6         | 1                   | CAP CER 11UF 10V X5R 0201     | GRM033R61A105ME15D       |
| C7         | 1                   | CAP CER 10UF 25V X5R 0603     | GRM188R61E106MA73D       |
| C8         | 1                   | CAP CER 27PF 50V COG/NPO 0201 | GRM033SC1H770JA01D       |
| R1         | 2                   | RES SMD 0 OHM JUMPER 1/20W 0201| ERJ-1GN0R00C             |
| R2         | 3                   | RES 10K OHM 1% 1/20W 0201     | RMCF0201FT10K0            |
| R3         | 1                   | RES SMD 10.7K OHM 1% 1/20W 0201| CRCW020110K7FKED         |
| R4         | 1                   | RES SMD 45.3K OHM 1% 1/20W 0201| RO201FR-0745K3L          |
| R5         | 2                   | RES SMD 680 OHM 0.5% 1/20W 0201| RR0306P-681-0            |
| Thermistor | 1                   | THERMISTOR NTC 10KOHM 3380K 0201| NTG063JF03FTB          |
| Schottky Diode | 4               | DIODE SCHOTTKY 30V 200MA 0402 | CD8QRO230R               |
| RF μC      | 1                   | IC RFID TRANSP 13.56MHZ 24VQFN | RF430FRL152HCRGER        |
| Inst. Amp. | 1                   | IC INST AMP 1 CIRCUIT 85ON    | INA333AIDRGR            |
| Voltage Regulator | 1               | IC REG LINEAR 3.3V 150MA 6SON | TPS70933DVR             |

Table T1. Bill of Materials.
| Location                  | Male (µm) | Female (µm) |
|---------------------------|-----------|-------------|
| Forearm & Wrist           | 67.8      | 80.3        |
| Forehead & fossa          | 95.9      | 90.4        |
| Cheek                     | 115.4     | 85.0        |
| Shin & Leg & Knee         | 100.6     | 78.3        |
| Calf                      | 124.4     | 116.2       |
| Heel                      | 792.8     | 478.1       |
| Buttock                   | 147.8     | N.A.        |
| Hand & Thumb              | 246.8     | N.A.        |
| Elbow                     | 112.7     | 97.1        |
| Back                      | 88.1      | 59.6        |
| Palm                      | N.A.      | 647.4       |
| Shoulder                  | 101.2     | N.A.        |
| Stomach                   | N.A.      | 79.9        |

Table T2 Thickness of the epidermis across various body locations (14). For locations with epidermal thickness not explicitly stated in Ref. 14 (wrist, leg/knee, hand/thumb, elbow, shoulder, stomach), computations of hydration levels utilized the epidermal thickness of an adjacent location. N.A. indicates no test performed on the gender/location.
| Subject | Sex | Age | Race/Ethnicity |
|---------|-----|-----|---------------|
| 1       | F   | 24  | Asian         |
| 2       | F   | 30  | White         |
| 3       | F   | 19  | Asian         |
| 4       | M   | 30  | Asian         |
| 5       | F   | 20  | White         |
| 6       | F   | 20  | Asian         |
| 7       | F   | 19  | White         |
| 8       | M   | 24  | Asian         |
| 9       | F   | 19  | White         |
| 10      | M   | 24  | Asian         |
| 11      | F   | 19  | Asian         |
| 12      | M   | 24  | Asian         |
| 13      | F   | 21  | White         |
| 14      | M   | 25  | White         |
| 15      | F   | 20  | White         |
| 16      | M   | 20  | White         |
| 17      | M   | 20  | Asian         |

Table T3 Demographics of Healthy/Normal Subjects
| Subject | Panel(s)   | Diagnosis            | Sex | Age | Race/Ethnicity            |
|---------|-----------|----------------------|-----|-----|---------------------------|
| 18      | 4A        | Atopic Dermatitis    | F   | 55  | Black/African American    |
| 19      | 4B,C      | Atopic Dermatitis    | M   | 20  | White/Asian               |
| 20      | 4D        | Atopic Dermatitis    | M   | 19  | Asian                     |
| 21      | 4E        | Atopic Dermatitis    | F   | 54  | Asian                     |
| 22      | 4F-H      | Atopic Dermatitis    | M   | 52  | Asian                     |
| 23      | 5A, S12F,G| Psoriasis            | F   | 52  | White                     |
| 24      | 5B,C      | Psoriasis            | M   | 49  | White                     |
| 25      | 5D, S12H  | Psoriasis            | F   | 77  | American Indian           |
| 26      | 5H        | Urticaria            | F   | 48  | Black/African American    |
| 27      | 5I-K      | Urticaria            | F   | 37  | Asian                     |
| 28      | 6A-K, S12A-C| Atopic Dermatitis  | F   | 64  | White                     |
| 29      | Fig 5D,E  | Atopic Dermatitis    | M   | 48  | White                     |
| 30      | Fig S12I,J| Rosacea              | M   | 45  | Black/African American    |

Table T4 Demographics of Diseased Patients.
Supplementary Note 1: Instructions for encapsulation procedure.

1. Clean a glass slide with acetone, isopropyl alcohol, and blow dry with nitrogen.

2. Spin coat a layer of poly (methyl) methacrylate (495 PMMA A5, MicroChem Corp., USA) on the glass slide at 3000 rpm, and bake at 180 °C for 3 minutes.

3. Pour 75 % by weight of Ecoflex gel (Smooth-On, Inc., USA) and 25 % Ecoflex 00-30 (Smooth-On, Inc., USA) into a container. Then add 2 % by weight of light blue dye (Silc Pig, Smooth On, Inc, USA) to the container. Centrifuge at 2000 rpm for 30s.

4. Spin coat a layer of this silicone mixture onto the PMMA coated glass slide at 3000 rpm, and then let cure on a hotplate at 70 °C for 5 minutes.

5. Place a cut piece of fiberglass on top of the cured PDMS and apply light pressure to ensure robust Van der Waals adhesion.

6. Spin coat an additional layer of the silicone mixture on top of the fiberglass at 3000 rpm and let cure on a hotplate at 70 °C for 5 minutes.

7. Treat the surface of the bottom layer silicone with ultraviolet (UV) light to create reactive –OH groups on the surface of the silicone.

8. Sputter SiO₂ onto the back of the flexible printed circuit board (f-PCB) and place onto the cured silicone slide to allow a covalent dehydration reaction between the -OH groups on the surface of the silicone and the SiO₂.

9. Clean both halves of the aluminum top shell mold with acetone, isopropyl alcohol, and blow dry with nitrogen.

10. Pour Ecoflex 00-30 into a container and add 2 % by weight of light blue dye. Centrifuge at 2000 rpm for 30s.

11. Pour Ecoflex 00-30 into the concave mold and put both parts of the mold together. Cure in hot press (Carver Press, Carver Inc., USA) at 250 °C and 1000 lbs for 1.5 minutes.

12. Cut out the cured top shell to the proper shape using the die cutter.
13. Apply Ecoflex 00-30 to the edges of the f-PCB and place the top shell on top. Let cure on a hotplate at 70 °C for 10 minutes.

14. Cut out the final sensor using the die cutter and peel off the glass slide.

**Supplementary Note 2: A simplified, analytical model**

A simplified model is established to predict the effect of some key design parameters. As shown in Fig. S4A, the model consists of a disk-shaped heater (radius \(R\), heating power \(q\) per unit area, total heating power \(Q = \pi R^2 q\) negligible thickness) on a semi-infinite, homogenous skin (thermal conductivity \(k_{\text{skin}}\) and thermal diffusivity \(\alpha_{\text{skin}}\)). A sensor with negligible size is placed right beside the heater (at \(r = R\) in the polar coordinate system). The temperature change in the sensor is (11)

\[
\Delta T_{\text{sensor}} = \frac{qR}{k_{\text{skin}}} \int_0^{\infty} \left[ J_0 (x) J_1 (x) \operatorname{erfc} \left( -x \sqrt{\frac{1}{2} \alpha_{\text{skin}} R^2} \right) \right] \frac{dx}{x}, \tag{S1}
\]

where \(J_0 (x)\) and \(J_1 (x)\) are the Bessel functions of the first kind with zero- and first-orders, respectively, and \(\operatorname{erfc}(x)\) is the complementary error function. Combined with the micro-mechanics model Eq. (1) and Eq. (2), \(\Delta T_{\text{sensor}}\) can be related to the skin water content \(\phi_{\text{skin}}\). In some previous works (11,12), the heater itself serves as the sensor such as that the average temperature in heater is the sensor temperature, which is

\[
\Delta T_{\text{heater}} = \frac{2qR}{k_{\text{skin}}} \int_0^{\infty} \left[ J_1 (x) \right]^2 \operatorname{erf} \left( x \sqrt{\frac{1}{2} \alpha_{\text{skin}} R^2} \right) \frac{dx}{x^2}. \tag{S2}
\]

Referring the design with the sensor separate from the heater as design 1 and the one with sensor/heater being the same as design 2, the simplified model shows that the sensitivity of temperature change to skin water content of design 1 is \(~30\%\) smaller than that of design 2 (Fig. S4A).

**Supplementary Note 3: Determining water content from experimental measurements of \(\Delta T\)**
To determine the water content $\varphi_E$ (epidermis) and $\varphi_D$ (dermis) from an experimental curve of temperature change $\Delta T$ vs. time $t$, $\varphi_E$ and $\varphi_D$ are extracted through minimization of the quantity below

$$\frac{1}{t_{total}} \int_0^{t_{total}} \left( \Delta T (t) - \Delta \hat{T} (t; \varphi_E, \varphi_D) \right)^2 dt,$$

where $t_{total}$ is the total heating time, $\Delta \hat{T} (t)$ is the temperature predicted by FEA and micro-mechanics model, and $\Delta T(t)$ is the experimental measurement.

**Supplementary Note 4: Error analysis**

*Error in the determined $\varphi_E$ and $\varphi_D$ from error in temperature measurement*

Given a curve of $\Delta T$ vs. $t$, $\varphi_E$ and $\varphi_D$ can be determined by the fitting method shown in Supplementary Note 3. Adding an error to the temperature change such that $\Delta T$ becomes $\Delta T(1+\delta)$ and performing the fitting again, the differences between the fitted water contents are the errors arising from the relative error in temperature measurement $\delta$.

*Error in the determined $\varphi_E$ and $\varphi_D$ from error in epidermis thickness*

Epidermis thickness has a small effect on the relationship of $\Delta T$ vs. $\varphi_E$ and $\varphi_D$. For a typical epidermis thickness $h = 100 \, \mu m$, fitting is performed to obtain $\varphi_E$ and $\varphi_D$ from the experimental curve of $\Delta T$ vs. $t$. Changing the epidermis thickness by $\pm 20\%$ and performing the fitting again for the same experimental curve, the differences between the fitted water contents are the errors arising from the error in epidermis thickness. The average errors for $\varphi_E$ and $\varphi_D$ ranging from $5\%$ to $95\%$ are $2.9\%$ for epidermis and $1.9\%$ for dermis (for $20\%$ error in epidermis thickness).

**Supplementary Note 5: Conversion of ADC result to Temperature**

The relationship between the thermistor resistance $R$ and temperature $T$ derived from the vendor datasheet is:
\[ R = -\left( \frac{1}{1.52 \times 10^{-4}} \right) \log \left( \frac{T - 7.42433}{79.54344} \right) \]

Referring to the circuit schematic in Fig. 2A, the output voltage for the instrumentation amplifier is:

\[ V_{out} = g \times V_{DD} \times \left( \frac{R_2}{R_1 + R} - \frac{R}{R_3 + R} \right) \]

where \( R_1 = R_2 = 10 \, k\Omega \), \( R_3 = 10.7 \, k\Omega \), and \( V_{DD} = 2.1 \, V \). and \( g \) is the amplifier gain given by

\[ g = 1 + \frac{100k\Omega}{R_g} \]

\( R_g = 45.3 \, k\Omega \) (gain resistor). \( V_{out} \) is converted to a 10-bit digital output by the \( \mu \)C ADC which has an input range of 0 – 0.9V. Thus

\[ ADC_{bits} = V_{out} \times \frac{2^{10}}{0.9 \, V} - 1 \]

As given in the datasheet for the \( \mu \)C.
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