Claims

1. An interstitial-fluid cytokine sensor module (FIGS. 5-1 to 5-3) for continuous measurement of interleukin-6 (IL-6), comprising:

   a) a flexible polyimide substrate having conductive traces that terminate in a hot-swap zero-insertion-force (ZIF) tail (FIG. 5-8);

   b) at least one gold working electrode, a counter electrode, and an Ag/AgCl reference electrode micro-patterned on the substrate (FIG. 5-2);

   c) a monolayer of IL-6-specific thiolated aptamers immobilized on the working electrode and tagged with an electro-active reporter;

   d) a permeable, anti-fouling hydrogel layer overlying the electrodes (FIG. 5-2);

   e) a dissolvable microneedle array that penetrates the stratum corneum, dissolves, and leaves microchannels to convey interstitial fluid to the hydrogel-covered electrodes (FIG. 5-3);

   f) non-volatile memory storing calibration coefficients, a unique identifier, wear-timer start value, and dose-ceiling data (FIG. 5-11); and

   g) circuitry configured to perform periodic square-wave voltammetry, apply the calibration coefficients, and communicate IL-6 concentration over a multi-drop I²C sensor bus,

   wherein the module is single-use, automatically disables after 24 hours of elapsed wear-time, and is adapted for plug-and-play operation with a closed-loop infusion controller.

2. The module of claim 1, wherein the microneedles comprise a hyaluronic-acid/carboxymethyl-cellulose matrix that dissolves within ten minutes to form open channels less than 40 µm wide.

3. The module of claim 1, further comprising a second, non-binding aptamer reference electrode and on-board logic that subtracts the reference signal from the working-electrode signal to cancel common-mode drift (FIG. 5-5).

4. The module of claim 3, wherein a deviation greater than 10 percent between the two IL-6 channels for more than three consecutive measurements triggers a sensor-fault flag in the memory map.

5. The module of claim 1, wherein the memory map reserves address 0x00–0x1F for calibration factors, 0x20–0x3F for sensor wear-timer data, 0x40–0x6F for manufacturing and lot information, and 0x70–0x7F for checksum values (FIG. 5-11).

6. The module of claim 1, wherein the circuitry is configured to deliver IL-6 concentration values at least once per minute with a limit of detection of 1 pg mL^{-1} and a linear dynamic range extending to 10 ng mL^{-1} (FIG. 5-6).

7. The module of claim 1, wherein a transient ±50 mV square-wave interrogation lasting less than one second produces a measurable redox-current change proportional to aptamer binding.

8. The module of claim 1, wherein the module's firmware enforces a hard power-down when the wear-timer reaches 24 hours, and sets a "module expired" flag that prevents further data transmission (FIG. 5-10).

9. The module of claim 1, wherein the ZIF tail comprises individual conductors for I^2C SCL, I^2C SDA, VDD, VBUS, GND, TXD, RXD, and a general-purpose interrupt line (FIG. 5-8).

10. The module of claim 1, wherein the hydrogel layer is a cross-linked poly(ethylene glycol) diacrylate film between 25 µm and 75 µm thick with pore diameters under 200 nm.

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11. A closed-loop immunomodulation system (FIG. 5-9) comprising:

    a) the IL-6 sensor module of claim 1;

    b) a controller in data communication with the sensor module over the sensor bus; and

    c) an infusion pump containing an anti-IL-6 biologic drug,

    wherein the controller is programmed to activate the pump when measured IL-6 concentration exceeds a configurable threshold and to suspend the pump when IL-6 falls

below the threshold.

12. The system of claim 11, wherein the controller increases the biologic-drug dose proportionally to the deviation of IL-6 from said threshold.

13. The system of claim 11, wherein the controller aborts pump activation if the sensor module indicates a drift or fault state on the safety ladder (FIG. 5-10).

14. The system of claim 11, further comprising at least one additional therapy-control loop that is automatically paused while IL-6 exceeds the threshold.

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15. A method of continuously sensing IL-6 in a human subject, comprising:

a) applying the sensor module of claim 1 to an arm of the subject;

b) allowing the microneedle array to dissolve, thereby establishing fluidic contact between interstitial fluid and the aptamer-covered electrodes;

c) interrogating the electrodes by square-wave voltammetry once per minute;

d) computing IL-6 concentration using calibration data stored in the module memory;

e) transmitting the computed IL-6 value over the sensor bus to a bedside controller; and

f) after 24 hours of cumulative wear, deactivating the module and prompting replacement.

16. The method of claim 15, further comprising subtracting a non-binding-aptamer reference signal from the working-electrode signal to correct for baseline drift.

17. The method of claim 15, wherein step (e) further comprises storing each IL-6 value with a timestamp in an electronic patient record.

18. The method of claim 15, wherein the controller compares the IL-6 value to a predetermined cytokine-storm threshold and administers an anti-IL-6 monoclonal antibody infusion when the threshold is exceeded.

19. The method of claim 18, wherein the infusion rate is reduced gradually as IL-6 concentration decreases toward the threshold.

20. The method of claim 15, wherein a checksum in the module memory is verified before step (a) to authenticate the module.

End of claims