Combinatorial wetting in colour: an optofluidic nose

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Title: Highly sensitive optofluidic chips for biochemical liquid assay fabricated by 3D femtosecond laser micromachining followed by polymer coating

Optofluidic chip fabricated by femtosecond laser direct writing consists of a microfluidic channel whose internal walls are coated with a low refractive index polymer and an optical waveguide for high sensitive biochemical liquid assay.

As featured in: Lab on a Chip

We present a colourimetric litmus test for simple differentiation of organic liquids based on wetting, which achieves chemical specificity without a significant sacrifice in portability or ease-of-use. Chemical specificity is derived from the combination of colourimetric wetting patterns produced by liquids in an array of inverse opal films, each having a graded wettability, but using different surface groups to define that gradient.

Colourimetry is a powerful form of chemical sensing. Without expensive equipment or extensive training, a colourimetric test gives a user at-home access to increasingly sophisticated chemical and biological diagnostic methods. The colour response provides an elegant visualization to this class of sensor, but also poses the greatest challenge to its development. While some target properties of an unknown can be easily coupled to colour change in an indicator material (e.g. pH), it is generally challenging to couple a colourimetric response that is sensitive to a general physical or chemical property.

Recently, we developed a platform for colourimetry based on wetting in silica inverse-opal films (IOFs), whose surface chemistry was graded such that the lyophobicity of the porous network increased with depth, which we called a Wetting In Colour Kit (WICK). When immersed in a liquid, the structure is infiltrated up to a fixed depth, and displays a structural colour pattern that is highly sensitive to the liquid’s wettability to the surface chemistry. When this procedure is applied to an IOF that varies in total thickness laterally across the sample (and where the individual layers steps can be seen as regions of distinct colour), distinct depths of infiltration can be visualized by a shift in the rainbow pattern corresponding to the number of unfilled layers, as shown in Fig. 1A. Intuitively, this shift will proceed in the direction of the thicker area as more of the lattice is filled.

A scheme of colourimetry that is sensitive to wettability (a generic property of liquids) can be applied in principle to any sensing problem that involves liquids. However, the sensitivity of WICK to such a generic property of liquids also means that no chemical information about the unknown can be discerned without any prior-given information. Fig. 1B illustrates this principle in a WICK, whose vertical gradient of wettability is applied by first functionalizing the IOF with 1H,1H,2H,2H-tridecafluorooctyl (13FS) groups (by exposure to vapours of the corresponding trichlorosilane), then exposing it to oxygen plasma for a short time (30 s), and then functionalizing it with 3,3,3-trifluoropropylsilyl (3FS) groups (this type of functionalization will hereafter be abbreviated 3FS→13FS, see Supplementary Methods and Ref. 2 for a more detailed description of this method). While the two ethanol-water mixtures shown (80%EtOH, 90%EtOH) produce visibly distinct colour patterns, it is relatively easy to find different liquids whose wetting behaviour exactly mimics those of the above ethanol-water mixtures. In this WICK, n-octane and acetone mimic the response of 80% EtOH and 90% EtOH respectively, as shown in Fig. 1B. In this example, if it is known beforehand that the unknown is a mixture of ethanol and water, WICK would be able to measure the ethanol concentration colourimetrically (with up to 2.5% sensitivity). However, if no information is given beforehand, then it is impossible to identify the unknown.

Here we show that chemically specific information can be extracted from a combination of colourimetric wetting responses displayed by a WICK array, with each element displaying a vertically graded wettability that is designed to exhibit a partial wetting response in most organic liquids (e.g. surface tension in the 20–30 mN m\(^{-1}\) range), but each using distinct types of surface groups to achieve the wetting gradient. Combinatorial sensing, exploited in our olfactory system as well as by several synthetic systems, is a useful approach to extracting chemically specific responses from an array of individual weakly-specific sensors. A wetting-based response is potentially ideal for combinatorial sensing because of the broad range of materials that can elicit the response (any liquid) and its weakly specific dependence on the chemical interactions between the liquid components and the surface chemistry (the solid-liquid interfacial tension is influenced by the chemical affinity of the liquid to the solid surface). Fig. 1C shows how chemical specificity is added by comparing the responses of two different WICKs employing different surface groups to achieve the wetting gradient (left: DEC→13FS, DEC = n-decylsilyl groups; right: 3FS→13FS) in methanol (\(\gamma = 22.1 \text{ mN}\).
We produced WICK arrays consisting of six samples, each functionalized with a different (less lyophobic than 13FS) surface group: pentafluorophenylpropyl (5FP), 3,3,3-trifluoropropyl (3FS), n-decyl (DEC), p-tolyl (PTOL), trimethylsilyl (TMS), 3-phenylpropyl (3PP). The plasma exposure time (30 s) was chosen to eliminate trivial responses and maximize the range of wetting responses observed in our library of organic liquids.

To facilitate interpretation of the results, we developed a system to translate qualitative wetting patterns into numerical values. Each element of the WICK array was first characterized in a series of reference liquids. To serve as ideal reference liquids, a set of liquids would have to induce a wide range of wetting responses in each element, ideally covering the broad range of wetting depths observed in test liquids. Most importantly, the relative order of wettabilities of the reference liquids would ideally be the same in each element of the array. For example, methanol and octane would make a bad set of reference liquids because methanol wets more than octane in 3FS elements of the array. As reference liquids, we chose the set of water-ethanol mixtures (in increments of 5% EtOH by volume) and isopropanol alcohol (IPA). IPA was found to wet more than ethanol in all elements, and thus a suitable addition to extend the effective range of detectable responses covered by the reference liquids. Colour patterns produced by unknown liquids (test liquids) were then assigned a numerical score for each element of the array based on the reference liquid(s) that produced the most similar pattern. The scoring system is illustrated in Fig. 1D for o-xylene as a test liquid, having scores of 50 (3FS→13FS), 75 (3PP→13FS), and 85 (PTOL→13FS) in three elements of the array. To integrate IPA into the scoring system, it was assigned the numerical value of 110. When a test liquid produced a wetting response that fell in between that of adjacent reference liquids, a midpoint score (ending in 2 or 7) was assigned (e.g. a liquid that wet more than 80% EtOH but less than 85% EtOH in a given element would be assigned a score of 82, or 87 for a liquid whose response fell in between 85% EtOH and 90% EtOH).

Fig. S1 (Supplementary Information) shows the complete sample set of colour patterns and reference liquid scores from an array tested in 17 different organic solvents. Notably, each liquid yielded a unique combinatorial colour response and thus a unique set of scores. Fig. S2A (Supplementary Information) shows the reference liquid scores for a wide range of organic solvents in the 3FS→13FS and DEC→13FS elements of the array. Aliphatic compounds displayed higher scores (i.e. more wetting relative to reference liquids) in the DEC→13FS element than they displayed in the 3FS→13FS element. As a general trend, the elements of the array with fluorinated surface groups (3FS, 5FP) produced lower scores relative to the other elements of the array in the nonpolar hydrocarbons, with deviation from the reference line (given by the reference liquids) negatively correlating with polarity of the liquid. Also as expected, the scores of the linear alkanes in all elements decreased monotonically with increasing chain length (increasing surface tension), since the chemical affinity for the different surface groups should be of the same type. The monotonically varying scores of the linear alkanes form a nearly straight line in this plot.
It does not require image analysis, RGB subtraction, or any other complex analysis technique that places constraints on the type of equipment amenable for use in the field. Furthermore, as shown in Fig. S2, a significant enhancement of chemical specificity can be achieved by using an array with only two or three elements. This requires a minimal increase in complexity compared to the original WICK litmus paper concept.

Fig. 2A shows a two-dimensional principal component analysis (PCA), where the aforementioned 6-dimensional set of numerical wetting scores are projected onto a new two-dimensional set of principal component axes, accounting for 98% of the total variance. Qualitatively Fig. S2A and Fig. 2A look similar, indicative of the fact that the contrast between the wetting behaviour in fluorinated and non-fluorinated elements of the array was the largest source of variability between the different liquids (see Supplementary Information for a more detailed discussion of our PCA). However, the consideration of all six elements (Fig. 2A) allows us to distinguish iso-octane and cyclohexane from the linear alkane line. In Fig. S2B–D, analyses using fewer elements of the array are done, showing that even three elements are able to differentiate the 17 test liquids successfully, thus suggesting that the 6-dimensional set is largely redundant.

A hallmark of ideal combinatorial sensors is that they give information as to what the chemical makeup of an unknown (not previously entered in the library) is likely to be. To test the applicability of this principle to our WICK sensor, we tested the array in a randomized mixture of the linear alkanes between C6 and C10. Its response is shown in Fig. 2A. Naïvely, we would expect that its response should fall along the arc (nearly straight line) connecting the responses of consecutive linear alkanes and this is exactly what is observed.

While the sophistication and selectivity of this array-based sensor is below that of many other previously reported “artificial noses” that have a much higher effective dimensionality of the variability, the value of WICK array lies in its ease of use and technical simplicity relative to the information it is able to extract. Unlike most artificial noses, the reference-liquid scoring system allows measurements to be done easily by eye, by simply comparing the response produced by a test liquid to that of reference liquids. Shown in Fig. 2B, the relative nature of the reference-liquid scoring system also facilitates measurements that are fairly robust against sample-sample variability, potentially eliminating the need for costly quality-control procedures. Notably, unlike previously reported colour-based combinatorial sensors, it does not require image analysis, RGB subtraction, or any other complex analysis technique that places constraints on the type of equipment amenable for use in the field. Furthermore, as shown in Fig. S2, a significant enhancement of chemical specificity can be achieved by using an array with only two or three elements. This requires a minimal increase in complexity compared to the original WICK litmus paper concept.

Conclusions

Using arrays of WICKs, each with distinct chemical functionality, but exhibiting a nontrivial wetting response over a common range of liquids, we are able to extract chemical specificity from a sensing platform whose widespread applicability is derived from sensitivity to wettability, a general (non-chemically specific) property of all liquids. Furthermore, through the use of a simple-to-use reference-based scoring system, we are able to translate qualitatively perceptible degrees of wetting to numerical values that can be assigned by eye (using a reference card) without the need for sophisticated equipment or software in a manner that simultaneously desensitizes the system to inter-sample variability. In addition to the ability to differentiate a wider range of liquids, our WICK arrays also allow users to make rough predictions about the chemical nature of a previously uncharacterized unknown liquid by comparing relative degrees of wetting of the different elements.

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References

