trends

Micromachining of monocrystalline silicon and glass for chemical analysis systems

A look into next century's technology or just a fashionable craze?

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Miniaturization of already existing techniques in on-line analytical chemistry is an alternative to compound-selective chemical sensors. Theory indicates higher efficiency, faster analysis time and lower reagent consumption. Micromachining, a well known photolithographic technique for structures in the micrometer range, is introduced and documented with structures as examples for flow injection analysis, electrophoresis and a detector cell.

Introduction

The continuous monitoring of a chemical parameter, usually the concentration of a chemical species, is gaining increasing attention in biotechnology[1,2], process control[3,4], and the environmental[5,6] and medical sciences[7,8]. The chemical compound of interest is usually accompanied by interfering species. Due to the severe selectivity requirements, and the fact that developments were made by researchers in different fields starting from different points, many possibilities have been examined in the approach to this topic. Recently, we presented a general concept for a miniaturized total chemical analysis system[9].

Selective chemical sensors, flow injection analysis (FIA) and separation techniques (chromatography, electrophoresis) can be used as 'stand alone techniques', *i.e.* an instrument, standing in a lab, operated by a qualified technician. For monitoring purposes, the instrument needs to be fully automatic, from sampling through information evaluation. A state-of-the-art strategy is the so called total chemical analysis system (TAS), which periodically transforms chemical information into electronic information. Sampling, sample transport, any necessary chemical reactions, chromatographic or electrophoretic separations, and detection are automatically performed. Most of these methods are precise and reproducible, but also time consuming. Because the sample pretreatment serves to eliminate most of the interfering chemical compounds, the detector or sensor in a TAS does not need to be highly selective. Furthermore, calibration can be incorporated into the system. Examples of TAS can be found in the literature (gas chromatography monitor[10], on-line glucose analyzer[11]).

Concept for miniaturization

A miniaturized TAS must be defined both in relation to a chemical sensor and to a TAS (Fig. 1). If a TAS performs all sample handling steps extremely close to the place of measurement, then we propose that it be called a miniaturized total chemical analysis system (μ-TAS). The interface to the control and measurement electronics could include, for instance, tubing for mass flow and optical fibers.

The chemical sensor, the TAS and the μ-TAS must similarly be compared with respect to their time scale. There are three different times to consider (Fig. 2):

- The *response time* of the detector or sensor, which is defined as the time difference between a concentration change (step function) and a certain output value of the detector (*e.g.* 90% of the final output);
- the *analysis time* of an analysis system, which is defined as the time delay of the quantitative output of the detector obtained with respect to the initial time of sampling; and
- the *cycle time* of an analysis system, which is de-

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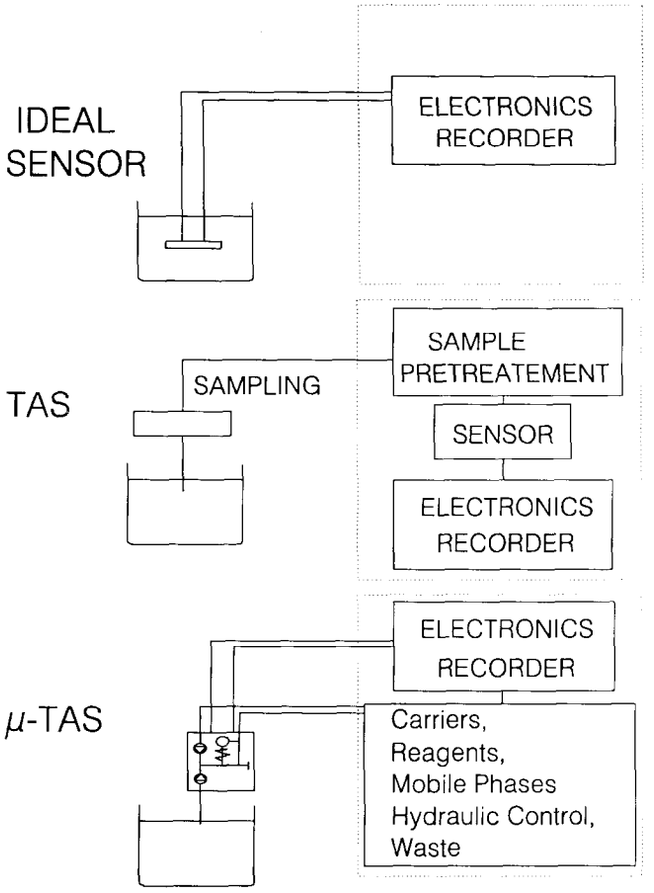

Fig. 1. Schematic diagram of an ideal chemical sensor, a total chemical analysis system (TAS) and a miniaturized TAS (μ-TAS).

fined as the reciprocal of the fastest possible injection frequency wherein no information is lost.

If the analysis time of a μ-TAS is comparable to the response time of a selective chemical sensor, then both become very similar in appearance and use, as illustrated in Fig. 2.

Several research groups have done basic developmental work on micro pumps and valves[12–14], small FIA systems[15], and open-tubular column chromatography[16,17]. The most advanced micro-technology is definitely capillary electrophoresis[18]. Recently, Monnig and Jorgenson[19] presented a high-speed separation using a 10-mm long capillary with elution taking 0.5 to 2 seconds. As will be shown later, our main reason for the miniaturization of the TAS is to realize an *enhancement of its analytical performance*, rather than a reduction of its size.

Theory of miniaturization

Let d be a typical length in a given system (for example the diameter of a tube). By multiplying each variable by d^n and the appropriate constants, it can be reduced to a dimensionless parameter which is independent of the spatial scale of the given system (for example the flow-rate will become the Péclet number). Similar systems of different sizes can then be easily compared. If we assume that a miniaturization is a simple three-dimensional down-scale (extensively discussed in ref. 9), we can easily demonstrate the behaviour of the relevant physical variables. There remains then one degree of freedom for the mechanical parameters: time.

Time constant system

In this case, the time scale is the same for the large and for the small system. Consequently, all relevant time variables (analysis time, transport time, response time) do not change. But a linear flow rate in a tube would decrease by d, a volume flow-rate by d^3, the Reynolds number by d^2 and a pressure drop needed would be a constant. This system behaviour is important for simple transportation and FIA systems. Diffusion would certainly be predominant. The main advantage is saving carriers or reagents. A 10-fold decrease in size, for example, would cause a 1000-fold decrease in carrier or reagent consumption.

Diffusion-controlled system

The diffusion-controlled system becomes important when molecular diffusion, heat diffusion or flow

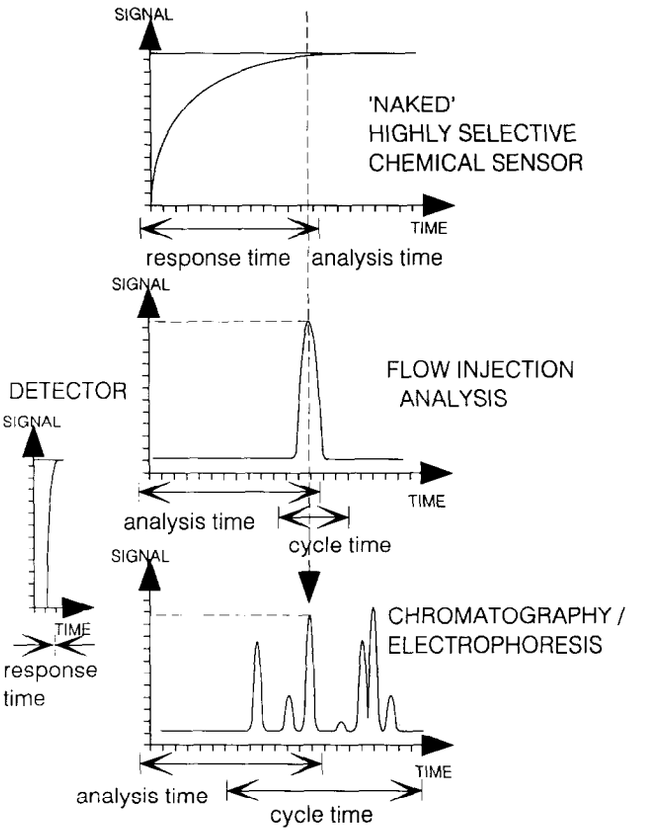

Fig. 2. Comparison of response time, analysis time and cycle time for an ideal chemical sensor, a flow injection analysis based and a chromatography based TAS.

characteristics control the separation efficiency in a given system. In this system the time scale is treated as a surface, *i.e.*, time is proportional to d^2. This system is in perfect agreement with standard chromatographic and electrophoretic bandbroadening theory, *e.g.* Van Deemter or Golay equations. All reduced parameters, including the Reynolds number, Péclet number (flow-rate), Fourier number (elution time) and Bodenstein number (pressure drop), remain constant regardless of the size of the system[20]. Hydrodynamic, heat and diffusion effects are compensated. This indicates that a down-scale to 1/10 of the original size (diameter of a tube) reduces the related time variables (analysis time, required response time of a detector) to 1/100. The pressure requirements increase by a factor 100, but the voltage requirements (for electrophoresis/electroosmosis) remain constant. The main advantage is a considerably higher speed of separation with a comparable efficiency. Some theoretical values comparing capillary electrophoresis (micellar solutions), capillary liquid chromatography and capillary supercritical fluid chromatography are given in Table I. It is important to note that the structures are a few microns in diameter (2.8–24 μm), a few centimeters long (6.5–20 cm) and need small volume detectors (1.6–47 picoliters). Although these values cannot replace experimental results, they give an indication of values forbidden by theory.

TABLE I. Calculated parameter sets for a given separation performance obtained with capillary electrophoresis (CE), liquid (LC) and supercritical fluid chromatography (SFC)
Assumed constants are: diffusion coefficients of the sample in the mobile phase $1.6 \cdot 10^{-9}$ m^2/s (CE, LC) and 10^{-8} m^2/s (SFC); viscosities of the mobile phase 10^{-3} Ns/m^2 (CE, LC) and $5 \cdot 10^{-5}$ Ns/m^2 (SFC); electrical conductivity of the mobile phase 0.3 S/m (CE), electrical permittivity·ζ potential $5.6 \cdot 10^{-11}$ N/V (CE).

Parameter		CE (micellar)	LC	SFC
Number of theoretical plates	N	100 000	100 000	100 000
Analysis time	$t(k' = 5)$ (min)	1	1	1
Heating power	P/L (W/m)	1.1	–	–
Capillary inner diameter	d (μm)	24	2.8	6.9
Capillary length	L (cm)	6.5	8.1	20
Pressure drop	Δp (atm)	–	26	1.4
Voltage	ΔU (kV)	5.8	–	–
Peak capacity	n	180	220	220
Signal bandwidth	σ_x (mm)	0.21	0.56	1.4
Signal bandwidth	σ_t (ms)	42	70	70
Signal bandwidth	σ_v (pl)	94	3.3	52

Micromachining

With its origins in the microelectronics industry, the photolithographic patterning of layer structures on the surface of silicon wafers has become a well-known high-tech standard procedure. Besides its semiconductor qualities, monocrystalline silicon is abundant and inexpensive, can be produced and processed under controlled conditions to unparalleled standards of purity and perfection, has excellent mechanical and chemical properties (yield strength better than steel, Young's modulus about identical, Knoop hardness comparable to quartz, chemical inertness comparable to glass) and is highly amenable to miniaturization (down into the micrometer range). The surface treatment to obtain mechanical structures is called micromachining[21] and includes fabrication steps such as film deposition, photolithography, etching and bonding. A simple process for obtaining a channel in silicon is shown in Fig. 3. It is obvious that the two-dimensional shape of the channel layout is given by the photomask, but does not affect the complexity of the process at all. As soon as a variation in depth (third dimension) or material (*e.g.* a metal layer) is needed, additional processes have to be added to the sequence.

Silicon based physical and chemical sensors and actuators are a focus of interest nowadays[22]. Compared to conventional machining, photolithographical processes allow cheap mass fabrication of complicated microstructures. Hundreds to thousands of

Glossary

Micromachining is the surface treatment of a solid material to obtain mechanical microstructures by using film deposition, photolitography, etching and bonding.

Film deposition processes include spin coating, thermal oxidation, physical (PVD) and chemical vapour deposition (CVD), low pressure CVD, plasma enhanced CVD, sputtering, etc. A large variety of metals, inorganic oxides, polymers and other compounds can be deposited.

Photolithography can be done using visible light for structures larger than 1 μm. For special applications such as submicron patterning, UV, X-ray or e-beam photolithography is used.

Etching is performed either as a wet chemical process or as a plasma process. Isotropic as well as anisotropic processes are known.

Bonding is the assembly of a piece of silicon onto silicon, glass or other substrates.

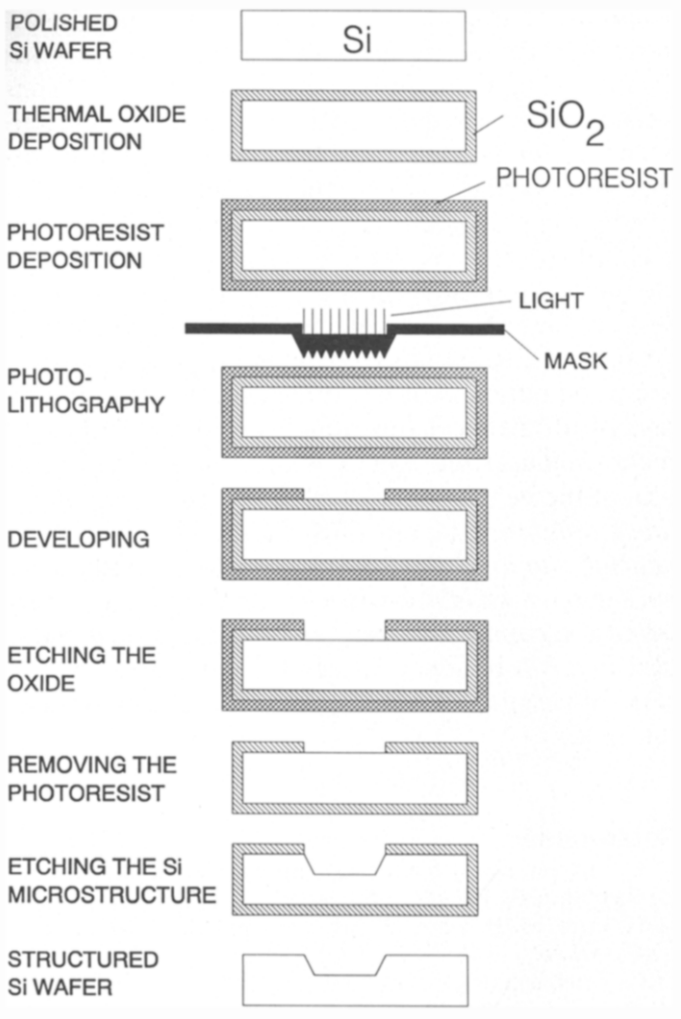

Fig. 3. Process steps of a standard one mask micromachining procedure.

structures are fabricated in the same batch. Precision and reproducibility of the structure elements are excellent (see Fig. 4). Although silicon allows monolithic integration of electronics, sensors and actuators, micromachining has to be done under clean room conditions and needs high-tech instrumentation, both of which represent a substantial financial investment.

Examples of structures

Two examples of photolithographically fabricated structures are presented here. The chemical analysis system shown in Fig. 5 combines a FIA technique with a capillary electrophoretic separation. The device consists of two glass plates, 40 × 155 mm. The upper plate contains the etched channel system (30 μm wide, 10 μm deep) and the lower plate the platinum electrode pairs (20 × 30 μm each). The carrier liquids are fed through the holes into the system using electroosmotic/electrophoretic flow. The flow in the system can be controlled by applying appropriate voltages to the different external electrolyte

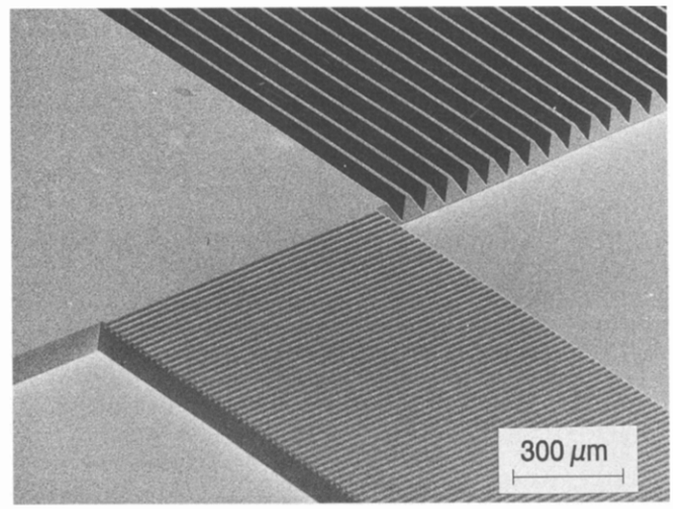

Fig. 4. Scanning electron micrograph of a micromachined silicon structure, demonstrating the precision and reproducibility of the process.

containers and to the electrodes at the end of some of the channels. The sample is injected, automatically diluted, derivatized and then injected into the electrophoresis capillary. The injection procedure is performed in four steps (see Fig. 5B): (1) The sample is directed through the first injection volume and then to waste. (2) The carrier takes the sample plug into the mixing chamber, where a reproducible tailing of the peak is formed, and through the second injection

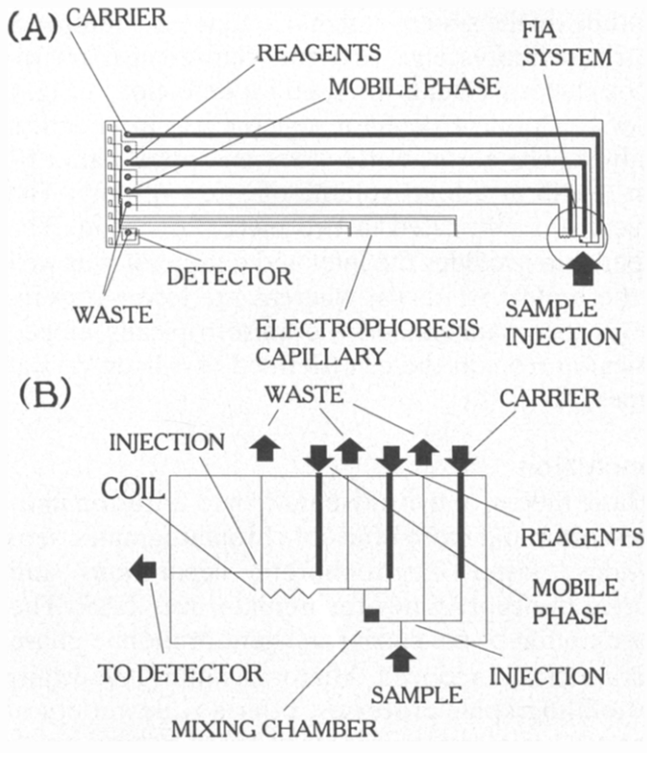

Fig. 5. Layout (A) and detail (B) of an electroosmotically driven flow injection analysis device used for automated injection, dilution and capillary electrophoresis of a sample.

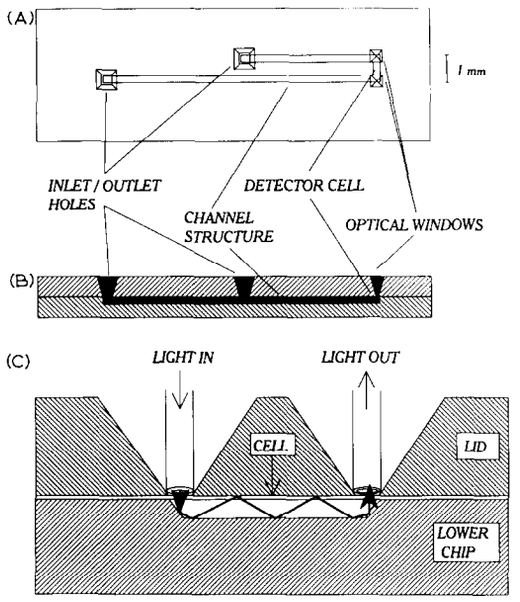

Fig. 6. Layout (A) and cross-sectional view (B and C) of an optical, small volume flow cell. The optical pathlength is considerably larger than the cross-section of the channel.

volume to another waste outlet. (3) At a preselected time (*i.e.* dilution factor), the second carrier containing a reagent takes the diluted sample plug into a mixing coil, through the third injection volume and to another waste outlet. (4) Finally the mobile phase carries the sample towards the detector. Electrophoretic separation could be effected in this channel depending on the system design. Conductivity, amperometric or fluorescence (external fluorescence microscope) measurements are used for detection[23]. Fig. 6 shows an optical detector cell for use in chemical analysis. The absorption follows an optical path of 1 mm length at a total volume of a few nl only. The structure is fabricated in two pieces of silicon. The upper chip provides the inlet and outlet holes as well as the optical windows, whereas the lower chip includes the channels and the anisotropically etched optical mirrors in the cell (defined by silicon crystal planes)[24].

Conclusion

Basic theory of hydrodynamics and diffusion indicates faster and more efficient chromatographic separations, faster electrophoretic separations and shorter transport times for miniaturized TAS. The consumption of the carrier, reagent or mobile phase is dramatically reduced. Micromachining, especially photolithographic processes, offer a wide variety of analytical microstructures which were absolutely inaccessible until now.

Because there has been little direct experimental evidence to date supporting the above theory, one could argue that miniaturized chemical analysis systems are just a fashionable craze. However, it is difficult to foresee the impact a new technological concept will have when it is in its early stages of development. After all, the early experiments with microelectronics did not predict the overwhelming success of this technology either. The history of silicon chip technology teaches that a well documented and theoretically positive idea can be accepted within a few decades. An inherent problem is that a heavy investment in R&D has to be made if positive results are to be obtained at all. Even easy fabrication and analytical chemical functionality will not suffice to make miniaturized total chemical analysis systems part of the next century's technology. A *swing of political opinion* in favour of this research, a strong *financial support* for R&D, a healthy *competition among research labs* worldwide, and a stronger interest in the *competitive marketing* of these new products in a >5 billion US$ per annum market would certainly trigger an increased rate of development in this field.

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Rapid signal processing techniques for Fourier transform infrared remote sensing

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A description is given of digital filtering and pattern recognition methods that implement an automated detection algorithm for passive Fourier transform infrared (FTIR) remote sensing data. The digital filtering step allows spectral information to be extracted from the interferogram data without the use of the Fourier transform. The detection is performed with only a 76-point segment of the FTIR interferogram, thereby simplifying the data collection requirements of the spectrometer.

Introduction

Fourier transform infrared (FTIR) remote sensors are environmental monitoring devices that employ an interferometer-based optical system to collect infrared spectral data in the outdoor environment. The resulting data can be analyzed for the presence of characteristic spectral bands corresponding to target analytes.

Infrared remote sensors can be operated in two ways. The spectrometer can be used with an external blackbody infrared source, or the sensor can be employed in a passive mode simply to collect whatever ambient infrared background radiation is present in the field of view. The passive technique is the more flexible of the two implementations, as the sensor consists of a single unit.

Specific application environments for passive FTIR sensors include monitoring at hazardous waste sites, leak detection at chemical plants, and regulatory monitoring of smokestack emissions. In these applications, the spectrometer can be positioned in a stationary configuration or mounted in a ground or airborne vehicle. The goal of the analysis in each of these applications is the automated detection of specific target analytes.

Two fundamental problems limit the applicability of passive FTIR sensors in demanding monitoring applications. First, the sensor must be rugged enough to operate under the conditions required for the application. Second, in the passive FTIR experiment, no stable infrared spectral background exists for use in processing the collected data. Standard laboratory spectral processing techniques that employ a background or reference spectrum cannot be used.

The most fragile component of a typical FTIR remote sensor is the interferometer drive mechanism, which must allow the collection of a stable interferogram of 1024 or 2048 points. The required interferogram length is dictated by the spectral resolution required to detect the target analyte(s) of interest. This relationship between interferogram length and spectral resolution derives from an inherent characteristic of the fast Fourier transform (FFT), the data processing tool used to obtain infrared spectra from the collected interferograms.

One aproach to increasing the potential ruggedness of an FTIR remote sensor is to adopt a simplified 'short-scan' interferometer design. The drive mechanism for such a system would allow only the collection of a 100–200 point interferogram segment. Conceptually, this system would be much more rugged than a conventional design as the moving mirror of the interferometer would need to maintain optical alignment for only a very short distance. The drawback to such a system is that a conventional spectral-based analysis cannot be performed, as the

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