Interface-Stabilized Fiber Sensor for Real-Time Monitoring of Amniotic Fluid during Pregnancy

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Abstract: Diseases in pregnancy endanger millions of fetuses worldwide every year. The onset of these diseases can be early warned by the dynamic abnormalities of biochemicals in amniotic fluid, thus requiring real-time monitoring. However, when continuously penetrated by detection devices, the amnion is prone to loss of robustness and rupture, which is difficult to regenerate. Here, we present an interface-stabilized fiber sensor for real-time monitoring of biochemical dynamics in amniotic fluid during pregnancy. The sensor is seamlessly integrated into the amnion through tissue adhesion, amniotic regeneration and uniform stress distribution, posing no risk to the amniotic fluid environment. The sensor demonstrates a response performance of less than 0.3% fluctuation under complex dynamic conditions and an accuracy of more than 98% from the second to the third trimester. By applying it to early warning of diseases such as intrauterine hypoxia, intrauterine infection, and fetal growth restriction, fetal survival increases to 95% with timely intervention.

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1. Introduction

The incidence and prevalence of diseases in pregnancy are worrying worldwide, threatening the health of fetus. More than 20,000,000 high-risk pregnancies and 2,600,000 fetal deaths occur worldwide each year.[1-2] Among them, the incidence of intrauterine hypoxia, intrauterine infection and maternal-fetal blood type incompatibility were 38.5%, 10% and 25%, respectively,[3-4] which can be early warned by the abnormalities of biochemicals in the amniotic fluid. For example, lactate upregulation and proton accumulation in the amniotic fluid are closely related to intrauterine hypoxia,[5] while glucose decrease is found in intrauterine infection.[6] Other biochemicals, including nitric oxide, uric acid and bilirubin in the amniotic fluid, assess fetal development.[7] Therefore, if real-time monitoring of biochemicals in amniotic fluid is possible during pregnancy, it would be feasible to intervene promptly and prevent adverse outcomes at the onset of these diseases.

B-ultrasound imaging and amniocentesis are currently used clinically for amniotic fluid assessment.[8-9] B-ultrasound imaging provides information related to amniotic fluid volume and fetal morphology but is incapable of sensing biochemicals directly.[10-13] Amniocentesis can analyze biochemicals in amniotic fluid extracted with the puncture needle.[14-15] However, the biochemical information obtained from the sampling point by amniocentesis is not real-time. Attempting to perform multiple amniocentesis procedures for real-time monitoring leads to amnion rupture, bloody amniotic fluid and fetal anomalies, increasing the risk of miscarriage.[16-19] To the best of our knowledge, no technology is available for real-time monitoring of the biochemical dynamics of amniotic fluid during pregnancy.

The major obstacle to real-time monitoring of amniotic fluid is attributed to the peculiarities of the amnion. During fetal growth, the amnion acts as a protective shield with antimicrobial, antifibrosis, and anti-inflammatory properties.[20-21] However, the amnion with a 20–50 μm thickness tends to lose its robustness when continuously penetrated by a detecting device. Specifically, a force as low as ~0.28 N under deformation causes rupture of the amnion. Besides, compared with other tissues, the amnion contains fewer immune cells and stress repair factors, resulting in poor regenerative capacity.[21] Moreover, stress concentration resulting from dynamic deformation of the amnion leads to increased expression of matrix metalloproteinases and extracellular matrix degradation, which in turn
exacerbates amnion rupture. Therefore, to achieve real-time monitoring of amniotic fluid, it is crucial to stabilize the device-amnion interface and thereby maintain amniotic fluid homeostasis.

Here, we report an interface-stabilized electrochemical fiber sensor (IEFS) that is minimally invasively implanted into the uterus to enable real-time biochemical monitoring of amniotic fluid during pregnancy. The IEFS first seamlessly integrated into the amnion immediately via the adhesion after implantation. Subsequently, the IEFS released collagen in situ to promote cell aggregation. During gestation, the local stress distribution was uniform to prevent amnion rupture. Animal experiments showed that the gestation period of pregnant rats, survival rate and development of fetal rats, core tissues and organs were not significantly different from those of the control group after IEFS implantation, verifying the safety of both mother and fetus. Real-time data collected after implantation showed high sensitivity, selectivity, stability and accuracy of the IEFS. Upon abrupt diseases in pregnancy, the IEFS promptly monitors biochemical abnormalities in the amniotic fluid and provides an early warning, securing enough time for opportune and reasonable therapy (Figure 1a).
Figure 1. Interface-stabilized electrochemical fiber sensor (IEFS) for in situ amniotic fluid analysis during pregnancy. a) Schematic illustration of the IEFS implanted in the uterus for real-time monitoring of biochemical signals during pregnancy. The signals monitored by the sensor were wirelessly transmitted through a flexible chip attached to the skin. b) Schematic illustration of the structure of IEFS that consists of a multi-ply sensing fibers core (composed of the respective sensing fibers and reference electrodes) and...
restorative gel sheath. c) Photograph of the skin surface of a pregnant rat after implanted with an IEFS. Scale bar, 1 mm.

2. Results and Discussion

The IEFS consists of a restorative gel sheath and a multi-ply fibers core composed of the respective sensing fibers and reference fibers. (Figure 1b). The sensing fiber was prepared by depositing sensing functional materials onto a carbon nanotube (CNT) fiber electrode (Figure S1, Supporting Information, details are provided in Experimental Section). Here, the CNT fiber electrode provides both remarkable electrical and mechanical properties with conductivity up to $1 \times 10^4$ S·cm$^{-1}$ and bending stiffness down to $1 \times 10^{-8}$ nN·m$^2$. The hierarchically aligned structure gives the CNT fiber high specific strength and electrical conductivity, and a large number of hierarchical gaps produce high degrees of freedom and thus good flexibility. The reference fiber was prepared by depositing Ag/AgCl on CNT fiber and then coating with polyvinyl butyral. For each sensing function, a sensing fiber was used as the working electrode, while an Ag/AgCl fiber was used as the reference electrode, forming a two-electrode system. The sensing fibers and reference electrodes were coated with polydimethylsiloxane as an encapsulation layer to ensure stable signals and prevent current crosstalk. The sensing fibers with different functions were then twisted to form the multi-ply fibers core. The restorative gel was prepared by loading Type I collagen onto silk fibroin, which was coated onto the twisted multi-ply fibers core to obtain the IEFS (Figure S2, Supporting Information). Due to its one-dimensional configuration, the IEFS was easily implanted into the target tissue by injection positioned under B-ultrasound guidance, causing only a 0.4 mm wound (Figure S3, Supporting Information). The implanted IEFS morphologically resembled hairs (Figure 1c).

After implantation, IEFS seamlessly integrated into the amnion through gel adhesion, restorative cell growth and uniform stress distribution, forming a stable interface with the amnion (Figure 2a). The gel was uniformly distributed on the surface of the fiber core with a thickness of approximately 30 μm (Figure 2b), and type I collagen was evenly dispersed in the microporous structure of silk fibroin (Figure 2c and Figure S4, Supporting Information). The restorative gel expanded and sealed the wound within 15 minutes and then adhered seamlessly to the amnion (Figure 2d). The adhesion force reached 250 N·m$^{-1}$ with no significant decrease and no amniotic fluid leakage after implantation for 7 days.
Furthermore, the microporous structure of the gel remained intact and the weight of silk fibroin remained largely unchanged with no significant degradation. Under complex deformations, the IIFS prevented the wound from expanding by dissipating the internal stress around the hole. The fracture strength of the amnion was maintained after IIFS implantation, whereas the fracture strength after clinical puncture was reduced to 58.8% (Figure 2e).
Figure 2. Interface stability between implanted IEFS and amnion. a) Schematic illustration of the seamless integration of IEFS with the amnion to form a stable interface. b) Fluorescence micrograph of the IEFS composed of a sensing fibers core (black) and a restorative gel sheath (yellow). Scale bar, 100 μm. c) Fluorescence micrograph of the restorative gel composed of sericin (brown) and collagen (green). Scale bar, 10 μm. d) Changes in the expansion ratio and adhesion strength after implantation of IEFS. The expansion ratio is defined by the ratio of the diameter increment to the initial diameter of IEFS. n = 3. e) Stress-strain curves of the amnion before and after implantation of puncture needle and IEFS. The tensile rate was 10 mm·min⁻¹. f) The representative histograms show the E-cadherin in amnion tissue without and with IEFS implantation for 3 days. g) mRNA expression of α-SMA in amnion tissue without and with IEFS implantation.
implantation for 3 days. n = 4. ***P ≤ 0.001. h, i) Immuno-fluorescence staining for TGF-βi (red) and DAPI (blue) in the amnion after implantation of IEFS and IEFS without restorative gel for 3 days, respectively. Scale bar, 100 μm. n = 4. j) Comparison of the Young’s moduli and bending stiffness for amnion, IEFS and SUS304. k) The Stress simulation of the IEFS and SUS304 in amnion under bending conditions. l) mRNA expression of MMP-8 and MMP-9 in the amnion 3 days after IEFS and SUS304 implantation. n = 4. m) Immunofluorescence staining for Vimentin (Vim, red) and DAPI (blue) in the amnion after IEFS and SUS304 implantation for 3 days. Vim is responsible for maintaining the integrity of the cytoskeleton. The diameter of both SUS304 and IEFS is 100 μm. Scale bar, 200 μm. All data presented as mean ± s.d.

The IEFS promoted the conversion of amniotic epithelial cells into reparative amniotic mesenchymal cells through the release of collagen-I in the restorative gel (Figure S6, Supporting Information). Type I collagen accelerated the regeneration of the ruptured amnion, as verified by the upregulation of E-cadherin and α-smooth muscle actin (α-SMA) expression (Figure 2f–g and Figure S7, Supporting Information). Amniotic mesenchymal cells remodel amnion surroundings by secreting abundantly amnion proteins, including transforming growth factor β-induced protein ig-h3 (TGF-βi), which is a very distinctive amnion protein involved in the wound healing cascade. Immunofluorescence results revealed that the accumulation of TGF-βi increased at the implant sites after the IEFS implantation. The amniotic mesenchymal cells infiltrated around the IEFS, maintaining the overall integrity of the amnion (Figure 2h). As a comparison, the IEFS without restorative gel caused destruction of the amnion structure, resulting in a hole of about 45,000 μm² (Figure 2i). As strong evidence of the integrity of the amnion, the infection-related indicator of the IEFS group was similar to the non-implanted control group, by analysing the proinflammatory cytokines of Interleukin-6 (IL-6), IL-1β expression and the calculation of Colony-forming units in amniotic fluid (Figure S8, Supporting Information). In contrast, the levels of IL-6 and IL-1β in the gel-free group were 2.10-fold and 2.02-fold compared with the control group, respectively.

The IEFS exhibited a low Young’s modulus of 8 MPa and bending stiffness of 3×10⁻⁶ nN·m², which matched the mechanical properties of the amnion (Figure 2j). Theoretical simulation demonstrated that the local stress of stainless steel fiber (SUS304, the material of clinical puncture needle) on the amnion under dynamic deformation was 1236 Pa and that of IEFS was 127 Pa (Figure 2k). As a result, the expression of matrix metalloproteinase-8 (MMP-8) and MMP-9 for SUS304 implantation, which are indicators of local stress, were 2.14 and 2.20 times higher than that of the IEFS group, respectively (Figure 2l). The interstitial collagenase MMP degrades the extracellular matrix and alters the collagen structure, which further leads to amnion rupture. After the stainless steel fiber implantation, the
amnion rupture area was approximately 70,650 μm², while the IEFS produced no additional rupture area (Figure 2m).

Benefiting from the stabilized device-amnion interface, the biocompatibility of the IEFS in vivo was ensured. The device was co-cultured with various cells for 24 h, 48 h and 72 h. Calcein-AM/propidium iodide staining and cell counting Kit-8 assay indicated that the RAW 264.7, HUVEC, HACAT and C2C12 cells in the IEFS group had normal proliferation ability, and no significant difference from the control group (Figure S9, Supporting Information). Hematoxylin-eosin (H&E) staining and immunofluorescence analysis of integrin alpha m (CD11b) in the maternal uterus that no obvious inflammatory cell infiltration was identified after implantation of IEFS for 7 days (Figure 3a, b). Routine blood and biochemical tests were carried out to analyze the peripheral blood circulation. No significant differences from the control group were found after 7 days of IEFS implantation (Figure 3c, d). In addition, the H&E staining images of the major organs, including the heart, liver, spleen, lung, kidney, and ovary, were analogous to those of the control group (Figure S10a, Supporting Information).
Figure 3. Biocompatibility of the implanted IEFS. a) H&E staining images of the uterus without and with IEFS implantation for 1, 3 and 7 days. Scale bar, 50 μm, n = 3. b) Confocal microscopy images of the uterus without and with IEFS implantation for 1, 3 and 7 days. The nucleus is visualised in blue (DAPI) and CD11b is indicated in red. Scale bar, 50 μm. n = 3. c) Blood levels of aspartate aminotransferase (AST, U·L\(^{-1}\)), alanine aminotransferase (ALT, U·L\(^{-1}\)), urea nitrogen (UREA, mM), creatinine (CREA, μM) and total bile acid (TBA, μM) from pregnant rat without and with IEFS implantation for 1, 3 and 7 days. n = 3. d) Average counts of white blood cell (WBC, 10\(^9\)·L\(^{-1}\)), red blood cell (RBC, 10\(^9\)·L\(^{-1}\)), hematocrit (HCT, %), blood haemoglobin (HGB, g·L\(^{-1}\)) and platelet (PLT, 10\(^10\)·L\(^{-1}\)) from pregnant rat without and with IEFS implantation for 1, 3 and 7 days.
The effect of IEFS implantation on fetal growth was further evaluated. Brain and limb development of the fetus was verified by B-ultrasound imaging after implantation of IEFS for 7 days, and no significant difference was observed (Figure 3e, f). The gestational age and offspring survival rate of the pregnant rat with IEFS implantation were also similar to the control group (Figure 3g). The body weight of the fetus was recorded from postnatal day 1 to day 21. The IEFS group was consistent with the control group (Figure 3h). The H&E analysis of the brain and the open field test revealed that the brain development and the cognitive behavioral ability in the fetus at postnatal day 21 of the IEFS group remained consistent with the control group (Figure 3i–j). Furthermore, all the routine blood and biochemical indexes of the fetus at postnatal day 21 were within the normal reference range (Figure S10b, c, Supporting Information). Meanwhile, H&E staining images of the heart, liver, spleen, lung, and kidney of the fetus at postnatal day 21 were analyzed, and there were no abnormal cell morphology and structure (Figure S10d, Supporting Information).

The electrochemical sensing performance of the IEFS was then characterized, and the sensing principles are described in Figure S11a–d, Supporting Information. Biochemical substances in amniotic fluid during pregnancy show dynamic changes due to different physiological activities of the fetus (e.g., lactate, 8.0–10.0 mM; glucose, 0.5–2.0 mM; nitric oxide, 3.0–4.5 μM; pH, 7.1–7.4). [28-30] Appropriate response range and sensitivity are required for the IEFS. The current responses of IEFS to lactate, glucose, and nitric oxide were tested chronoamperometrically in 6–16 mM lactate solutions, 0–2.5 mM glucose solutions, and 0.1–5.0 μM nitric oxide solutions, respectively (Figure 4a–c). A linear relationship between current and analyte concentration was found with sensitivities of 4.68 μA·mM⁻¹ to lactate, 3.21 μA·mM⁻¹ to glucose, and 47 nA·μM⁻¹ to nitric oxide (Figure S11e–g, Supporting Information). The linear correlation of open-circuit potential with pH in the range of 7.0–8.0 was demonstrated with a sensitivity of 28 mV·pH⁻¹ (Figure 4d and Figure S11h, Supporting Information). These results showed that the response range and sensitivity of the IEFS were fully adequate to assess the dynamics of the corresponding biochemicals in the amniotic fluid during pregnancy. In addition,
all the sensing units showed repeatability with relative standard deviations of 4.3%, 5.6%, 7.8% and 5.1% for lactate, glucose, nitric oxide, and pH, respectively (Figure S11i–l, Supporting Information). The IEFS was retained in phosphate-buffered saline for 30 days, and the signal intensity remained stable throughout the continuous monitoring (Figure S12, Supporting Information).

**Figure 4.** Electrochemical sensing performance of the IEFS. a–c) Chrono-amperometric response of the IEFS to lactate, glucose, and nitric oxide (NO) in respective analyte solutions, respectively. d) Open-circuit potential response of the IEFS to pH in analyte solutions. e) The impedance magnitude changes of the lactate-sensing fiber after bending for 1000 cycles. f) SEM images of the lactate-sensing fiber after bending for 1000 cycles. Scale bar, 100 μm. g) Electrochemical sensing signals (lactate: 6 mM, glucose: 1 mM, NO: 3 μM, and pH: 7.2) measured using the IEFS in different simulating motion states: walking, shaking, sitting,
jumping, and stooping. \textit{h–k}) Comparison of \textit{ex-situ} analysis (including lactate, glucose, NO and pH) of amniotic fluid samples collected from pregnant rats using the clinical gold standard, with in vivo real-time analysis using IEFS. The arrows indicate the injection of saline solutions of lactate, glucose, nitric oxide and citric acid into the amniotic fluid of pregnant rats, respectively. \textit{i–o}) Accuracy of the IEFS to lactate, glucose, NO, and pH after implantation for different days within a gestation period of the pregnant rat. The accuracy is defined by the ratio of in vivo analysis data by IEFS to the \textit{ex-situ} data by clinical gold standard from collected amniotic fluid samples. All data presented as mean ± s.d. n = 4.

To avoid interference from various metabolites in the amniotic fluid, it is necessary to ensure the signal selectivity of IEFS. Various interfering substances were added to the target solution, and the changes in current or potential were recorded. The results showed that IEFS had excellent selectivity for other interfering substances (Figure S13, Supporting Information).

Besides, for continuous and stable monitoring, the interference of physical activity must be considered. The impedance over a specific frequency range was measured to assess the electrochemical stability of the sensor, as it reflects not only the internal structural changes of the electrodes but also the stability of the electrode-analyte interface. After 1,000 bending cycles, the impedance of each sensing fiber remained stable with a fluctuation of ±0.3% (Figure 4e and Figure S14a–c, Supporting Information). In addition, the morphology of the sensing fibers was identical after deformations (Figure 4f and Figure S14d, Supporting Information). The structural integrity is attributed to the flexibility of the CNT-based fibers and their inherent structural and electrical stability. The response signals showed no significant fluctuation during simulated walking, shaking, sitting, jumping and stooping (Figure 4g). These results demonstrated that the IEFS was electrochemically stable under physical activity and possibly amniotic fluid dynamics, thus meeting the challenging requirements for continuous and stable monitoring.

In vivo sensing performance was evaluated after implantation of IEFS into the amniotic fluid of pregnant rats. Real-time electrochemical data obtained separately from the IEFS showed a timely response to changes in analyte concentration and matched well with clinical gold standard in vitro breakpoint measurements (Figure 4h–k). As gestation progresses, the fetus in the amniotic fluid and the uterus gradually increase in size. The long-term fixation of IEFS in the amniotic fluid environment...
benefits from the strong adhesion between the restorative gel and tissue, and its electrochemical performance remains stable with less than 0.3% impedance fluctuation (Figure S15, Supporting Information). The long-term accuracy of the IEFS in vivo was then further evaluated. Real-time data collected from the implantable IEFS showed consistency with data from clinical discontinuous monitoring (>98% accuracy) in vitro, covering mid to late gestation in pregnant rats (Figure 4I–O).
Figure 5. AFEWS for early warning of diseases in pregnancy. a) Block diagram shows how the IIFS works in AFEWS. b) Photograph of a pregnant rat after implantation of the AFEWS. The implant position is indicated by a blue arrow. Scale bars, 3 cm. c) The glucose (top) and nitric oxide (NO, bottom) concentrations in amniotic fluid of rats under infection and fetal growth restriction recorded by AFEWS. d) The pH and lactate concentration in amniotic fluid of a rat under the hypoxic conditions and after treatment recorded by
AFEWS. e) The fetal rat’s survival rate of the pregnant rats under intrauterine hypoxia with or without warning from pregnancy to parturition. f, g) mRNA expressions of Erythropoietin (EPO) and erythropoietin receptor (EPOR) in the brain of fetal rats at postnatal 21 days under intrauterine hypoxia with or without warning; the ratio of EPO and EPOR mRNA expressions of the brain from fetal rats. Without AFEWS group hypoxia time was 1 hour. n = 4. h) Immunofluorescence staining for Neuronal nuclei (NeuN, red) and DAPI (blue) in the brain of fetal rats at postnatal 21 days under intrauterine hypoxia with or without warning. Without warning group hypoxia time was 1 hour. Scale bar, 50 μm. n = 4. All data presented as mean ± s.d. NS, no significant difference. * P ≤ 0.05, ** P ≤ 0.01, and ***P ≤ 0.001.

The amniotic fluid early warning system (AFEWS) was obtained by integrating the IEFS with a flexible wireless transmitter module for real-time monitoring of amniotic fluid biochemicals and early warning of diseases in pregnancy (Figure 5a). Specifically, the sensing end of IEFS was immersed in amniotic fluid, while the other end was connected to a flexible chip module on the skin. The detected biochemical information was converted into electrical signals by IEFS, and then collected and processed by the flexible chip, and wirelessly transmitted to mobile terminals such as mobile phones or laptops through the Bluetooth module, thus realizing real-time continuous monitoring of biochemicals (Figure S16, Supporting Information).

After AFEWS implantation, the pregnant rat was energetic and moved freely with no difference from the normal rat (Figure 5b and Figure S17, Supporting Information). Successive trends of biochemical substances in the amniotic fluid were observed from the mid-pregnancy to the late-pregnancy period by the AFEWS (Figure S18, Supporting Information), and the stability and safety was guaranteed (Figure S19 and S20, Supporting Information). Glucose in the amniotic fluid is characteristic for the diagnosis of intrauterine infection, which reflects an inflammatory condition caused by leukocyte infiltration. Using AFEWS (Figure 5c), we found that the glucose concentration dropped from 1.5 to 0.5 mM within 56 hours upon intrauterine infection, while the glucose concentration remained at 1.5 mM in the normal group. Moreover, nitric oxide in the amniotic fluid closely correlates with fetal growth. The concentration of nitric oxide dropped from 3.6 to 1.2 μM within 72 hours of fetal growth restriction, while the nitric oxide concentration remained at 3.6 μM in the normal group.

Furthermore, in intrauterine hypoxia, the accumulation of dissolved carbon dioxide leads to an acidity increase, followed by the production of lactate through anaerobic respiration. Lactate concentration above 7.2 mM indicates that the fetuses are at urgent risk. As shown in Figure 5d, real-time
monitoring data from the AFEWS revealed that the normal pH of amniotic fluid in pregnant rats is approximately 7.35, while the normal lactate concentration is ~5 mM. When intrauterine hypoxia occurred, the pH dropped rapidly from 7.4 to 6.7, while the lactate concentration increased from 5.2 to 7.2 mM within 10 minutes. After monitoring lactate concentration higher than 7.2 mM, the AFEWS issued an early warning, and relevant treatment measures were taken in time. After the intervention, the pH and lactate concentration in the amniotic fluid gradually returned to normal.

Under the conditions of early warning by the AFEWS, the final survival rate of fetal rats was 95%, approaching the level of unaffected fetal rats (Figure 5e). In contrast, in the absence of early warning, the survival rates of fetal rats decreased with the duration of hypoxia, which were 82.4%, 13.3%, 7.9% and 0 after 0.5, 1.0, 1.5 and 2.0 hours of hypoxia, respectively. After 1 hour of hypoxia, the erythropoietin and erythropoietin/Erythropoietin receptor ratio (reflected by relative mRNA expression) in the brains of the infant rats (postnatal 21 days) were significantly reduced compared to the AFEWS warning group, indicating significantly impaired brain development in the infant rats (Figure 5f, g). Neuronal nuclei are another indicator that reflects the maturity of a neuron. Immunofluorescence staining of neuronal nuclei in the brains of infant rats indicated that the level of mature neurons in the AFEWS warning group was higher than that without AFEWS and was close to that in the control group (Figure 5h). H&E staining also demonstrated similar results. The cortical and hippocampal neurons were different in size without AFEWS. The nucleus was shrunken and deformed, and some cells were lost. However, there was no significant difference in neurons in the AFEWS group compared to the control group (Figure S21, Supporting Information). Therefore, the AFEWS was effective in providing early warning of pregnancy diseases and improving the survival rate and development of fetal rats. As a complement to the clinical puncture needle technique (Table S1, Supporting Information), the sensor showed a greater advantage in early warning of sudden onset diseases, such as acute intrauterine hypoxia and neonatal sepsis, providing a valuable time window for timely intervention.

3. Conclusion

In summary, by designing an interface-stabilized fiber sensor, we demonstrate a strategy for the continuous, real-time and selective monitoring of a wide range of biomarkers in amniotic fluid during pregnancy. The difficulty that the amnion is prone to rupture when the sensing device penetrates continuously is successfully overcome, thus maintaining amniotic fluid homeostasis and ensuring maternal-fetal safety. The method is valuable for the early diagnosis of diseases in pregnancy and
understanding the biochemical dynamics of the amniotic fluid. Real-time monitoring of amniotic fluid and early warning of sudden abnormalities have been achieved in a close-loop diagnostic system, representing a qualitative advance in pregnancy testing methods. This method also shows advantages if reconfigured to continuously monitor other biomarkers in amniotic fluid for personalised prevention, diagnostic and therapeutic of a wide range of gestational diseases.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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An interface-stabilized electrochemical fiber sensor is designed for real-time monitoring of biochemical dynamics in amniotic fluid during pregnancy. The sensor seamlessly integrates into the amnion through tissue adhesion, amniotic regeneration and uniform stress distribution. The sensor demonstrates response performance with fluctuation of less than 0.3% under complex dynamic conditions and accuracy of more than 98% in pregnant rats.