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Dynamic Complex Emulsions as Amplifiers for On-Chip Photonic Cavity Enhanced Resonators

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Abstract

Despite the recent emergence of microcavity resonators as label-free biological and chemical sensors, practical applications still require simple and robust methods to impart chemical selectivity and reduce cost of fabrication. We introduce the use of hydrocarbon-in-fluorocarbon-in-water (HC/FC/W) double emulsions as a liquid top cladding that expands the versatility of optical resonators as chemical sensors. The all-liquid complex emulsions are tunable droplets that undergo dynamic and reversible morphological transformations in response to a change in the chemical environment (*e.g.*, exposure to targeted analytes). This chemical-morphological coupling drastically modifies the effective refractive index, allowing the complex emulsions to act as a chemical transducer and signal amplifier. We detect this large change in refractive index by tracking the shift of the enveloped resonant spectrum of a silicon nitride (Si₃N₄) racetrack resonator-based sensor, which correlates well with a change in the morphology of the complex droplets. This combination of soft materials (dynamic complex emulsions) and hard materials (on-chip resonators) provides a unique platform for liquid-phase, real-time, and continuous detection of chemicals and biomolecules, for miniaturized and remote, environmental, medical, and wearable sensing applications.

Graphical Abstract

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Supporting Information. The Supporting Information is available free of charge on the ACS Publications website. Experimental details, general materials, fabrication of complex emulsions, fabrication of optical resonators, measurement of optical shift

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Keywords

complex emulsions; photonic sensor; ring resonator cavity; chemical sensor; SiN photonics

Rapid and sensitive analysis of the composition and concentration of liquid samples is necessary for environmental monitoring, food safety, and biomedical applications.^{1–3} Traditional methods of measurement often require expensive equipment and dedicated laboratory space, hindering their practical uses in remote sites. Advances in chemical sensors have enabled robust and practical analytical tools for on-site detection and quantification of various chemical and biomolecular analytes.^{1,3} However, challenges remain in optimizing the performance—*i.e.*, selectivity, sensitivity, stability, and reproducibility—while maintaining portability and cost effectiveness. High selectivity and sensitivity often significantly increase the cost of fabrication. For example, immobilization of recognition units (*e.g.*, antibodies) onto solid-state surfaces requires extensive processes to minimize variability between samples and to prevent degradation.⁴ Thus, we have chosen to combine two sensing methods, dynamic complex emulsions and on-chip photonic cavity resonators, that complement one another. Specifically, we introduce low-cost complex liquid emulsions as a modular and selective recognition unit onto a sensitive optical resonator, to bypass issues arising from immobilization, improve reproducibility, and reduce cost of fabrication. This decoupling of recognition and transduction units may allow for parallel improvement of both components leading to a generalized universal sensor.

Complex emulsions are essential components in food, medicine, and functional nanoparticles.^{5,6} Recently, extensive development on the controlled fabrication of these complex emulsions using microfluidic techniques has led to various biomedical applications, including drug delivery,^{7–9} cell-encapsulations,¹⁰ artificial cells,^{11,12} and biochemical analysis.¹³ Of particular interest is the use of all-liquid complex emulsions, consisting of two or more immiscible liquids in a continuous medium, as responsive systems for biosensing applications. For example, we have shown that responsive double emulsions can dynamically alter their internal morphology¹⁴ in response to chemical and biomolecular analytes.^{15–19} These sensing applications relied solely on the coupling of the internal morphology of the complex droplets and their optical properties²⁰ leading to a detectable optical readout (*e.g.*, change in opacity^{15,16} or fluorescent emission^{17–19}). Briefly, the curvature of the internal interface (HC-FC interface) dictates the scattering of light passing through the emulsions.²⁰ That is, each droplet acts as a tunable lens. This optical transduction, while successful in certain applications, limits the generalization of the technique and introduces complications in the preparation of the samples due to the possibility of optical interference.^{16,19} Thus, an improved method of recognition and transduction, potentially “optics-free,” is necessary to realize a generalized sensor for chemical and biological analytes.

Optical resonators, or whispering gallery mode (WGM) resonators, are an emerging class of analytical tools that have found applications in biosensing,^{21,22} micro gas chromatography,²³ and aqueous-phase sensors.²⁴ They function by detecting the interactions between analytes and the evanescent wave emerging from the recirculating light confined within a microcavity.^{25–28} Specifically, this “leakage” of light from the microcavity interrogates the surrounding environment and alters its resonant frequency based on modification of its effective refractive index. Thus, this behavior allows optical resonators to use light as a probe without the requirement of a transparent analyte. Sensors based on photonic technology have relied on functionalization, or the physical or covalent solid-state immobilization of selectors onto the surface of the resonators to impart selectivity. However, such methods pose challenges when attempting to obtain reproducible devices with uniform and consistent sensing areas.²⁹ Additionally, the sensitivity of the device may be reduced if the binding of the analyte does not significantly change the transmission spectrum of the resonator.^{25–28} This limitation can be overcome by the use of a responsive cladding layer comprising complex emulsions.

We report a combination of dynamic complex emulsions and on-chip optical resonators as a unique platform for liquid-phase sensing of chemical analytes. The present method uses a silicon nitride (Si₃N₄)-based racetrack optical resonator cavity as the sensor to detect the change in the effective refractive index of the environment. Unlike the previously reported sensors that detect the interactions of the target analytes using immobilized, functionalized layer of selectors at the surface of the resonators, we leverage a modular sensing layer comprising complex emulsions that also simultaneously serves as the signal amplifier, Figure 1. Specifically, the transformation of a complex emulsion into different morphologies (double, Janus, and inverted) in response to the chemical environment determines the effective refractive index, enabling the specific detection of chemical analytes that would normally not induce changes in the refractive index. This change in the effective refractive

index can be measured reproducibly by tracking resonant wavelengths in the transmission spectra of the optical resonators.

EXPERIMENTAL DESIGN

Dynamic complex emulsions.

Our sensing approach relies on the dynamic transformation of the internal morphology of a layer of all-liquid complex emulsions upon changes in the chemical environment. These complex emulsions—comprising two immiscible oils, hydrocarbon (HC) and fluorocarbon (FC) oils—can be fabricated through a thermally induced phase separation to produce uniform composition of the two domains, Figure 2a–c.¹⁴ Briefly, the two oils are first heated above their upper critical temperature to form a single dispersed phase before emulsification in a surfactant solution through a microfluidic device. The choice of the surfactants in the continuous phase dictates the resulting morphology of the complex emulsions, Figure 2d. Specifically, the relative concentration (and/or the effectiveness) between HC-surfactant and FC-surfactant, which stabilize the HC/water (HC/W) and FC/water (FC/W) interfaces respectively, controls the balance of the interfacial tensions at the water interfaces, $\gamma_{\text{HC/W}}$ and $\gamma_{\text{FC/W}}$. When $\gamma_{\text{HC/W}} > \gamma_{\text{FC/W}}$, the FC/W interface is preferred leading to HC-in-FC-in-water (HC/FC/W) double droplets, and the inverse is necessary to attain FC-in-HC-in-water inverted morphology (FC/HC/W). Thus, adjusting this balance between the two interfacial tensions gives rise to the dynamic change in the morphology of the emulsions. Similarly, exposure to an analyte can affect the relative value of the interfacial tensions, producing morphological changes.

This unique chemical-morphological-optical coupling in complex emulsions has shown utility in sensing applications.^{15–19} Particularly, the change in transmissive or emissive properties of the emulsion changes as a function of physical morphology upon the interaction with chemical or biomolecular analytes. Because morphology of complex emulsions are controlled by interfacial tensions,¹⁴ a selective interaction between the analyte and a responsive surfactant can alter the interfacial tensions, providing the driving force for such transformations. Additionally, we have found that the complex emulsions are stable on the timescale of at least several weeks under normal conditions. That is, when they remain submerged in the surfactant solution at room temperature without aggressive mechanical stimulation, their overall size, dispersity, and composition remain constant. These previously reported techniques rely primarily on optical visualization through optical microscopy or detection of light intensity. Such a requirement limits generalization of the technique and introduces complications in the preparation of the samples due to the possibility of optical interference.^{16,19} An alternative way of probing complex emulsions without optical microscopy leverages the use of on-chip resonators to measure a change in the effective refractive index that corresponds directly to the droplet morphology. This method bypasses the need for optically transparent samples and is sensitive to the difference between the refractive indices of the HC and FC domains.

Design of on-chip resonators and photonic devices.

Whispering gallery mode (WGM) optical resonators—such as micro-disk, micro-ring, race-track, and other photonic cavity resonant structures—are receiving increased attention as methods for near-infrared (NIR)^{24,30} on-chip spectroscopy, which is the measurement of characteristic optical absorption and transmission spectra for gaseous and liquid analytes. We used a silicon nitride (Si₃N₄)-based micro-ring resonator cavity as the sensor to detect morphological changes in the complex emulsions, Figure 3. A tunable light source with a central emitting wavelength of 1550 nm was connected with a lens-tip optical fiber to couple input light into our device via edge coupling. The light mode in the straight waveguide interacts with the photonic cavity through the gap between the bus waveguide and the cavity loop. When the optical path length of the cavity loop is an integral multiple of the input light wavelength, the light is coupled into the resonator and circulates within the loop, enhancing light interaction with ambient particles, as expressed following equation:

$$\lambda_{\text{res}} = n_{\text{eff}} L_{\text{res}} / m \quad (1)$$

where λ_{res} is the resonance wavelength, n_{eff} is the effective refractive index which is altered upon sensing, L_{res} is the resonator length, and m is the integer related with the order of resonance mode. This resonance wavelength that is trapped within the cavity loop depends on the geometry of the resonators, the coupling efficient between the ring and the bus waveguide, and the surrounding environment or cladding which is directly related with the effective index. The detection outcome is based on the transmitted light signal from the photonic device after the light-particle interaction within the device where both attenuation and refractive index shift occur. Thus, the liquid-phase samples used in the photonic device do not require transparency, a key advantage over conventional measurements that rely on free-space optical transmission.^{16–19,29}

We chose resonators with a racetrack geometry to increase coupling length and coupling efficiency in this experiment compared to a micro-ring structure, while also relaxing the lithography tolerance requirements.²² The resonator geometry was designed and fabricated to be 50 ~m in radius (r) and coupling distance (L) of 50 ~m with a gap (g) of 1050 nm between the bus waveguide and the resonator, to achieve a measured critical coupling at near 1550 nm. The silicon nitride (Si₃N₄) waveguide fabricated from low pressure chemical vapor deposition (LPCVD) was designed for single-mode operation (TE). The waveguide loss was measured to be ~0.1 dB m⁻¹ and the quality factor of the resonator was ~10⁵. Transmitted light following the interaction of the Si₃N₄ sensor's evanescent wave with the environment is measured by the detector. A change in the effective refractive index, induced by the target analyte, causes a shift in the resonant peak and enables sensing of the analyte.²¹ However, a critical limit remains in the fact that most chemical analytes (at low concentrations) do not alter the refractive indices significantly. Thus, we chose the complex emulsions as the amplifier that can alter the refractive index sufficiently, enabling the detection of analytes.

Combination of complex emulsions and optical resonators as sensors.

We fabricated our sensors by depositing a monolayer of the prefabricated monodispersed complex emulsions on top of the optical resonators. Because the FC domain was chosen to have higher density than the HC, the complex emulsions self-assembled into a gravity-aligned hexagonally close-packed layer (Figure 2b). This self-alignment of the complex emulsions is highly reproducible and is crucial to the sensing scheme of our device. Additionally, we observed using side-view microscopy that the droplets remain spherical under our experimental conditions. As the on-chip resonator interacts with the surrounding media, the transmission spectra are affected by the effective refractive index. Characteristically, the resonant wavelength shifts toward a higher wavelength with the increase in the effective refractive index, and vice versa. In this scheme, the complex emulsions act as a thin layer of top cladding that can drastically change the effective refractive index in close proximity to the resonator. Specifically, in the double emulsion morphology (FC encapsulating HC, HC/FC/W), the refractive index of the cladding will be that of the FC ($n_{\text{FC}} = 1.30$). When driven toward Janus and inverted morphologies, the value of the effective refractive index will move closer to that of the HC ($n_{\text{HC}} = 1.50$). Notably, this range of the absolute change in the refractive index from $n \sim 1.3$ to ~ 1.5 is significantly larger than the effects arising from most chemical or biomolecular analyte interaction with the evanescent mode. We exploit this mode of signal transduction to enhance the sensitivity of the on-chip resonators.

Figure 3d demonstrates the experimental set-up where the dynamic complex emulsions are deposited as a modular cladding layer on top of the resonators. The analytes were introduced directly to the layer of complex emulsions that alters the morphology, leading to the change in the effective refractive index. As a proof-of-concept study, we chose the change in the balance of the hydrocarbon and fluorocarbon surfactants (SDS and Zonyl) to induce morphological change.

RESULTS AND DISCUSSION

Fabrication and characterization of the photonic resonators.

The photonic racetrack resonators were designed and fabricated in MIT Microsystems Technology Laboratories (MTL) cleanroom facility. Briefly, six-inch silicon wafers were first cleaned using standard methods and loaded into a tube furnace for 3 μm SiO_2 growth. Subsequently, we deposited a high-quality silicon nitride layer (Si_3N_4) of 400 nm using low pressure chemical vapor deposition (LPCVD). Photonic racetrack resonators were then patterned via photolithography and reactive ion dry etching techniques. Detailed procedures are provided in the Supporting Information. Figures 4a–d show optical and scanning electron micrographs of the racetrack resonators. We used finite element analysis to verify that the evanescent field from the optical resonators will interact with the complex emulsions. The first two transverse modes, transverse electric (TE) and transverse magnetic (TM), supported by the cavity waveguide are presented in Figure 4e–f. The confinement factor is defined as the mode intensity retained in the waveguide, which is 56% and 30% electric field intensity for TE and TM modes, respectively. This mode allows the field intensity of 26% and 36% in TE and TM modes respectively to be at the vicinity of the

waveguide for sensing the changes in the morphology and the effective refractive index of the complex emulsions. We note here that the waveguide design (*i.e.*, the waveguide dimensions) can be optimized to improve the sensing performance. To do so, the trade-off between the contributions of the waveguide confinement factor and the resonator quality factor must be evaluated. Specifically, the increase in the evanescent field that would amplify the light-particle interaction might reduce the resonator quality factor, diminishing the overall sensitivity. As a proof of concept, we chose the single-mode waveguide designed for TE mode operation because it offers a balance between the confinement factor and the quality factor.²⁴

We then measured the transmittance spectra of the photonic resonators using the optical vector analyzer (OVA), comprising a tunable laser and a detector from Luna technologies (Luna Innovations Incorporated). We edge-coupled the OVA using a lens-tip fiber to deliver light in and out of the resonator using an automatic alignment system. The laser has a tuning range from 1520 to 1600 nm, with a resolution of 0.5 pm. We obtained the spectra of the racetrack resonator with air cladding (prior to the addition of the complex emulsions) as a blank reference. The transmission spectra have a characteristic critical coupling as a result of the racetrack geometry. That is, the series of resonant wavelengths can be grouped together using the envelope-assisted method.³¹ And by observing the entire envelope, we can easily distinguish and track the shift in the critical coupling wavelength with higher resolution.³¹ Compared to the analysis that relies on tracking of individual resonant peaks, the analysis of enveloped resonant peaks reduces the probability of false-positives (*e.g.*, peak shifts resulting from temperature fluctuation) and allows the integration of facile signal processing units for miniaturized sensor packaging.

Coupling of transmission spectra and morphology of emulsions.

We validated the performance of our sensor comprising the racetrack resonator and a layer of monodispersed complex emulsions by measuring the transmission spectra as a function of the morphology of the emulsions. We chose to tune the emulsion morphology by adjusting the mass ratio between the HC-surfactant (SDS) and the FC-surfactant (Zonyl). Additionally, because these two surfactants do not directly alter the refractive index, this demonstration highlighted the effects arising solely from the change in the effective refractive index of the complex emulsions with the photon-particle interaction in the photonic device and suggests the generality of the sensors for other analytes. In pure Zonyl solution, the emulsions assume the morphology in which the FC domain is preferred over the HC domain, in such a way that the lower index FC domain ($n_{\text{FC}} = 1.3$) is proximate to the resonators. With the stepwise addition of HC-surfactant (SDS) into the continuous domain, the preferred domain gradually shifts from FC to HC, resulting in the transformation from double emulsions to Janus emulsions and ultimately to inverted emulsions. This transformation brings the higher index HC domain ($n_{\text{HC}} = 1.5$) closer to the resonator, increasing the effective refractive index proximate to the waveguide. We used the mass fraction of SDS (f_{SDS}) as a metric of droplet morphologies. Specifically, we obtained double emulsions (HC/FC/W) when $f_{\text{SDS}} = 0$ and inverted emulsion when f_{SDS} approaches 1. The observed morphologies at different values of f_{SDS} were confirmed using optical micrographs and were consistent with previous reports from our group

Figure 5a depicts representative transmission spectra obtained from our sensing device. The wavelengths of the resonant peaks depend on the effective refractive index of the top cladding. More importantly, we fit Lorentzian peaks over the series of resonant peaks to determine the enveloped critical coupling wavelength. With increasing f_{SDS} , we observed a shift in the critical coupling toward higher wavelength. Figure 5b shows the spectra obtained from the control experiments without complex emulsions. Here, the change in the surfactant ratio had no significant effect on the shift in the critical coupling resonant wavelength, Figure 5b inset. This result is expected because SDS does not change the refractive index of the aqueous solution significantly.

We then defined the value of the peak shift (λ_{env}) by the difference between the critical coupling at certain f_{SDS} and the critical coupling at $f_{\text{SDS}} = 0$. Figure 5c summarizes the peak shifts of the transmission spectra in TE mode as a function of f_{SDS} . We observed that the change in λ_{env} decreases at higher values of f_{SDS} and attributed this behavior to the minimal geometric variation of the complex emulsions at those morphologies. That is, the effective refractive index depends less on the morphological changes when f_{SDS} approaches 1. These shifts in the critical coupling were also verified by depositing complex emulsions that were fabricated in separate vials containing different values of f_{SDS} .

From the above results, we hypothesized that the sensing response of the complex droplets depends on the overall size of the emulsions. In our initial experiment, we chose the droplets to have smaller diameters (~ 30 nm) than the feature size of the racetrack resonators (50 nm radius). We expected that larger droplets will have less area in which they can influence the effective refractive index, as the volume between each droplet is then filled with the aqueous surfactant solution. Using the monodispersed complex emulsions with larger diameters (~ 100 nm), we observed an unreliable trend in the peak shift and attributed this behavior to the fact that the variation in effective refractive index may change drastically depending on the subtle movement of the larger droplets and the “dead space” filled by surfactant solutions. To test this hypothesis, we created a mixture of complex emulsions with two different diameters (30 and 100 nm) and deposited a monolayer on the racetrack resonators. The mixture of the larger and smaller emulsions self-assembled into a closed-pack layer such that the excluded areas created by larger droplets were occupied by the smaller droplets (Figure S2, supporting information). Using this layer, we then observed similar peak shifts as a function of f_{SDS} as observed in the case with only 30 nm complex emulsions. Furthermore, the quality factors of the cavity resonance were on the order of 10^5 and showed no significant distinctive variations with the change in the morphology of the emulsions. We suspected that the loss in the sensing scheme may depend more on the size of the emulsions and their packing behavior.

Finite difference time domain (FDTD) simulation

We further validated our experimental results by performing the finite-difference time-domain (FDTD) simulation to correlate the peak shift as a function of complex emulsion transformation (Figure 6a). A model of the Si_3N_4 racetrack resonator structure was built to have a critical coupling at the wavelength region near 1550 nm. We then simulated the refractive index in the ambient environment to vary from 1.30 to 1.40 in order to mimic the

effective refractive index change in the sensing environment during the complex emulsions' morphological change from double emulsions to inverted emulsions as illustrated in the Figure 2d. As the concentration of SDS increases, more of the inverted emulsions (FC/HC/W) formed and the refractive index increased from 1.3 to 1.4 in the vicinity of the cavity waveguide due to the fact that HC domain has the higher refractive index. We observed the shift of the simulated resonance peaks toward higher wavelength in the FDTD analysis with the increase in the ambient refractive index (Figure 6b). These peak shifts in the enveloped resonance spectra are consistent with the measured spectra obtained in the complex emulsion sensing.

CONCLUSION

We report a unique coupling of optical resonators and complex emulsions that offers a mode of chemical sensing that neither component can achieve alone. The change in the effective refractive index induced by the morphological changes in the complex emulsions in response to the chemical analyte led to the significant shifts in the resonance wavelength measured by the optical resonators. This signal is significantly larger comparing to that captured by the resonators without the complex emulsions. In our previous publications, we have shown that complex emulsions can be tuned to detect the presence of bacteria^{16,19} and Zika virus,¹⁷ the activities of enzymes,^{15,18} and UV light and pH changes.¹⁴ These sensors made use of carefully tuned responsive surfactants that interact with analytes to change the interfacial tension and drive the morphological changes. Thus, the sensing system described in this manuscript would be compatible with the previous demonstrations and would enhance their performance by removing the need for optical measurements. Additionally, complex droplets will be able to detect analytes that are surface-active without further functionalization, for biomedical applications and environmental monitoring. We anticipate that complex emulsions may be used as a modular layer to improve the miniaturization of optical sensing systems and can be tuned using responsive surfactants to selectively target certain analytes. Furthermore, due to the reversibility of the morphological change of the complex emulsions, we expect that a continuous measurement that relies on a continuous sliding scale mechanism would be easily implemented. Tuning this novel combination of hard and soft sensors toward biologically relevant biomarkers is a topic of on-going investigations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

- (1). Wongkaew N; Simsek M; Griesche C; Baumner AJ Functional Nanomaterials and Nanostructures Enhancing Electrochemical Biosensors and Lab-on-a-Chip Performances: Recent Progress, Applications, and Future Perspective. *Chem. Rev* 2018, *acs.chemrev.8b00172*. 10.1021/acs.chemrev.8b00172.
- (2). Mako TL; Racicot JM; Levine M Supramolecular Luminescent Sensors. *Chem. Rev* 2019, *119* (1), 322–477. 10.1021/acs.chemrev.8b00260. [PubMed: 30507166]
- (3). Swager TM Sensor Technologies Empowered by Materials and Molecular Innovations. *Angew. Chemie Int. Ed* 2018, *57* (16), 4248–4257. 10.1002/anie.201711611.
- (4). Farka Z; Ju ík T; Ková D; Trnková L; Skládal P Nanoparticle-Based Immunochemical Biosensors and Assays: Recent Advances and Challenges. *Chem. Rev* 2017, *117* (15), 9973–10042. 10.1021/acs.chemrev.7b00037. [PubMed: 28753280]
- (5). Shang L; Cheng Y; Zhao Y Emerging Droplet Microfluidics. *Chem. Rev* 2017, *117* (12), 7964–8040. 10.1021/acs.chemrev.6b00848. [PubMed: 28537383]
- (6). Li W; Zhang L; Ge X; Xu B; Zhang W; Qu L; Choi C-H; Xu J; Zhang A; Lee H; et al. Microfluidic Fabrication of Microparticles for Biomedical Applications. *Chem. Soc. Rev* 2018, *47* (15), 5646–5683. 10.1039/C7CS00263G. [PubMed: 29999050]
- (7). Li Y; Yan D; Fu F; Liu Y; Zhang B; Wang J; Shang L; Gu Z; Zhao Y Composite Core-Shell Microparticles from Microfluidics for Synergistic Drug Delivery. *Sci. China Mater* 2017, *60* (6), 543–553. 10.1007/s40843-016-5151-6.
- (8). He F; Wang W; He X-H; Yang X-L; Li M; Xie R; Ju X-J; Liu Z; Chu L-Y Controllable Multicompartmental Capsules with Distinct Cores and Shells for Synergistic Release. *ACS Appl. Mater. Interfaces* 2016, *8* (13), 8743–8754. 10.1021/acsami.6b01278. [PubMed: 26977710]
- (9). Liu D; Zhang H; Herranz-Blanco B; Mäkilä E; Lehto V-P; Salonen J; Hirvonen J; Santos HA Microfluidic Assembly of Monodisperse Multistage PH-Responsive Polymer/Porous Silicon Composites for Precisely Controlled Multi-Drug Delivery. *Small* 2014, *10* (10), 2029–2038. 10.1002/sml.201303740. [PubMed: 24616278]
- (10). Chen Q; Utech S; Chen D; Prodanovic R; Lin JM; Weitz DA Controlled Assembly of Heterotypic Cells in a Core-Shell Scaffold: Organ in a Droplet. *Lab Chip* 2016, *16* (8), 1346–1349. 10.1039/c6lc00231e. [PubMed: 26999495]
- (11). Trantidou T; Friddin M; Elani Y; Brooks NJ; Law RV; Seddon JM; Ces O Engineering Compartmentalized Biomimetic Micro- and Nanocontainers. *ACS Nano* 2017, *11* (7), 6549–6565. 10.1021/acsnano.7b03245. [PubMed: 28658575]
- (12). Kamiya K; Takeuchi S Giant Liposome Formation toward the Synthesis of Well-Defined Artificial Cells. *J. Mater. Chem. B* 2017, *5* (30), 5911–5923. 10.1039/c7tb01322a. [PubMed: 32264347]
- (13). Shibata H; Heo YJ; Okitsu T; Matsunaga Y; Kawanishi T; Takeuchi S Injectable Hydrogel Microbeads for Fluorescence-Based in Vivo Continuous Glucose Monitoring. *Proc. Natl. Acad. Sci. U. S. A* 2010, *107* (42), 17894–17898. 10.1073/pnas.1006911107. [PubMed: 20921374]
- (14). Zarzar LD; Sresht V; Sletten EM; Kalow JA; Blankschtein D; Swager TM Dynamically Reconfigurable Complex Emulsions via Tunable Interfacial Tensions. *Nature* 2015, *518* (7540), 520–524. 10.1038/nature14168. [PubMed: 25719669]
- (15). Zarzar LD; Kalow JA; He X; Walish JJ; Swager TM Optical Visualization and Quantification of Enzyme Activity Using Dynamic Droplet Lenses. *Proc. Natl. Acad. Sci* 2017, *114* (15), 3821–3825. 10.1073/pnas.1618807114. [PubMed: 28348236]
- (16). Zhang Q; Savagatrup S; Kaplonek P; Seeberger PH; Swager TM Janus Emulsions for the Detection of Bacteria. *ACS Cent. Sci* 2017, *3* (4), 309–313. 10.1021/acscentsci.7b00021. [PubMed: 28470048]
- (17). Zhang Q; Zeininger L; Sung KJ; Miller EA; Yoshinaga K; Sikes HD; Swager TM Emulsion Agglutination Assay for the Detection of Protein-Protein Interactions: An Optical Sensor for Zika Virus. *ACS Sensors* 2019, *4* (1), 180–184. 10.1021/acssensors.8b01202. [PubMed: 30624045]

- (18). Lin C-J; Zeininger L; Savagatrup S; Swager TM Morphology-Dependent Luminescence in Complex Liquid Colloids. *J. Am. Chem. Soc* 2019, 141 (9), 3802–3806. 10.1021/jacs.8b13215. [PubMed: 30785273]
- (19). Zeininger L; Nagelberg S; Harvey KS; Savagatrup S; Herbert MB; Yoshinaga K; Capobianco JA; Kolle M; Swager TM Rapid Detection of Salmonella Enterica via Directional Emission from Carbohydrate-Functionalized Dynamic Double Emulsions. *ACS Cent. Sci* 2019, 5 (5), 789 10.1021/acscentsci.9b00059. [PubMed: 31139715]
- (20). Nagelberg S; Zarzar LD; Nicolas N; Subramanian K; Kalow JA; Sresht V; Blankschtein D; Barbastathis G; Kreysing M; Swager TM; et al. Reconfigurable and Responsive Droplet-Based Compound Micro-Lenses. *Nat. Commun* 2017, 8, 14673 10.1038/ncomms14673. [PubMed: 28266505]
- (21). Hu J; Sun X; Agarwal A; Kimerling LC Design Guidelines for Optical Resonator Biochemical Sensors. *J. Opt. Soc. Am. B* 2009, 26 (5), 1032 10.1364/JOSAB.26.001032.
- (22). Hu J; Carlie N; Petit L; Agarwal A; Richardson K; Kimerling L Demonstration of Chalcogenide Glass Racetrack Microresonators. *Opt. Lett* 2008, 33 (8), 761 10.1364/ol.33.000761. [PubMed: 18414524]
- (23). Shopova SI; White IM; Sun Y; Zhu H; Fan X; Frye-Mason G; Thompson A; Ja S On-Column Micro Gas Chromatography Detection with Capillary-Based Optical Ring Resonators. *Anal. Chem* 2008, 80 (6), 2232–2238. 10.1021/ac702389x. [PubMed: 18271605]
- (24). Singh R; Ma D; Kimerling L; Agarwal AM; Anthony BW Chemical Characterization of Aerosol Particles Using On-Chip Photonic Cavity Enhanced Spectroscopy. *ACS Sensors* 2019, 4, 571–577. 10.1021/acssensors.8b00587. [PubMed: 30762345]
- (25). Su J Label-Free Biological and Chemical Sensing Using Whispering Gallery Mode Optical Resonators: Past, Present, and Future. *Sensors (Switzerland)* 2017, 17 (3), 1–18. 10.3390/s17030540.
- (26). Wade JH; Bailey RC Applications of Optical Microcavity Resonators in Analytical Chemistry. *Annu. Rev. Anal. Chem* 2016, 9 (1), 1–25. 10.1146/annurev-anchem-071015-041742.
- (27). Foreman MR; Swaim JD; Vollmer F Whispering Gallery Mode Sensors. *Adv. Opt. Photonics* 2015, 7 (2), 168 10.1364/AOP.7.000168. [PubMed: 26973759]
- (28). Bogaerts W; de Heyn P; van Vaerenbergh T; de Vos K; Kumar Selvaraja S; Claes T; Dumon P; Bienstman P; van Thourhout D; Baets R Silicon Microring Resonators. *Laser Photonics Rev.* 2012, 6 (1), 47–73. 10.1002/lpor.201100017.
- (29). Zeininger L; Weyandt E; Savagatrup S; Harvey KS; Zhang Q; Zhao Y; Swager TM Waveguide-Based Chemo- and Biosensors: Complex Emulsions for the Detection of Caffeine and Proteins. *Lab Chip* 2019, 19 (8), 1327–1331. 10.1039/C9LC00070D. [PubMed: 30896702]
- (30). Grist SM; Schmidt SA; Flueckiger J; Donzella V; Shi W; Talebi Fard S; Kirk JT; Ratner DM; Cheung KC; Chrostowski L Silicon Photonic Micro-Disk Resonators for Label-Free Biosensing. *Opt. Express* 2013, 21 (7), 7994 10.1364/oe.21.007994. [PubMed: 23571890]
- (31). Zhang W; Serna S; Le Roux X; Vivien L; Cassan E Highly Sensitive Refractive Index Sensing by Fast Detuning the Critical Coupling Condition of Slot Waveguide Ring Resonators. *Opt. Lett* 2016, 41 (3), 532 10.1364/OL.41.000532. [PubMed: 26907416]

Figure 1. Schematic diagram of the sensing platform comprising an array of dynamic complex emulsions (with the different fluid phase represented as red and clear spheres) and an on-chip optical racetrack resonator and bus waveguide (in black).

Figure 2.

Complex emulsions. (a) Schematic of the composition of the complex emulsions (side view) showing hydrocarbon (HC) and fluorocarbon (FC) domains, and the chemical structures of the hydrocarbon oil (toluene), the fluorocarbon oils (perfluorotributylamine, FC43, and HFE7500), and the two surfactants (SDS and Zonyl) used in this study. (b) Optical micrograph (top view) of the complex emulsions in 1% SDS. The outer rings are HC and the inner circles are FC. The higher refractive index of HC magnifies the FC domains. (c) Size distribution of the emulsions were obtained from image analysis. (d) The transformation of complex emulsions into different morphologies—double (HC/FC/W), Janus, and inverted (FC/HC/W)—in response to the chemical environment dictates the effective refractive index, allowing the detection of chemical analytes that would normally not induce changes in the refractive index.

Figure 3. Schematic of the racetrack resonator. (a) Optical fiber coupling set-up for on-chip sensing. (b) Image of the as-fabricated sensor chip. (c) Illustration of the racetrack resonator configuration. (d) Experimental test set-up for sensing measurement using on-chip resonators and complex emulsions.

Figure 4. Characterization of the racetrack resonators. Optical micrographs (a) and scanning electron micrographs (b, c, d) of the racetrack resonator. Finite element analysis of the resonator, with the first TE (e) and TM (f) modes, respectively.

Figure 5.

Responses to changes in morphology of the complex emulsions. (a) Transmission spectra of optical resonator in TE mode with complex emulsions with different morphology as the top cladding. The fraction of 1 wt% SDS surfactant, f_{SDS} , where the remaining fraction is 1% Zonyl, dictates the morphology of the complex emulsions and the local effective index of refraction. Lorentzian peak fits of the resonant wavelengths are provided as guides to the eyes. (b) Control experiment without the complex emulsions. The change in the ratio of the two surfactants does not significantly shift the critical coupling of the resonators. (c) The peak shift of the envelope resonant spectra as a function of the fraction of the surfactant SDS.

Figure 6.

Finite difference time domain (FDTD) analysis of the use of complex emulsions for sensing via a racetrack resonator. (a) Electrical field intensity map of the Si₃N₄ racetrack resonator at critical coupling condition. (b) Spectral analysis of the resonance peaks in TE mode under various effective refractive indices in the environment, simulating the change due to the complex emulsion transformation