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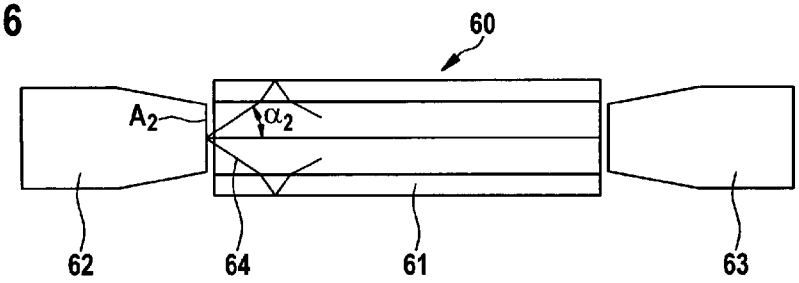
(54) Title: WAVEGUIDE CELL WITH ENHANCED NUMERICAL APERTURE

Fig. 6



(57) Abstract: A waveguide cell (60) is described, the waveguide cell (60) comprising a capillary tubing (61) enclosing a cell volume of the waveguide cell (60), the capillary tubing (61) having a first end and a second end opposite to the first end, a fluid inlet located at the first end of the capillary tubing, a fluid outlet located at the second end of the capillary tubing, a first optical fiber (62) located at the first end of the capillary tubing, the first optical fiber being configured for coupling light into the cell volume of the waveguide cell, the first optical fiber being implemented as a first tapered optical fiber, and a second optical fiber (63) located at the second end of the capillary tubing, the second optical fiber being configured for uncoupling light from the cell volume of the waveguide cell, the second optical fiber being implemented as a second tapered optical fiber.

WAVEGUIDE CELL WITH ENHANCED NUMERICAL APERTURE

BACKGROUND ART

[0001] The present invention relates to a waveguide cell, to a photometric apparatus, and to a separation system. The present invention further relates to a method of determining an optical property of a liquid in a waveguide cell.

[0002] US Patent 4,392,712 describes a light distributor comprising a plurality of optical fibers each having a tapered portion. International Patent application WO 94/04892 describes spectroscopic systems for the analysis of small and very small quantities of substances. US Patent 6,281,975 discloses a capillary flow cell with bulbous ends. US Patent 6,542,231 relates to a fiber-coupled liquid sample analyzer with liquid flow cell. International Patent application WO 2009/043968 describes an active optical fiber and a method for fabricating an active optical fiber. International Patent application WO 2009/143217 discloses light-guiding flow cells and analytical devices using the same.

DISCLOSURE

[0003] It is an object of the invention to provide an improved liquid core waveguide cell and a corresponding method of determining an optical property of a liquid in a waveguide cell. The object is solved by the independent claim(s). Further embodiments are shown by the dependent claim(s).

[0004] A waveguide cell according to an embodiment of the present invention comprises a capillary tubing enclosing a cell volume of the waveguide cell, the capillary tubing having a first end and a second end opposite to the first end, a fluid inlet located at the first end of the capillary tubing, a fluid outlet located at the second end of the capillary tubing, a first optical fiber located at the first end of the capillary tubing, the first optical fiber being configured for coupling light into the cell volume of the waveguide cell, the first optical fiber being implemented as a first tapered optical fiber, and a second optical fiber located at the second end of the capillary tubing, the second optical fiber being configured for uncoupling light from the cell volume of the waveguide cell, the second optical fiber being implemented as a second tapered

optical fiber.

[0005] According to embodiments of the present invention, the first optical fiber and the second optical fiber are implemented as tapered optical fibers. Compared to conventional optical fibers, tapered optical fibers are capable of transforming numerical aperture. In particular, a tapered optical fiber is capable of transforming a standard numerical aperture of light launched into an input side of the optical fiber into an augmented numerical aperture of light obtained at the fiber's tapered end. The capillary tubing of the waveguide cell can accept large numerical apertures which are considerably higher than the numerical apertures provided by conventional optical fibers.

[0006] By employing light with large numerical aperture, light throughput is increased, and signal-to-noise ratio of the detected signals is improved as well. The increased light throughput permits to reduce the cell volume of the waveguide cell. Thus, waveguide cells with a cell volume below 10 µl or even below 4 µl can be realized. The smaller the cell volume, the better the resolution of the respective waveguide cell.

[0007] Especially for small cell volumes below 10 µl, the use of tapered optical fibers has several advantages. Because of the small cell volume, the chromatographic resolution of the waveguide cell is quite good. The light throughput is higher than before, and therefore, even for waveguide cells with small cell volumes, a good signal-to-noise ratio is obtained. Furthermore, by selecting a capillary tubing having a minimum length, it is possible to realize a waveguide cell with good sensitivity.

[0008] According to a preferred embodiment, the capillary tubing is capable of accepting a light cone with a numerical aperture of at least 0.4.

[0009] According to a preferred embodiment, the first tapered optical fiber has a numerical aperture of at least 0.4. According to a further preferred embodiment, the second tapered optical fiber has a numerical aperture of at least 0.4.

[0010] According to a preferred embodiment, the waveguide cell is configured to guide light by total internal reflection.

[0011] According to a preferred embodiment, the capillary tubing is an air-clad capillary. According to a preferred embodiment, the capillary tubing is an air-clad capillary that can accept light with a numerical aperture of 0.4 or more. According to a preferred embodiment, the capillary tubing is an air-clad capillary, with light being reflected at an outer glass-air boundary of the capillary tubing.

[0012] According to a preferred embodiment, the cell volume is less than 10 microliter. According to a preferred embodiment, the cell volume is less than 4 microliter.

[0013] According to a preferred embodiment, an inner diameter of the capillary tubing is below 700 µm.

[0014] According to a preferred embodiment, the length of the capillary tubing is in a range between 8 mm and 60 mm. According to a preferred embodiment, the length of the capillary tubing is in a range between 8 mm and 12 mm.

[0015] According to a preferred embodiment, the fluid inlet is configured for supplying a flow of liquid to the cell volume of the waveguide cell. According to a preferred embodiment, the fluid outlet is configured for withdrawing a flow of liquid from the cell volume of the waveguide cell.

[0016] According to a preferred embodiment, the first tapered optical fiber is configured for transforming a numerical aperture of light.

[0017] According to a preferred embodiment, the first tapered optical fiber is configured for receiving light at a regular numerical aperture and for transforming said light into light having an augmented numerical aperture.

[0018] According to a preferred embodiment, the first tapered optical fiber is configured for transforming a regular numerical aperture of light launched into the first tapered optical fiber at a first end into an increased numerical aperture of light at a tapered end of the first tapered optical fiber.

[0019] According to a preferred embodiment, the second tapered optical fiber is configured for transforming a numerical aperture of light.

[0020] According to a preferred embodiment, the second tapered optical fiber is configured for receiving light at an augmented numerical aperture at its tapered end and for transforming said light into light having a regular numerical aperture.

[0021] According to a preferred embodiment, the second tapered optical fiber is configured for transforming an augmented numerical aperture of light received at its tapered end into a regular numerical aperture.

[0022] According to a preferred embodiment, the second optical fiber is configured for receiving light having an augmented numerical aperture at its tapered end and for transforming said augmented numerical aperture into a regular numerical aperture.

[0023] According to a preferred embodiment, the enhanced numerical aperture of the first tapered optical fiber causes an increase of light throughput of the waveguide cell.

[0024] According to a preferred embodiment, the enhanced numerical aperture of the first tapered optical fiber causes an increase of light throughput of the waveguide cell and a corresponding increase of photo current.

[0025] According to a preferred embodiment, the enhanced numerical aperture of the first tapered optical fiber causes a reduction of noise of a detected signal.

[0026] According to a preferred embodiment, the enhanced numerical aperture of the first tapered optical fiber causes an improvement of a signal-to-noise ratio of a detected signal.

[0027] According to a preferred embodiment, the enhanced numerical aperture of light provided by the first tapered optical fiber causes an increase of light throughput and a corresponding increase of photo current, which in turn leads to an improved signal-to-noise ratio.

[0028] According to a preferred embodiment, the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an increase of light throughput.

[0029] According to a preferred embodiment, the enhanced numerical aperture of

light received by the second tapered optical fiber corresponds to an increase of light throughput and a corresponding increase of photo current.

[0030] According to a preferred embodiment, the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to a reduction of noise of a detected signal.

[0031] According to a preferred embodiment, the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an improvement of signal-to-noise ratio of a detected signal.

[0032] According to a preferred embodiment, the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an increase of light throughput and a corresponding increase of photo current, which in turn leads to an improved signal-to-noise ratio.

[0033] According to a preferred embodiment, the waveguide cell is used in at least one of these application areas: absorbance spectroscopy, Raman spectroscopy, fluorescence spectroscopy, high performance liquid chromatography. capillary electrophoresis.

[0034] A photometric apparatus according to an embodiment of the present invention is configured for determining an optical property of a liquid, the photometric apparatus comprising a light source; a liquid core waveguide cell according to any of the preceding claims; and a spectroscopic detection unit.

[0035] A fluid separation system according to embodiments of the present invention is configured for separating compounds of a sample fluid in a mobile phase, the fluid separation system comprising: a mobile phase drive, preferably a pumping system, configured to drive the mobile phase through the fluid separation system; a separation unit, preferably a chromatographic column, configured for separating compounds of the sample fluid in the mobile phase; and a photometric apparatus according to the preceding claim, the photometric apparatus being configured to detect separated compounds of the sample fluid.

[0036] Embodiments of the present invention might be embodied based on most

conventionally available HPLC systems, such as the Agilent 1290 Series Infinity system, Agilent 1200 Series Rapid Resolution LC system, or the Agilent 1100 HPLC series (all provided by the applicant Agilent Technologies - see www.agilent.com - which shall be incorporated herein by reference).

[0037] One embodiment of an HPLC system comprises a pumping apparatus having a piston for reciprocation in a pump working chamber to compress liquid in the pump working chamber to a high pressure at which compressibility of the liquid becomes noticeable.

[0038] One embodiment of an HPLC system comprises two pumping apparatuses coupled either in a serial or parallel manner. In the serial manner, as disclosed in EP 309596 A1, an outlet of the first pumping apparatus is coupled to an inlet of the second pumping apparatus, and an outlet of the second pumping apparatus provides an outlet of the pump. In the parallel manner, an inlet of the first pumping apparatus is coupled to an inlet of the second pumping apparatus, and an outlet of the first pumping apparatus is coupled to an outlet of the second pumping apparatus, thus providing an outlet of the pump. In either case, a liquid outlet of the first pumping apparatus is phase shifted, preferably essentially 180 degrees, with respect to a liquid outlet of the second pumping apparatus, so that only one pumping apparatus is supplying into the system while the other is intaking liquid (e.g. from the supply), thus allowing to provide a continuous flow at the output. However, it is clear that also both pumping apparatuses might be operated in parallel (i.e. concurrently), at least during certain transitional phases e.g. to provide a smooth(er) transition of the pumping cycles between the pumping apparatuses. The phase shifting might be varied in order to compensate pulsation in the flow of liquid as resulting from the compressibility of the liquid. It is also known to use three piston pumps having about 120 degrees phase shift.

[0039] The separating device preferably comprises a chromatographic column providing the stationary phase. The column might be a glass or steel tube (e.g. with a diameter from 50 µm to 5 mm and a length of 1 cm to 1 m) or a microfluidic column (as disclosed e.g. in EP 1577012 A1 or the Agilent 1200 Series HPLC-Chip/MS System provided by the applicant Agilent Technologies, see e.g.

http://www.chem.agilent.com/Scripts/PDS.asp?lPage=38308). For example, a slurry can be prepared with a powder of the stationary phase and then poured and pressed into the column. The individual components are retained by the stationary phase differently and separate from each other while they are propagating at different speeds through the column with the eluent. At the end of the column they elute one at a time. During the entire chromatography process the eluent might be also collected in a series of fractions. The stationary phase or adsorbent in column chromatography usually is a solid material. The most common stationary phase for column chromatography is silica gel, followed by alumina. Cellulose powder has often been used in the past. Also possible are ion exchange chromatography, reversed-phase chromatography (RP), affinity chromatography or expanded bed adsorption (EBA). The stationary phases are usually finely ground powders or gels and/or are microporous for an increased surface, though in EBA a fluidized bed is used.

[0040] The mobile phase (or eluent) can be either a pure solvent or a mixture of different solvents. It can be chosen e.g. to minimize the retention of the compounds of interest and/or the amount of mobile phase to run the chromatography. The mobile phase can also been chosen so that the different compounds can be separated effectively. The mobile phase might comprise an organic solvent like e.g. methanol or acetonitrile, often diluted with water. For gradient operation water and organic is delivered in separate bottles, from which the gradient pump delivers a programmed blend to the system. Other commonly used solvents may be isopropanol, THF, hexane, ethanol and/or any combination thereof or any combination of these with aforementioned solvents.

[0041] The sample fluid might comprise any type of process liquid, natural sample like juice, body fluids like plasma or it may be the result of a reaction like from a fermentation broth.

[0042] The fluid is preferably a liquid but may also be or comprise a gas and/or a supercritical fluid (as e.g. used in supercritical fluid chromatography – SFC – as disclosed e.g. in US 4,982,597 A).

[0043] The pressure in the mobile phase might range from 2-200 MPa (20 to 2000 bar), in particular 10-150 MPa (100 to 1500 bar), and more particular 50-120 MPa (500

to 1200 bar).

[0044] The HPLC system might further comprise a sampling unit for introducing the sample fluid into the mobile phase stream, a detector for detecting separated compounds of the sample fluid, a fractionating unit for outputting separated compounds of the sample fluid, or any combination thereof. Further details of HPLC system are disclosed with respect to the aforementioned Agilent HPLC series, provided by the applicant Agilent Technologies, under www.agilent.com which shall be in cooperated herein by reference.

[0045] According to embodiments of the present invention, a method of determining an optical property of a liquid in a waveguide cell, the waveguide cell comprising a capillary tubing that encompasses a cell volume, the method comprising coupling light into the cell volume of the waveguide cell via a first tapered optical fiber at a first end of the capillary tubing, and uncoupling the light, after the light has traversed the cell volume, from the cell volume of the waveguide cell via a second tapered optical fiber at a second end of the capillary tubing, the second end being opposite to the first end.

[0046] Embodiments of the invention can be partly or entirely embodied or supported by one or more suitable software programs, which can be stored on or otherwise provided by any kind of data carrier, and which might be executed in or by any suitable data processing unit. Software programs or routines can be preferably applied in or by the control unit.

BRIEF DESCRIPTION OF DRAWINGS

[0047] Other objects and many of the attendant advantages of embodiments of the present invention will be readily appreciated and become better understood by reference to the following more detailed description of embodiments in connection with the accompanied drawing(s). Features that are substantially or functionally equal or similar will be referred to by the same reference sign(s). The illustration in the drawing is schematically.

[0048] Fig. 1 shows a setup of a liquid core waveguide cell;

[0049] Fig. 2 shows the properties of a waveguide cell in dependence on the

proportions of the respective waveguide cell;

[0050] Fig. 3 shows a waveguide cell with conventional optical fibers;

[0051] Fig. 4 indicates a numerical aperture of a waveguide cell filled with solvent as a function of the refractive index n_{ext} outside of the waveguide cell;

[0052] Fig. 5 shows a tapered optical fiber;

[0053] Fig. 6 shows a waveguide cell equipped with two tapered optical fibers, the waveguide cell having a cell volume of 4 µl;

[0054] Fig. 7 shows a waveguide cell with two tapered optical fibers, the waveguide cell having a cell volume of 1 µl;

[0055] Fig. 8 depicts accessible concentration limit of detection (CLOD) as a function of cell volume for two different waveguide cells; and

[0056] Fig. 9 shows a CLOD (concentration limit of detection) enhancement factor as a function of cell volume.

[0057] In detail, Fig. 1 shows a liquid core waveguide cell configured for determining an optical property of a solution. The waveguide cell 1 comprises a capillary tubing 2 that contains the liquid. The capillary tubing 2 may e.g. be made of glass or fused silica. A first fitting 3 is fixed to a first end of the capillary tubing 2, and a second fitting 4 is fixed to a second end of the capillary tubing 2, which is opposite of the first end. The first fitting 3 comprises an inlet 5 configured for supplying a liquid to the waveguide cell 1, as indicated by arrow 6. Via the inlet 5, the waveguide cell 1 may be filled with a liquid that is to be analyzed. The second fitting 4 comprises an outlet 7 configured for withdrawing liquid from the waveguide cell 1, as indicated by arrow 8.

[0058] For determining an optical property of the liquid contained in the capillary tubing 2, the waveguide cell 1 further comprises a first optical fiber 9 that is mounted to the first fitting 3. The first optical fiber 9 is configured for emitting a light cone 10. The light emitted by the first optical fiber 9 traverses the liquid contained in the capillary tubing 2, with the light being totally reflected multiple times when traversing the liquid. In case the capillary tubing 2 is made of glass or fused silica, the total reflection occurs

at the outer glass/air interface 11 of the capillary tubing 2. The waveguide cell 1 further comprises a second optical fiber 12 configured for receiving light after the light has passed through the liquid in the capillary tubing 2. The second optical fiber 12 is configured to guide the received light to a detection unit. For example, the detection unit may be configured to determine absorbance $A=\log(I_0/I)$ as a function of wavelength. A waveguide cell of the kind shown in Fig. 1 may e.g. be used in diverse spectroscopic applications, for example in absorbance spectroscopy, in Raman spectroscopy and in fluorescence spectroscopy. A waveguide cell of the kind shown in Fig. 1 may also be applied in high performance liquid chromatography (HPLC) or in capillary electrophoresis (CE), in particular for detecting and analyzing various different components of a liquid sample.

[0059] Figs. 2A, 2B and 2C illustrate various different design considerations for designing a liquid core waveguide cell. In Fig. 2A, a waveguide cell 18 is shown, with the waveguide cell 18 comprising a first optical fiber 19, a capillary tubing 20 and a second optical fiber 21. In Fig. 2A, the dimensions of the capillary tubing are chosen such that the length L_1 of the capillary tubing 20 is quite small, whereas the inner diameter ID_1 is comparatively large. Due to the large inner diameter ID_1 of the capillary tubing 20, light throughput is quite large, because light throughput is proportional to $A \cdot NA^2$, with A being the cross-sectional area of the optical fiber, and with NA being the numerical aperture of the light provided by the first optical fiber 19. In terms of light throughput, the waveguide cell shown in Fig. 2A is convincing.

[0060] Furthermore, in Fig. 2A, the length L_1 of the capillary tubing 20 is quite small. Therefore, the cell volume of the waveguide cell is quite small as well, which is advantageous in view of the waveguide cell's resolution: A comparatively small cell volume corresponds to a high resolution when analyzing a flow of liquid. As a rule of thumb, the cell volume should not exceed 1/10 of the sample volume.

[0061] The length L_1 of the waveguide cell determines the waveguide cell's sensitivity. The absorbance A can be expressed in terms of the waveguide cell's sensitivity S and the concentration c of a light-absorbing moiety as follows:

$$A = \log\left(\frac{I_0}{I}\right) = S \cdot c = \varepsilon \cdot L \cdot c$$

[0062] The last relationship results from the law of Lambert-Beer, which can be written as follows:

$$I = I_0 \cdot 10\text{^}(-\varepsilon \cdot L \cdot c)$$

[0063] In this formula, ε is an extinction coefficient, and L is the length of the waveguide cell. The sensitivity S of the waveguide cell is directly proportional to the length L of the waveguide cell. Hence, for obtaining a waveguide cell of good sensitivity, it is necessary that the waveguide cell has a certain length. The waveguide cell shown in Fig. 2A, which has a relatively small length L_1, is therefore not suitable for obtaining a good sensitivity. In summary, a waveguide cell like the one shown in Fig. 2A, which has a comparatively large inner diameter ID_1 and a small length L_1, is characterized by good chromatographic resolution, good light throughput and rather low sensitivity.

[0064] In Fig. 2B, another waveguide cell 22 is shown. The waveguide cell 22 comprises a first optical fiber 23, a capillary tubing 24 and a second optical fiber 25. In the waveguide cell 22 of Fig. 2B, both the inner diameter ID_2 and the length L_2 are rather large. Because of the large inner diameter ID_2, the light throughput of the waveguide cell 22 is good. Furthermore, as the length L_2 is quite large, the sensitivity $S = L_2 \cdot \varepsilon$ is quite good as well (with ε denoting the extinction coefficient). Therefore, the waveguide cell 22 may detect small concentrations of a certain sample component or analyte. Hence, in a waveguide cell 22 as shown in Fig. 2B, both the light throughput and the sensitivity of the waveguide cell 22 are satisfactory. However, both the inner diameter ID_2 and the length L_2 of the waveguide cell 22 are rather large, and therefore, the cell volume is quite large as well. This implies that the resolution of the waveguide cell 22 is quite low. In terms of resolution, the waveguide cell 22 shown in Fig. 2B does not yield satisfactory results.

[0065] To achieve a satisfactory resolution, it is desirable to reduce the cell volume of the waveguide cell. However, in order not to impair sensitivity, the length of the waveguide cell should be maintained. Hence, the cell's inner diameter as well as the

diameter of the fiber(s) have to be reduced.

[0066] A waveguide cell with reduced inner diameter is shown in Fig. 2C. The waveguide cell 26 comprises a first optical fiber 27, a capillary tubing 28 and a second optical fiber 29. The length L_3 of the capillary tubing 28 is quite large, whereas the inner diameter ID_3 of the capillary tubing 28 is relatively small. Due to the small inner diameter ID_3, the cell volume of the waveguide cell 26 is small, and accordingly, the resolution of the waveguide cell 26 is quite good. The length L_3 is quite large, and accordingly, the sensitivity $S = L_3 \cdot \varepsilon$ is satisfactory (with ε denoting the extinction coefficient). However, due to the small inner diameter ID_3, the light throughput of the waveguide cell 26 is too small, and as a consequence, the signal-to-noise ratio is not satisfactory.

[0067] None of the waveguide cells shown in Figs. 2A, 2B and 2C provides a combination of good sensitivity, high resolution and acceptable light throughput. Embodiments of the present invention are aimed at providing a waveguide cell with good sensitivity, high resolution and acceptable light throughput.

[0068] Fig. 3 shows the light path in a waveguide cell 30. The waveguide cell 30 comprises a first optical fiber 31, a capillary tubing 32 and a second optical fiber 33. The first optical fiber 31 is configured for emitting a light cone 34. The second optical fiber 33 is configured for receiving the light after it has passed through the liquid contained in the capillary tubing 32. The waveguide cell 30 may e.g. have a cell volume of 10 µl. In order to achieve a good sensitivity, the length of the waveguide cell 30 may be chosen as 10 mm. The angle α_1 corresponds to half of the aperture angle of the light cone 34. The numerical aperture NA_1 of the light cone 34 emitted by the first optical fiber 31 can be expressed as follows:

$$NA_1 = n_{solv} \cdot \sin(\alpha_1)$$

[0069] with n_{solv} denoting the index of refraction of the liquid contained in the capillary tubing 32, and with α_1 denoting half of the aperture angle of the light cone 34. In the example of Fig. 3, the numerical aperture NA_1 is determined by the properties of the first optical fiber 31. For a typical optical fiber, the numerical aperture lies in the range between 0.21 and 0.25. Hence, in Fig. 3, the numerical aperture NA_1 of the light

cone 34 lies in the range between 0.21 and 0.25. Once the numerical aperture NA_1 is known, the light throughput T_1, which is also referred to as the "etendue", is proportional to:

$$T_1 \propto A_1 \cdot n_{solv}{}^2 \cdot \Omega_1$$

with A_1 denoting the cross-sectional area of the optical fiber 31, with n_{solv} denoting the refractive index of the liquid, and with Ω_1 denoting a solid angle of the light cone 34. The solid angle Ω_1 can be expressed as $\Omega_1 = \pi \cdot \sin(\alpha_1)^2$, and therefore:

$$T_1 \propto A_1 \cdot NA_1{}^2$$

with A_1 denoting the cross-sectional area of the optical fiber 31, and with NA_1 being the numerical aperture of the light cone 34. From this formula, it can be seen that the light throughput T_1 is limited by the rather small numerical aperture NA_1 of the first optical fiber 31, which is typically in the range between 0.21 and 0.25.

[0070] In case the capillary tubing 32 is filled with an aqueous solution, the refractive index n_{solv} of the aqueous solution may be approximately 1.33. In case the capillary tubing 32 is made of glass, the refractive index n_{tub} of the capillary tubing 32 is 1.5, and in case the capillary tubing 32 is made of fused silica, the refractive index n_{tub} is 1.45. Therefore, light rays in the light cone 34 that hit the inner surface of the capillary tubing 32 are refracted in the direction towards the normal 35, in accordance with the law of Snellius:

$$n_{solv} \cdot \sin(\delta_1) = n_{tub} \cdot \sin(\delta_2)$$

In this formula, δ_1 is the angle of incidence, and δ_2 is the angle of refraction.

[0071] Next, the refracted light ray hits the outer surface of the capillary tubing 32, and there, the light ray is totally reflected, because the angle δ_2 is larger than the angle of total reflection. Hence, the light rays in the light cone 34 are totally reflected at the outer surface of the capillary tubing 32 and remain within the cell volume of the waveguide cell 30.

[0072] In the example of Fig. 3, the numerical aperture NA_1 of the light cone 34 is

mainly determined by the properties of the first optical fiber 31. In fact, the capillary tubing 32 can accept a light cone 36 having a numerical aperture that is much larger than the numerical aperture NA_1 of the light cone 34 provided by the first optical fiber 31. Especially in case of an air-clad capillary, the capillary tubing 32 can accept incident light having a numerical aperture that is much larger than a typical numerical aperture of a typical optical fiber. In fact, the capillary tubing 32 can accept incident light having a numerical aperture of 0.4 or even more.

[0073] In the following, we will calculate the upper limit of the numerical aperture that can be accepted by a capillary tubing filled with a liquid.

[0074] The maximum angle of aperture of the light cone 36 corresponds to the angle of total reflection at the outer surface of the capillary tubing 32, which can be calculated as follows:

$$n_{solv} \cdot \sin(\delta_{1min}) = n_{ext}$$

[0075] with n_{solv} being the refractive index of the liquid in the tubing, with n_{ext} denoting the refractive index at the exterior of the tubing, and with δ_{1min} denoting the angle of incidence relative to the capillary tubing 32. The angle δ_{1min} can be expressed as

$$\sin(\delta_{1min}) = \frac{n_{ext}}{n_{solv}}.$$

[0076] The angle α_{1max}, which is shown in Fig. 3, and which corresponds to half of the angle of aperture, can be related to δ_{1min} as follows:

$$\sin(\delta_{1min}) = \cos(\alpha_{1max}).$$

[0077] Hence, the angle α_{1max} can be written as:

$$\alpha_{1max} = \operatorname{acos}\left(\frac{n_{ext}}{n_{solv}}\right).$$

[0078] Now, the maximum angle α_{1max} is known, and hence, the upper limit of the numerical aperture NA_{max} that can be accepted by the capillary tubing 32 can be

written as:

$$NA_{max}(n_{solv}, n_{ext}) = n_{solv} \cdot \sin(\alpha_{1max}) = n_{solv} \cdot \sin\left(a\cos\left(\frac{n_{ext}}{n_{solv}}\right)\right).$$

[0079] In Fig. 4, the upper limit of the acceptable numerical aperture $NA_{max}(n_{solv}, n_{ext})$ is shown as a function of the refractive index n_{ext}, which is the refractive index at the exterior of the capillary tubing 32. The refractive index n_{solv}, which is the refractive index of the liquid in the capillary tubing 32, is equal to 1.33, which corresponds to an aqueous solution. The curve 40 indicates the upper limit of the acceptable numerical aperture NA_{max} as a function of the refractive index n_{ext} at the exterior of the waveguide cell. It can be seen that the curve 40 reaches its maximum value when $n_{ext} = 1$, which is the refractive index of air. With increasing values of n_{ext}, the curve 40 drops continuously and reaches zero when $n_{ext} = 1.33$. Hence, it can be concluded that an air-clad capillary tubing is well suited for accepting incident light having a large numerical aperture of up to 0.88. For achieving a large light throughput, it is therefore recommendable to employ a light source having a large numerical aperture, because the larger the numerical aperture, the larger the light throughput will be.

[0080] As detailed in the preceding, the ideal waveguide cell requires fibers of large $A \cdot NA^2$ product together with small cross-sectional area at cell input allowing for a small cell diameter. A high NA tapered optical fiber is well suited for this purpose.

[0081] Fig. 5 shows a tapered optical fiber 50 comprising a core 51 surrounded by a cladding 52. At the input side of the tapered optical fiber 50, the diameter d_{in} of the core 51 may e.g. be 400 µm, and the clad/core ratio may e.g. be 1.1. At the output side of the tapered optical fiber 50, a tapered tip 53 is formed, the tapered tip 53 having a reduced diameter d_{out} . In general, the tapered tip 53 is formed by at least partly heating the optical fiber, pulling the ends of the optical fiber apart and cutting the optical fiber at the thinned portion. The core 51 may e.g. consist of fused silica, whereas the cladding 52 may be made of fluorine doped fused silica.

[0082] When light traverses the optical fiber 50 shown in Fig. 5, light throughput T, also referred to as the etendue, is a conserved quantity. Therefore, the following relationship is fulfilled:

$$A_{in} \cdot NA_{in}^{2} = A_{out} \cdot NA_{out}^{2},$$

with A_{in} denoting a cross-sectional area of the optical fiber at the input side, with NA_{in} being the numerical aperture of light launched into the optical fiber at the input side, with A_{out} denoting the fiber's cross-sectional area at the output side (i.e. at the tapered end 53), and with NA_{out} being the numerical aperture at the output side. With $A_{in} \propto d_{in}^{2}$ and $A_{out} \propto d_{out}^{2}$, the above relationship can be expressed as:

$$d_{in} \cdot NA_{in} = d_{out} \cdot NA_{out}$$

[0083] Hence, when launching light at standard numerical aperture of e.g. NA_{in} =0.22 into the large diameter d_{in} at the input side of the tapered optical fiber 50 of high numerical aperture, light of increased numerical aperture NA_{out} is obtained at the tapered end 53 of the optical fiber. Hence, the numerical aperture $NA_{out} = n_{solv} \cdot \sin(\alpha)$ at the output side is rather large. As illustrated in Fig. 5, the numerical aperture of light provided by the tapered optical fiber 50 is much larger than the numerical aperture of a regular optical fiber. The tapered optical fiber 50 is capable of transforming a standard numerical aperture of e.g. NA_{in} = 0.22 into an augmented numerical aperture NA_{out}, with the ratio of NA_{out} and NA_{in} being determined by the ratio of the diameters d_{in} and d_{out} at the fiber's input and output side.

[0084] Launching light at standard numerical aperture of e.g. NA_{in} = 0.22 into the large diameter d_{in} input side of a tapered fiber of high numerical aperture NA_{fiber} allows for a reduction of the output diameter d_{out} and, as a consequence, for a reduction of cell volume. For example, by means of tapering a high NA fiber of NA=0.66 illuminated at NA_{in} = 0.22 at the input side, a reduction of output diameter d_{out} by a factor of 3 and thus reduction of cell volume by a factor 9 is feasible while keeping light throughput T constant.

[0085] Therefore, the tapered optical fiber shown in Fig. 5 is well suited for being used in a waveguide cell. A tapered optical fiber of the kind shown in Fig. 5 may be used both for supplying light to the waveguide cell and for receiving light from the waveguide cell. By employing a tapered optical fiber, the waveguide cell's capability of accepting light with a large numerical aperture is taken advantage of. By providing a

light cone having a large numerical aperture to the waveguide cell, light throughput of the waveguide cell is considerably increased, and the signal-to-noise ratio is improved.

[0086] Fig. 6 shows a waveguide cell 60 according to a first embodiment of the present invention. The waveguide cell 60 comprises a capillary tubing 61, a first tapered optical fiber 62 configured for supplying light to the waveguide cell 60, and a second tapered optical fiber 63 configured for receiving light that has been transmitted through the waveguide cell 60. The length of the capillary tubing 61 is chosen to be 10 mm, which is the same length as in Fig. 3. However, compared to the waveguide cell shown in Fig. 3, the cell volume has been reduced considerably. While the cell volume of the waveguide cell 30 shown in Fig. 3 amounts to 10 µl, the cell volume of the waveguide cell 60 shown in Fig. 6 is equal to 4 µl. Correspondingly, the cross-sectional area A_2 at the tapered tip of the first tapered optical fiber 62 is considerably smaller than the corresponding cross-sectional area A_1 of the optical fiber 31 shown in Fig. 3. The first tapered optical fiber 62 supplies a light cone 64 to the waveguide cell 60, with α_2 denoting half of the angle of aperture of the light cone 64. Due to the tapered end of the first tapered optical fiber 62, the angle α_2 is considerably larger than the corresponding angle α_1 indicated in Fig. 3. As a consequence, the numerical aperture $NA_2 = n_{solv} \cdot \sin(\alpha_2)$ is much larger than the numerical aperture NA_1 of light supplied to the waveguide cell 30. In the waveguide cell 60, light throughput depends both on the cross-sectional area A_2 and on the numerical aperture NA_2 of the light cone 64. The light throughput T_2 is proportional to:

$$T_2 \propto A_2 \cdot NA_2^{\,2},$$

with A_2 denoting the cross-sectional area at the tapered end of the first tapered optical fiber 62 and with NA_2 denoting the numerical aperture of the light cone 64. The cross-sectional area A_2 is considerably smaller than the corresponding cross-sectional area A_1 shown in Fig. 3. Nevertheless, the increased numerical aperture NA_2 overcompensates the reduction of A_2, and because of the large numerical aperture NA_2 of the light cone 64, an acceptable light throughput T_2 is achieved. Hence, by using tapered optical fibers 62, 63, an acceptable light throughput can be obtained even in cases where the cell volume is rather small. Because of the small cell volume, the resolution of the waveguide cell 60 is quite good. Because of the large numerical

aperture of the incident light, the light throughput T_2 is quite good as well. Furthermore, a length of 10 mm is sufficiently large to accomplish a good sensitivity of the waveguide cell 60. In summary, due to the use of tapered optical fibers 62, 63, a waveguide cell 60 with large light throughput, small cell volume and high sensitivity is obtained.

[0087] Fig. 7 shows a waveguide cell 70 according to a second embodiment. The waveguide cell 70 comprises a capillary tubing 71, a first tapered optical fiber 72 configured for supplying light to the waveguide cell 70, and a second tapered optical fiber 73 configured for receiving light that has traversed the waveguide cell 70. The length of the capillary tubing 71 is equal to 10 mm, which is equal to the respective lengths of the waveguide cells shown in Fig. 3 and Fig. 6. However, the cell volume of the waveguide cell 70 has been further reduced. The cell volume of the waveguide cell 70 is about 1 µl. Correspondingly, the cross-sectional area A_3 at the tapered end of the first tapered optical fiber 72 is considerably smaller than the corresponding cross-sectional area A_2 of the tapered end of the first tapered optical fiber 62 shown in Fig. 6. Accordingly, the capillary tubing 71 is quite narrow. To achieve a good light throughput, the numerical aperture of the light cone 74 supplied by the first tapered optical fiber 72 has to be quite large. The angle α_3 indicated in Fig. 7, which is half of the aperture angle, is larger than the corresponding angle α_2 indicated in Fig. 6. Hence, the numerical aperture $NA_3 = n_{solv} \cdot \sin(\alpha_3)$ is also larger than the numerical aperture NA_2. The light throughput T_3 is proportional to:

$$T_3 \propto A_3 \cdot NA_3^2,$$

with A_3 denoting the cross-sectional area at the tapered end of the first tapered optical fiber 72 and with NA_3 denoting the numerical aperture of the light cone 74. Though the cross-sectional area A_3 is considerably smaller than before, the numerical aperture NA_3 has been further increased, and hence, an acceptable light throughput is obtained even for the very narrow capillary tubing 71. By employing tapered optical fibers, waveguide cells with very small cell volumes of for example 1 µl can be realized, which are characterized by an excellent chromatographic resolution. Due to the large numerical aperture NA_3, the light throughput is still acceptable, and the signal-to-noise ratio is quite good. The length of the capillary tubing 71 is equal to 10 mm. As

sensitivity mainly depends on the length of the capillary tubing, the sensitivity of the waveguide cell 70 is as good as in the embodiments shown in Fig. 3 and Fig. 6. By using tapered optical fibers, waveguide cells with very small cell volumes can be realized.

[0088] Fig. 8 shows an accessible concentration limit of detection (CLOD) as a function of cell volume (in µl) both for the case of a waveguide cell equipped with conventional optical fibers and for the case of a waveguide cell equipped with tapered optical fibers. Curve 80 corresponds to a waveguide cell with conventional optical fibers having a rather low numerical aperture of e.g. 0.22. As the cell volume gets smaller, the concentration limit of detection (CLOD) increases strongly.

[0089] Curve 81 corresponds to a waveguide cell with tapered optical fibers having a numerical aperture of 0.66. For cell volumes in the range of about 1 µl to 10 µl, the concentration limit of detection (CLOD) remains constant. Then, as the cell volume becomes smaller than 1 µl, the concentration limit of detection rises as the cell volume becomes smaller. In the entire range between 0.1 µl and 10 µl, the curve 71 is considerably below the curve 80, and hence, it can be concluded that by employing tapered optical fibers, a more sensitive waveguide cell is obtained, which can be used for detecting small concentrations of a certain species. Especially for small cell volumes below 10 µl, a waveguide cell with tapered optical fibers is superior to a waveguide cell with conventional optical fibers.

[0090] In Fig. 9, a CLOD enhancement factor is shown as a function of cell volume, with the CLOD enhancement factor indicating the ratio of the concentration limit of detection (CLOD) of a waveguide cell with tapered optical fibers and a waveguide cell with conventional optical fibers. It can be seen that for a cell volume of 10 µl, the enhancement factor is equal to 1. As cell volume gets smaller, the enhancement factor rises up to 3, and for cell volumes in the range between 0.01 and 1 µl, the enhancement factor is equal to 3.

CLAIMS

1. A waveguide cell (60) comprising

a capillary tubing (61) enclosing a cell volume of the waveguide cell (60), the capillary tubing (61) having a first end and a second end opposite to the first end,

a fluid inlet located at the first end of the capillary tubing (61),

a fluid outlet located at the second end of the capillary tubing (61),

a first optical fiber (62) located at the first end of the capillary tubing (61), the first optical fiber (62) being configured for coupling light into the cell volume of the waveguide cell (60), the first optical fiber (62) being implemented as a first tapered optical fiber, and

a second optical fiber (63) located at the second end of the capillary tubing (61), the second optical fiber (63) being configured for uncoupling light from the cell volume of the waveguide cell (60), the second optical fiber (63) being implemented as a second tapered optical fiber.

2. The waveguide cell of claim 1, comprising at least one of:

the capillary tubing is capable of accepting a light cone with a numerical aperture of at least 0.4;

the first tapered optical fiber has a numerical aperture of at least 0.4;

the second tapered optical fiber has a numerical aperture of at least 0.4.

3. The waveguide cell of claim 1 or any of the above claims, comprising at least one of:

the waveguide cell is configured to guide light by total internal reflection;

the capillary tubing is an air-clad capillary;

the capillary tubing is an air-clad capillary that can accept light with a numerical aperture of 0.4 or more;

the capillary tubing is an air-clad capillary, with light being reflected at an outer glass-air boundary of the capillary tubing.

4. The waveguide cell of claim 1 or any of the above claims, comprising at least one of:

the cell volume is less than 10 microliter;

the cell volume is less than 4 microliter;

an inner diameter of the capillary tubing is below 700 µm;

the length of the capillary tubing is in a range between 8 mm and 60 mm;

the length of the capillary tubing is in a range between 8 mm and 12 mm;

the fluid inlet is configured for supplying a flow of liquid to the cell volume of the waveguide cell;

the fluid outlet is configured for withdrawing a flow of liquid from the cell volume of the waveguide cell.

5. The waveguide cell of claim 1 or any of the above claims, comprising at least one of:

the first tapered optical fiber is configured for transforming a numerical aperture of light;

the first tapered optical fiber is configured for receiving light at a regular numerical aperture and for transforming said light into light having an augmented numerical aperture;

the first tapered optical fiber is configured for transforming a regular numerical aperture of light launched into the first tapered optical fiber at a first end into an increased numerical aperture of light at a tapered end of the first tapered optical fiber;

the second tapered optical fiber is configured for transforming a numerical

aperture of light;

the second tapered optical fiber is configured for receiving light at an augmented numerical aperture at its tapered end and for transforming said light into light having a regular numerical aperture;

the second tapered optical fiber is configured for transforming an augmented numerical aperture of light received at its tapered end into a regular numerical aperture;

the second optical fiber is configured for receiving light having an augmented numerical aperture at its tapered end and for transforming said augmented numerical aperture into a regular numerical aperture.

6. The waveguide cell of claim 1 or any of the above claims, comprising at least one of:

the enhanced numerical aperture of the first tapered optical fiber causes an increase of light throughput of the waveguide cell;

the enhanced numerical aperture of the first tapered optical fiber causes an increase of light throughput of the waveguide cell and a corresponding increase of photo current;

the enhanced numerical aperture of the first tapered optical fiber causes a reduction of noise of a detected signal;

the enhanced numerical aperture of the first tapered optical fiber causes an improvement of a signal-to-noise ratio of a detected signal;

the enhanced numerical aperture of light provided by the first tapered optical fiber causes an increase of light throughput and a corresponding increase of photo current, which in turn leads to an improved signal-to-noise ratio;

the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an increase of light throughput;

the enhanced numerical aperture of light received by the second tapered optical

fiber corresponds to an increase of light throughput and a corresponding increase of photo current;

the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to a reduction of noise of a detected signal;

the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an improvement of signal-to-noise ratio of a detected signal;

the enhanced numerical aperture of light received by the second tapered optical fiber corresponds to an increase of light throughput and a corresponding increase of photo current, which in turn leads to an improved signal-to-noise ratio.

7. The waveguide cell of claim 1 or any of the above claims, wherein the waveguide cell is used in at least one of: absorbance spectroscopy, Raman spectroscopy, fluorescence spectroscopy, high performance liquid chromatography. capillary electrophoresis.

8. A photometric apparatus for determining an optical property of a liquid, the photometric apparatus comprising

a light source;

a liquid core waveguide cell according to any of the preceding claims;

a spectroscopic detection unit.

9. A fluid separation system for separating compounds of a sample fluid in a mobile phase, the fluid separation system comprising:

a mobile phase drive, preferably a pumping system, configured to drive the mobile phase through the fluid separation system;

a separation unit, preferably a chromatographic column, configured for separating compounds of the sample fluid in the mobile phase;

a photometric apparatus according to the preceding claim, the photometric

apparatus being configured to detect separated compounds of the sample fluid.

10. The fluid separation system of the preceding claim, further comprising at least one of:

a sample injector adapted to introduce the sample fluid into the mobile phase;

a collection unit adapted to collect separated compounds of the sample fluid;

a data processing unit adapted to process data received from the fluid separation system;

a degassing apparatus for degassing the mobile phase.

11. A method of determining an optical property of a liquid in a waveguide cell (60), the waveguide cell (60) comprising a capillary tubing (61) that encompasses a cell volume, the method comprising

coupling light into the cell volume of the waveguide cell (60) via a first tapered optical fiber (62) at a first end of the capillary tubing (61),

uncoupling the light, after the light has traversed the cell volume, from the cell volume of the waveguide cell (60) via a second tapered optical fiber (63) at a second end of the capillary tubing (61), the second end being opposite to the first end.

12. The method of the preceding claim, comprising at least one of:

the first tapered optical fiber has a numerical aperture of more than 0.4;

the second tapered optical fiber has a numerical aperture of more than 0.4.

13. A software program or product, preferably stored on a data carrier, for controlling or executing the method of claim 11 or any of the above claims, when run on a data processing system such as a computer.

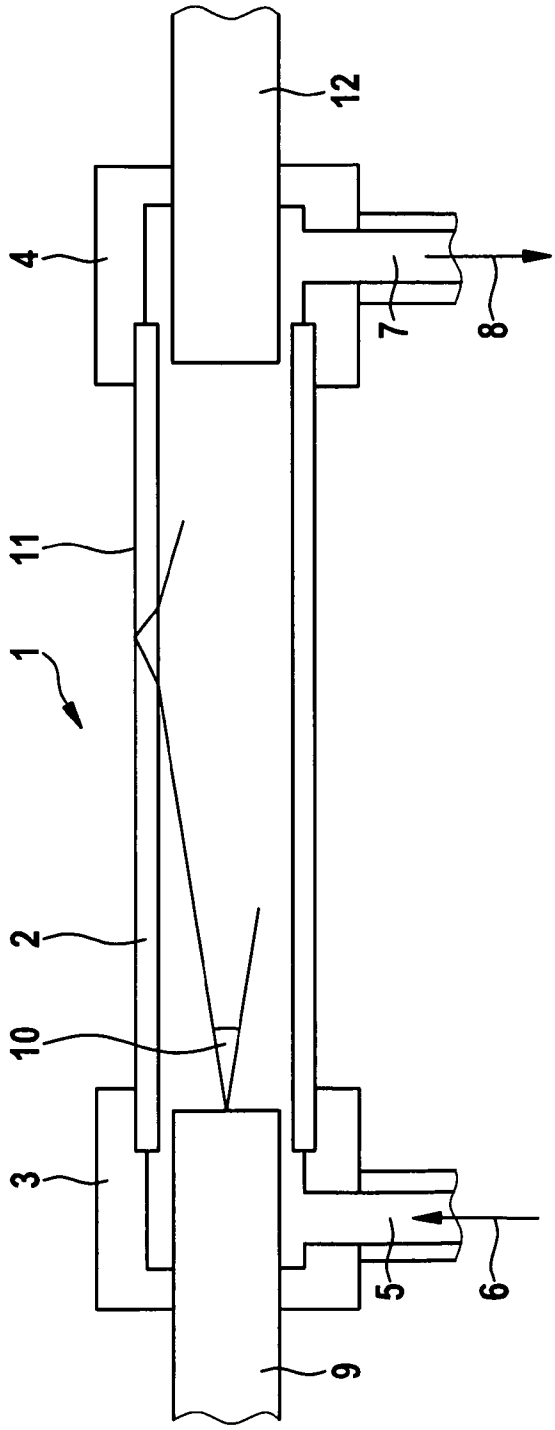


Fig. 1

Fig. 2A

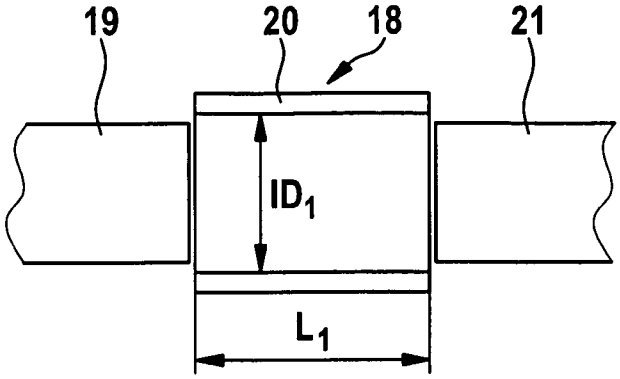


Fig. 2B

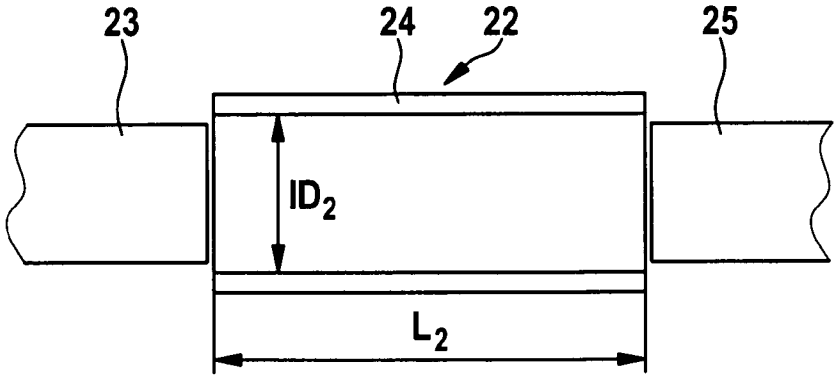
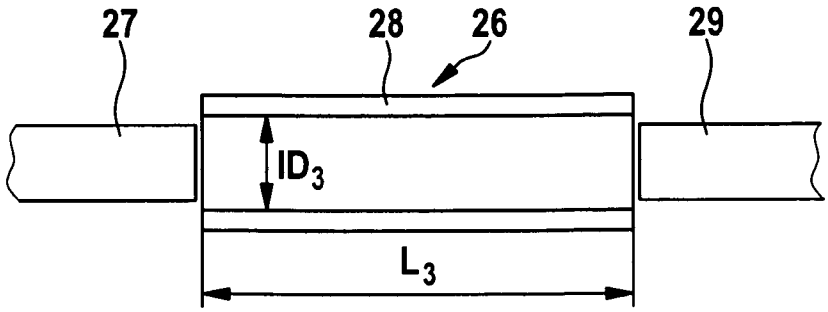


Fig. 2C



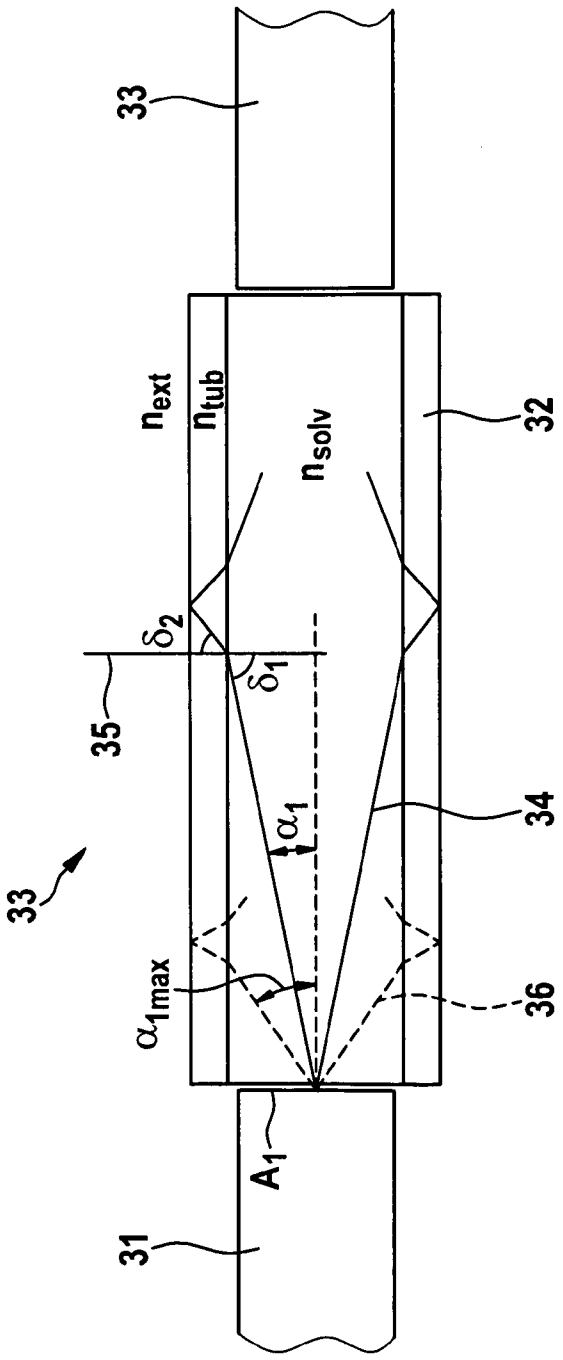

33
n_{ext}
n_{tub}
n_{solv}
32
δ_2
δ_1
35
α_1
34
33
α_{1max}
36
A_1
31

Fig. 3

Fig. 4

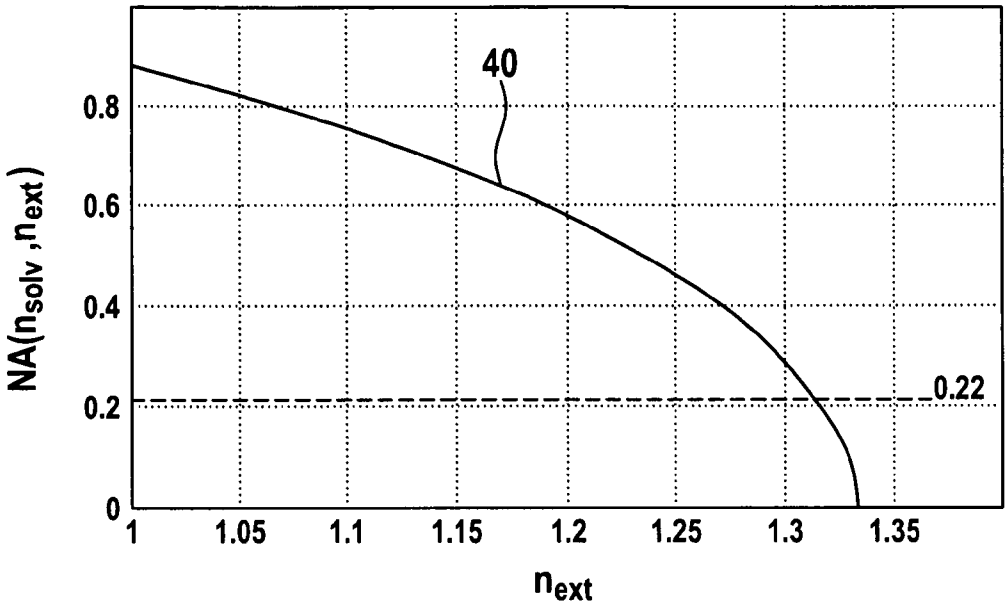
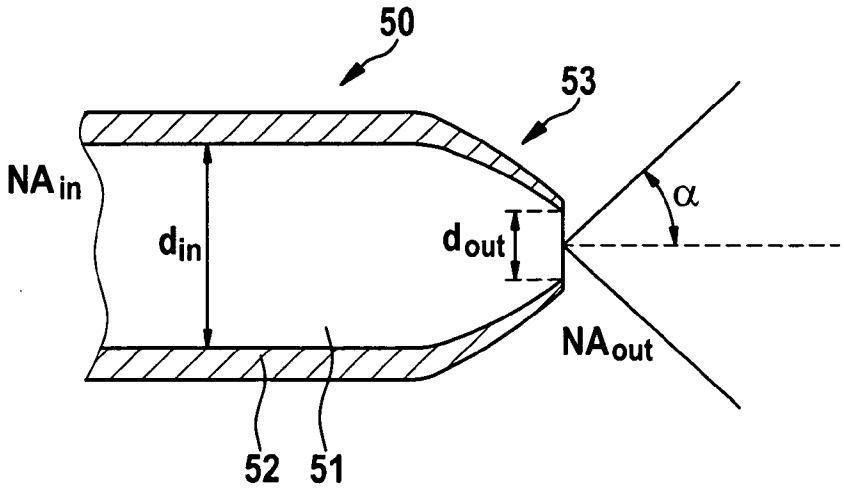

40
0.8
0.6
0.4
0.2
0
0.22
1
1.05
1.1
1.15
1.2
1.25
1.3
1.35
NA(n_solv ,n_ext)
n_ext

Fig. 5


50
53
NA in
d in
d out
α
NA out
52
51

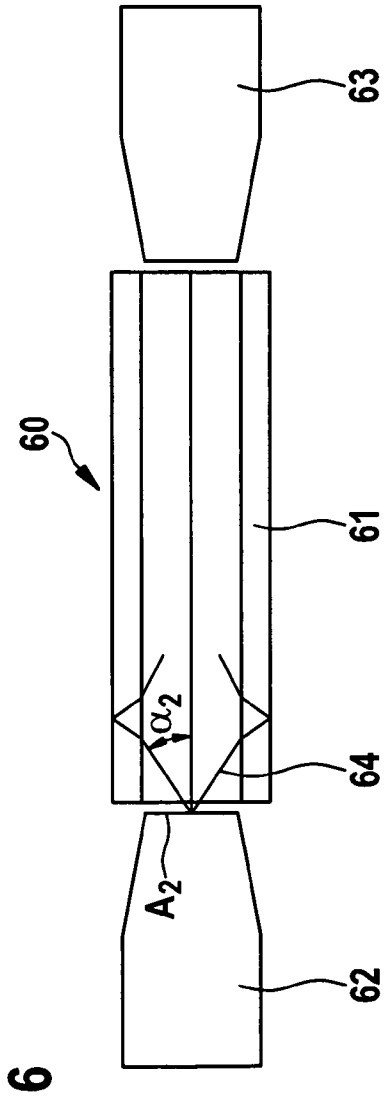


Fig. 6

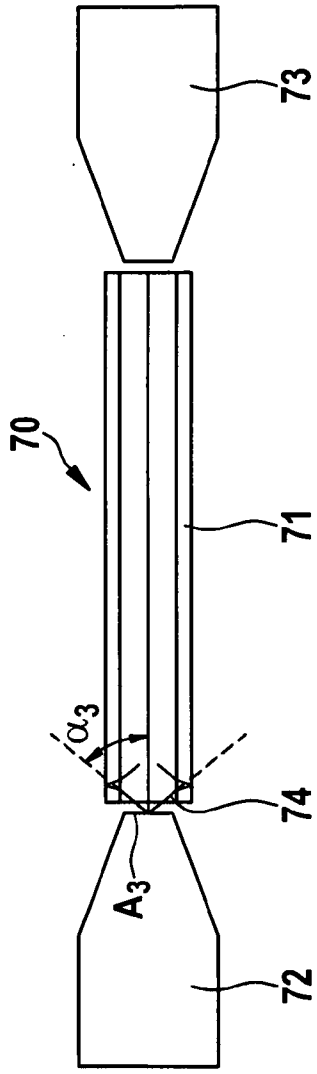


Fig. 7

Fig. 8

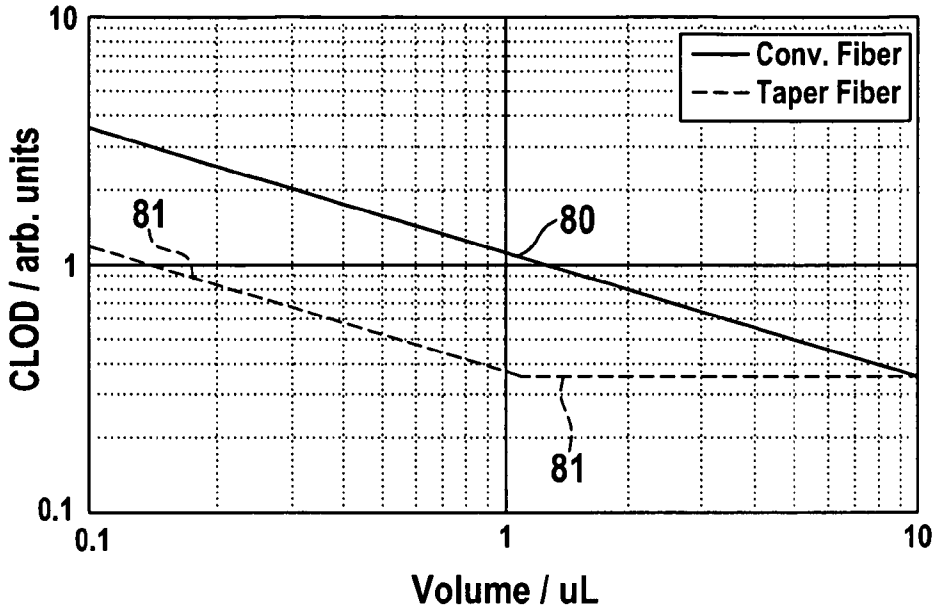
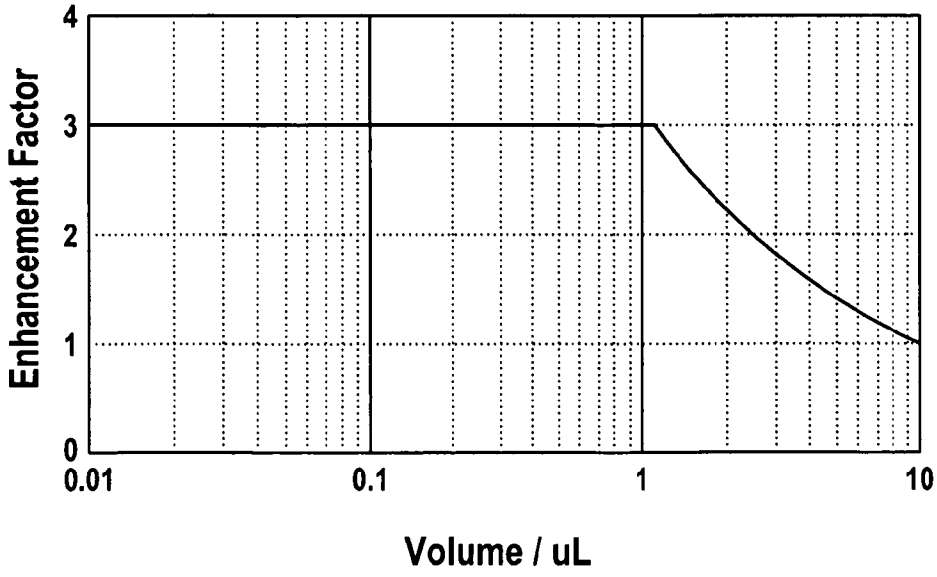

10
1
0.1
CLOD / arb. units
Conv. Fiber
Taper Fiber
81
80
81
0.1
1
10
Volume / uL

Fig. 9


4
3
2
1
0
Enhancement Factor
0.01
0.1
1
10
Volume / uL

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2010/066205

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N21/05 G01N30/74 G02B6/26
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	EP 0 597 552 A1 (LC PACKINGS INTERNATIONAL [NL]) 18 May 1994 (1994-05-18) col. 1 lines 1-20; col. 6 lines 5-15; col. 7 lines 23-56; col. 9 line 54 to col. 10 line 16figures 1,5	1,5-11, 13 1-13
Y	US 2002/071123 A1 (MILLER RICHARD L [US] ET AL BELZ MATHIAS [US] ET AL) 13 June 2002 (2002-06-13) paragraphs [0025], [0026], [0033]; figure 3	1-13
Y	WO 2006/127590 A2 (US GOV HEALTH & HUMAN SERV [US]; SMITH PAUL D [US]; MORGAN NICOLE Y [U) 30 November 2006 (2006-11-30) paragraphs [0001], [0071], [0072]	2-10,12, 13

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
19 July 2011	02/08/2011

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Spott, Thorsten

Form PCT/ISA/210 (second sheet) (April 2005)

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Y	WO 94/04892 A1 (MAECHLER MEINRAD [DE]) 3 March 1994 (1994-03-03) page 1 lines 7-9; page 5 lines 4-16; page 6 line 28 to page 7 line 3; page 12 lines 29-35;	4-10
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T	STEVE J LACKIE ET AL: "Instrumentation for cylindrical waveguide evanescent fluorosensors", 1 January 1991 (1991-01-01), BIOSENSORS WITH FIBEROPTICS, THE HUMANA PRESS INC, PAGE(S) 225 - 251, XP009150340, section 3.	

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2010/066205

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