Integrated microwave resonant device for dielectric analysis of microfluidic systems

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Abstract. Herein we present a device for performing non-contact dielectric spectroscopy upon liquids in a microfluidic environment. The device is comprised of a compression-sealed polytetrafluoroethylene (PTFE) chip with an embedded coaxial resonator, which is overmoded for dielectric measurements at six discrete frequencies between 1 and 8 GHz. A novel capacitive coupling structure allows transmission measurements to be taken from one end of the resonator, and an optimised microchannel design maximises sensitivity and repeatability. The use of a PTFE substrate and a non-contact measurement gives excellent chemical and biological compatibility. A simple ‘fingerprint’ method for identifying solvents is demonstrated, whereby a sample is characterised by air-referenced changes in complex frequency. Complex permittivity values are also obtained via a perturbation theory-based inversion. A combination of experimental and simulated results is used to characterise the device behaviour, limits of operation and measurement uncertainty. The high stability of temporal measurements, coupled with the robustness of the design, make this device ideal for analytical chemistry and industrial process control.

1. Introduction

Dielectric metrology has applications as an alternative and complimentary spectroscopic technique because of key advantages over other, more ubiquitous methods, including the potential for non-destructive, non-invasive and label-free measurements, which are not hampered by the presence of solid material within a liquid phase. This work describes the development of a device for liquid-phase dielectric measurements in a platform that enables in situ characterisation of chemical, biological and pharmaceutical processes. It is novel in three main respects: the resonator coupling structure, the use of an overmoded resonator to give multi-frequency information, and the microfluidic interface.

An integrated device – one comprised of a sensing technology and appropriate sample interface – is necessary for low volume, high throughput analytical procedures. Filling a waveguide with a solvent [1] or dipping a reflectance probe [2] into a solution are sufficient for several samples but not for the applications of modern chemistry and biology. Instead, the inclusion of microfluidic techniques enables the realisation of a more practical measurement system for such applications. Laminar flow can be exploited by appropriate micron-scale design, enabling the control of various parameters to a great degree of accuracy: concentration, temperature, mixing, etc. [3,4], whilst using extremely small volumes. Such a system is attractive because of its potential for low-cost, disposable, point-of-care devices, with the obvious safety benefits of a sealed device.

It is advantageous to focus dielectric measurements on the microwave region for solvent-based systems, because it is an interesting range where many dipolar relaxations can be observed [5-8], and
where the effects of dissolved species on these relaxations can be seen. A resonant structure was chosen for greater accuracy and less uncertainty when compared with equivalent broadband techniques [9]. They are more limited in scope by being fundamentally restricted to measuring discrete frequencies rather than continuous spectra, but the use of an overmoded resonator counters this problem. A resonant structure is also less dependent on the Vector Network Analyser (VNA) calibration, resulting in reduced systematic error. Using a coaxial resonator is beneficial due to ease of integration: the resonator can be perturbed by being positioned near to a sample, but not necessarily in contact with it. There are also a large number of well-defined TEM modes before hybrid and parasitic modes appear in the spectrum. Semi-rigid coaxial cable was selected as it is cheap, easy to machine, a standard size, and sufficiently robust for industrial applications. Although a coaxial resonator will have a lower quality factor ($Q$) than cavity or dielectric resonators (where $Q$ is the quotient of resonant frequency and half-power bandwidth), this disadvantage is outweighed by the advantages. Transmission rather than reflectance measurements were used for improved dynamic range.

## 2. Design

### 2.1. Perturbation Theory

The reader is referred to [10] for a full formulation of perturbation theory for microwave resonators, but a cursory description is provided here for sake of completeness. It should be noted that while the approach of [10] is formulated with respect to a cavity resonator, it is equally applicable for evanescent field perturbation at the end of a coaxial resonator.

A material can interact with the electromagnetic fields of the resonator according to its complex values of permittivity and permeability, which interact with the electric and magnetic fields respectively. Due to the difficulty of decoupling the effects of these two parameters, this device is intended for measurements of non-magnetic (i.e. zero permeability) materials, and as such magnetic field interactions will not be considered.

The stored energy of the empty and perturbed fields are related to their volume integrals, and can also be related to a normalised change in complex frequency in a derivation beginning with Maxwell’s equations [10], where complex frequency \( \tilde{f} \), as defined in equation (1):

\[
\tilde{f} = f_0 - i \frac{1}{2} f_B
\]

where \( f_0 \) is resonant frequency and \( f_B \) is half-power bandwidth. If complex permittivity is isotropic and unchanging, it can be calculated from measurements of centre frequency and bandwidth assuming some knowledge of the stored energy. In practice, this can be achieved by assuming the resonator fields are changed by a negligible amount upon the introduction of a sample material, so their volume integrals can be assumed to be constant. The expression then approximates to show a change complex permittivity is linearly proportional to the resulting change in complex frequency, so unknown materials can be characterised according to a measurement of a known calibration material. However, the unchanging field assumption does not hold for most reasonable values of permittivity, particularly for the relatively lossy solvents of interest to the applications described in the introduction, so measurements must be calibrating with a number of solvents as described in section 3.

### 2.2. Overmoded resonator

The open-ended half-wavelength resonator was formed of open-circuited 50 $\Omega$ RG401 semi-rigid coaxial cable, which was cut to 8 cm to give a fundamental resonance of $\sim$ 1.25 GHz. This resonance was chosen to give six modes in the frequency region of interest. It has copper conductors (6.35 mm outer diameter) and a PTFE spacer (inner diameter 1.6 mm, outer diameter 5.4 mm). These dimensions were chosen as a compromise between a suitably small aperture size for microfluidic channels, against resonator losses, which increase with frequency.
2.3. Coupling structure

Transmission measurements require two ports, and are most easily achieved by coupling with parallel coaxial feedlines located a small distance from either end of the resonator. However, this structure is difficult to perturb with a sample – for example, it is possible to pass a capillary between the resonator and a feedline, but the tolerances on the inner and outer diameters of capillaries generally yield a +/-10% uncertainty. Invasive couplings are also possible, whereby receptacles protrude orthogonally into the resonator, but these will not be able to couple to certain higher-order modes which have nulls adjacent to the connectors.

The cross-sectional and 3D views of figures 1 (a) and (b) show how transmission measurements can be taken from one end of the probe without having to couple at suboptimal points along the length of the resonator. The ground plane is necessary to minimise crosstalk between the connectors. This structure was designed to be weakly coupled, which means coupling has a minimal effect on the resonator fields, so it does not have to be accounted for during the inversion process. This design was simulated in COMSOL Multiphysics, and the relative dimensions and positions of the ground plane, receptacles and resonator were optimised to maintain weak coupling and maximise dynamic range.

2.4. Microfluidic interface

A 400 µm square channel, widening above the probe aperture, was micromilled in a PTFE chip. A recess in the back of the chip housed the resonator 100 µm below the channel in order to improve chemical and biological compatibility; to prevent fluid ingress into the resonator and to reduce corrosion of the copper conductors. Holes were drilled through the chip at either end of the channel to accept capillaries for fluidic inlet and outlet connections. These were fixed in place by standard fittings that screwed into the manifold. The use of a PTFE microfluidic setup meant that the system could be cleaned by flushing with acetone or other solvent, removing the need for disassembly between measurements and thus improving measurement reproducibility. A gasket layer of 100 µm PTFE film was placed between the machined chip and another, plain PTFE chip, and compression sealed in a brass manifold. The device can be added directly into existing flow systems because of the use of a PTFE substrate and standard fittings.

3. Experimental Methodology

The transmission coefficient was measured for each resonance with an Agilent E5071B VNA, and exported to LabVIEW, where a Lorentzian curve was fitted to the data in order to determine the centre frequency and bandwidth in real-time. A segmented frequency sweep was used to study all modes simultaneously. The frequency range of the VNA meant six modes could be measured with each sweep taking roughly 15 milliseconds. For each sample, air was pumped through the system and a reference measurement taken. Immediately following this, the sample solvent (HPLC-grade) was pumped through the device and a measurement again taken. This process was repeated 8 times for each solvent. The environment was maintained at constant temperature by passing a 1 m length of inlet capillary through a 20 °C water bath.

A 3D model of the integrated device was created in COMSOL, and simulations were used to calculate the centre frequency and bandwidth of each resonance within the frequency region of interest. A series of simulations were performed where resonant frequency and bandwidth were
calculated as the real and imaginary components of sample permittivity were swept from 1 → 30 and i0 → i15. Two important observations arose from investigating the relationships between these parameters. Firstly, each component of complex frequency could be seen to depend on both real and imaginary permittivity. This fact is ignored by the majority of groups that employ perturbation theory, which simply equate real and imaginary components. Secondly, the relationships between complex frequency and complex permittivity were non-linear. This is also commonly ignored, as the relationships between permittivity and frequency are normally treated as linear proportionalities, as described in section 2.1. An analytic inversion based upon perturbation theory was therefore deemed unsuitable as it would not be able to account for these behaviors. Instead, measurements of several known solvents over a range of real and imaginary permittivities were used to interpolate an inversion function for each mode from the associated changes in complex frequency. This was verified by comparing inverted measurements with previously obtained dielectric dispersion data, together with simulations of the same solvents.

4. Results and Discussion

The results were processed in two ways. The first takes the changes in the real and imaginary components of frequency (figure 2), where the change in complex frequency $\Delta f$ is defined in equation (2),

$$\Delta f = \Delta f_0 - i\frac{1}{2} \Delta f_B = g(\varepsilon_1 - i\varepsilon_2),$$

where $\varepsilon_1$ is permittivity, $\varepsilon_2$ is dielectric loss and $g$ is a non-linear function of complex permittivity $\varepsilon_1 - i\varepsilon_2$. This method of post-processing could be used for real-time monitoring of a liquid sample as it does not require the interpolation of an inversion function. The variance of the data was ten parts in a million, so error bars are not appropriate. The error bars do not overlap in any instance, so there is no ambiguity in distinguishing solvents. This system also lends itself to multi-dimensional classification.

Permittivity spectra of the measured samples are shown in figure 3, where interpolated measurements of chloroform, ethanol, methanol, acetone and acetonitrile, were used to calculate the complex permittivity of toluene. The grey lines represent the dielectric relaxations to which the measured changes in complex frequency were fitted. Relaxation parameters were taken from [5-8].

Table 1 shows the following sensor parameters: limit of detection, geometric uncertainty and maximum standard error. The standard error was used to calculate the limit of detection; that is, the minimum change in complex frequency that could be discerned above measurement noise. The uncertainty was taken as the maximum of a series of correlated simulations modelling fabrication.
Table 1. Sensor Characteristics

| Standard error | Limit of detection, $\varepsilon_{DR}$ | Uncertainty |
|----------------|---------------------------------------|--------------|
| $\pm 7$ kHz   | 1.00011                               | $\pm 1.7\%$ |

tolerances, which can be assumed to be the dominant source of uncertainty.

Given the large range of permittivities and the small number of solvents, it is not appropriate to define a resolution with the available data. The device is suitable for compositional measurements (for industrial, chemical and pharmaceutical purposes) as it has been exercised over a large range of permittivity, yet still demonstrates a low error.

5. Conclusion

A new method of interfacing a microwave measurement technique with a microfluidic circuit has been demonstrated. Three novel aspects (the coupling structure, the overmoded resonator and the microfluidic interface) were combined to obtain quasi-spectral complex permittivity measurements in a non-destructive, non-invasive and label-free measurement regime. Such a device can also be used to characterise colloids and suspensions. It is ideal for multi-sensor fusion, such as an ‘electronic tongue’ device, because of the excellent chemical and biological compatibility and the ease of development of fluidic functionality on the demonstrated platform.

References

[1] Kaatze U, Pottel R and Wallusch A 1995 *Meas. Sci. Tech.* **6** 1201-7
[2] Misra D K 1977 *IEEE Trans. Microw. Theory Tech.* **35** 925-8
[3] Marre S and Jensen K F 2010 *Chem. Soc. Rev.* **39** 1183-202
[4] Kumar V, Paraschivoiu, M and Nigam K D P 2011 *Chem. Eng. Sci.* **66** 1329-73
[5] Santarelli V, MacDonald J and Pine J 1967 *J. Chem. Phys.* **46** 2367-75
[6] Xu M, Eyring E and Petrucci S 1997 *J. Molec. Liq.* **73-4** 41-8
[7] Barthel J, Bachhuber K, Buchner R, Gill J B and Kleebauer M 1990 *Chem. Phys. Lett.* **167** 62-6
[8] Barthel J, Bachhuber K, Buchner R and Hetzenauer H 1990 *Chem. Phys. Lett.* **165** 369-73
[9] Gregory A and Clarke R 2006 *IEEE Trans. Dielectr. Elect. Insul.* **13** 727-43
[10] Pozar D M 2005 *Microwave Engineering 3rd Ed.* (New York: Wiley) chapter 6