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(54) **Micro-fluidic system**

(57) The invention relates to a micro-fluidic system comprising a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system, wherein the second material comprises a reinforced polytetrafluoroethylene.

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Description

[0001] The invention relates to a micro-fluidic system, to an element suitable for use in a micro-fluidic system, to the use of the element in a micro-fluidic system, to the use of a polymer in said micro-fluidic system and to a kit of parts comprising said element.

[0002] Micro-fluidic systems are known in the art. For example, in WO2004/022233 a modular micro-fluidic system has been described having at least one base board with a plurality of fluidly linked fluid supply apertures, optional intermediate level boards of equivalent construction, a plurality of micro-fluidic modules adapted to be detachably attached to the base board/ intermediate boards, each having one or more fluid inlets and/or outlets, and a plurality of fluid connections.

[0003] For example WO03/039736 relates to a micro reactor system for the continuous synthesis, which provides defined reaction chambers and conditions for said synthesis, as well as to the uses of said micro reactor in carrying out chemical reactions.

[0004] For example, WO2007/112945 discloses a micro reactor system assembly comprising a stack of at least n process modules, wherein n is an integer equal to or greater than 1, made from a rigid first material and comprising at least one reactive fluid passage for accommodating and guiding a reactive fluid, and at least n+1 heat exchange modules made from a ductile material other than said first material and comprising at least one heat exchange fluid passage for accommodating and guiding a heat exchange fluid, wherein each process module is sandwiched between two adjacent heat exchange modules.

[0005] However, the current micro-fluidic systems, make use of wetted parts that are made from poly-ether-ether ketone (PEEK). The disadvantage of PEEK is that it lacks in chemical resistance against abrasive and corrosive materials such as trifluoro acetic acid, trifluoromethane sulfonic anhydride (triflic anhydride) and boron trifluoroetherate.

[0006] Therefore, it is the object of the invention to provide a micro-fluidic system comprising at least one wetted part, wherein the wetted parts show a good chemical resistance against trifluoro acetic acid, trifluoromethane sulfonic anhydride (triflic anhydride) and boron trifluoroetherate and preferably also when used under elevated temperatures.

[0007] This object is achieved by a micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system, wherein the second material comprises a reinforced polytetrafluoroethylene.

[0008] As can be seen from the examples herein, a second element comprising a reinforced polytetrafluoroethylene has good chemical resistance against trifluoro acetic acid, trifluoromethane sulfonic anhydride (triflic anhydride) and boron trifluoroetherate.

[0009] Additionally, the micro-fluidic system of the invention may have one or more of the following advantages: the micro-fluidic system may have a good resistance to high stresses due to fluidic pressures or high temperatures and/or is able to undergo multiple heating and cooling cycles without being affected in terms of strength and/or chemical resistance.

[0010] As used herein, the term 'micro-fluidic system' generally refers to a system comprising an element through which materials, particularly fluids can be transported. For the avoidance of doubt the term 'fluids' encompasses liquids, gases and mixtures thereof, wherein the term 'liquids' includes liquids containing solid particles, such as slurries. The micro-fluidic system of the present invention comprises a first element of a first material comprising a channel for transporting fluids. The at least one cross-sectional dimension, e.g. width, depth, or diameter, is in the range from 0.05 to 10mm, for example in the range from 0.05 to 1 mm, for example in the range from 0.5 to 1.5 mm, for example in the range from 3 to 10 mm, for example in the range from 3 to 5mm. The use of dimensions of the channel in the order as mentioned, allows the incorporation of a greater number of channels in a smaller area and allows for the use of smaller fluid volumes.

[0011] The first material may for example be a transparent material, for example polymethylmethacrylate (PMMA) or glass. The first material is preferably different from the second material or in other words, preferably the first material and the second material are not the same.

[0012] At least one inlet in the channel is used as an entry point for the fluids, such as the chemicals in a chemical reaction to be executed in the micro-fluidic system, for example the reactants, solvents and catalysts. At least one outlet in the channel may be used as an exit point for the fluids, for example the products and by-products prepared in a chemical reaction, but may also be connected to another channel, which in its turn may again be connected to another channel etc.

[0013] The second element is in communication, for example fluid communication, with the channel and is contacted by the fluids (for example the chemicals or product and by-products of a chemical reaction) during operation of the micro-fluidic system. The second element may be any element with does not form an integral part with the first element. The second element is preferably detachable from the first element

[0014] Examples of the second element include but are not limited to valves, for example check valves, sealing elements, ferrules, nuts, elements in the back pressure regulator, luer connectors, unions, holder parts, etc.

[0015] Preferably, at least two, more preferably at least three, most preferably all elements of the micro-fluidic device that are in communication with the channel and that are in contact with the fluids during operation of the micro-fluidic system comprise a material that comprises a reinforced polytetrafluoroethylene.

[0016] The second element may be a sealing element. For example, when the first element is connected to a third element comprising a channel, a sealing element may connect and seal the channel in the first element to the channel in said third element. For example, when channel in the first element is connected to a back-pressure regulator, a sealing element may connect the back-pressure regulator to the channel in the first element. The second element is also referred to herein as 'wetted part'.

[0017] The second element may for example also be a connector, such as a nut-and-ferrule connector. A nut-and-ferrule connector may be provided at an outlet of the channel. In a nut-and-ferrule connector, a conically shaped ferrule holding a tube may be inserted in a counteracting conically shaped hole in a second element provided at an outlet of the channel. A nut may then be screwed into another element, for instance a holder part, which is provided with screw thread. The conically shaped ferrule contracts, clamps the tube and thus provides a sealed connection between the outlet of the channel and the tube. A nut-and-ferrule connector may also be combined into a single piece.
Similarly, also nut and ferrule connectors having a different shape, for example a flatbottom shape may be used as a second element.

[0018] For example, the second material essentially consists, for example consists of a reinforced polytetrafluoroethylene.

[0019] The micro-fluidic system of the invention may comprise further elements, for example to operate the micro-fluidic system. Example of further elements include but are not limited to a pump, a pressure regulator and a temperature sensor.

[0020] Preferably, the second material comprises a reinforced polytetrafluoroethylene having a tensile modulus of at least 1400MPa as measured on a machined piece using ASTM D638-10, at 23°C, on a type V specimen of 4 mm thickness at 1 mm/min testing speed.

[0021] For example, the tensile modulus of the reinforced polytetrafluoroethylene is at most 7000MPa, for example at most 6000MPa, for example at most 5000MPa, for example at most 4500MPa. For example the tensile modulus of the reinforced polytetrafluoroethylene is at least 1500MPa, for example at least 1600MPa, for example at least 1700MPa, for example at least 1800MPa, for example at least 1900 MPa, for example at least 2000MPa.

[0022] With reinforced is meant that the polytetrafluoroethylene (PTFE) has been made stronger by for example the addition of fillers, for example fibers to PTFE. Both natural and synthetic fibers, for instance wood, glass, carbon fibers or mica may be used to reinforce PTFE.

[0023] Preferably PTFE is reinforced with mica, for example with natural or with synthetic mica ($Mg_3K[AlF_2O(SiO_3)_3$), more preferably with synthetic mica, more preferably with synthetic fluorinated mica, also known as fluorophlogite or $KMg_3(AlSi_3O_{10})F_2$. For PTFE reinforced with synthetic fluorinated mica is commercially available as for example Fluorosint™ 500, Fluorosint™ 207, Fluorosint™ HPV, Fluorosint™ MT-01.

[0024] The amount of fillers, preferably fibers in PTFE may for example be in the range of from 10 to 40wt% based on the second material.

[0025] Preferably, the reinforced polytetrafluoroethylene is polytetrafluoroethylene is reinforced with a filler that is chemically compatible with polytetrafluoroethylene. With 'chemically compatible' is meant that the PTFE does not change its physical or mechanical properties as a result of contact with the filler as can be visually determined by inspecting the surface of $1cm^3$ of reinforced PTFE, prepared by machining, for cracks and defects using the naked eye and comparing this to the results of an unfilled PTFE.

[0026] Preferably, the amount of polytetrafluoroethylene in the second material of the micro-fluidic device is at least 60wt% based on the second material, for example at least 70wt% based on the second material. For example the amount of PTFE may be at most 85wt% based on the second material.

[0027] In another aspect, the invention relates to an element suitable for use as the second element in a micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid

materials during operation of the micro-fluidic system,
wherein the second material of the second element comprises a reinforced polytetrafluoroethylene.
In another aspect, the invention relates to the use of the element according to the invention in a micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system.

[0028] In another aspect, the invention relates to the use of a reinforced polytetrafluoroethylene in a second element of a micro-fluidic system, wherein the micro-fluidic system comprises

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and

- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system.

[0029] Preferred embodiments and examples of the micro-fluidic system, second parts, second materials and the reinforced polytetrafluoroethylene for all aspects of the invention are as described above.
[0030] In yet another aspect, the invention relates to a kit of parts comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system, wherein the second material comprises a reinforced polytetrafluoroethylene.

[0031] The micro-fluidic system of the invention can suitably be used to perform chemical reactions at a temperature in the range of for example from -20 to 200°C and/or at a pressure in the range of for example from atmospheric pressure (101.325 kPa) to 80bar, for example from atmospheric pressure to 20 bar.
[0032] It is noted that the invention relates to all possible combinations of features recited in the description, including the combination of features recited in the claims.
[0033] The invention will now be illustrated by way of the following examples without however being limited thereto.

Examples

[0034] Table 1 lists the engineering plastics that were used in this experimental section. The Tensile modulus was measured using the method described herein.

Table 1. Material Details:

Engineering plastic Tested	Chemical Name	Chemical Composition	Supplier	Tensile modulus (MPa)
Ketron PEEK- 1000	Polyetheretherketone	Un-filled PEEK	Quadrant Engineering Plastics	4340
Techtron-PPS HPV	Polyphenylene sulfide	Lubricant filled polyphenylene sulfide	Quadrant Engineering Plastics	3720
Techtron 1000 PPS	Polyphenylene sulfide	Un-filled polyphenylene sulphide	Quadrant Engineering Plastics	3450

(continued)

Engineering plastic Tested	Chemical Name	Chemical Composition	Supplier	Tensile modulus (MPa)
Techtron CM- PSGF	Compression moulded polyphenylene sulphide glass filled	40 % glass filled polyphenylene sulfide	Quadrant Engineering Plastics	5030
Symalit PVDF 1000	Polyvinylidene fluoride	Un-filled poly-1,1-difluoroethene	Quadrant Engineering Plastics	2070
Fluorosint-500	PTFE (polytetrafluoroethylene)	Mica filled PTFE	Quadrant Engineering Plastics	2200

[0035] Table 2 lists the reagents used to test the chemical compatibility of the engineering plastics, their supplier and in which concentrations they were used.

Table 2. Reagents employed:

Reagent Used	Quality	Concentration Used	Supplier	CAS No.
Trifluoroacetic acid	≥99.0 %	Neat	Aldrich	76-05-1
Trifluoromethane sulfonic acid	99 % Extra	Neat	Acros organics	1493-13-6
Boron trifluoride etherate	48 %	Neat	Acros organics	109-63-7

[0036] **Experimental Details:** Depending on the material under investigation, two types of tests were performed;

1. Surface treatment tests

2. Assessment of threaded parts

[0037] In all cases, tests were performed at atmospheric pressure in the presence or absence of heat depending on the reagent under evaluation.

1. Surface Tests: For surface testing, 0.5 ml of reagent was applied to the surface of a piece of engineered plastic. The effect of the reagent on the bulk plastic was assessed over a period of 30 min at room temperature (around 20°C). For some experiments, the plastic was heated on a hotplate to 5 ºC under the reagents boiling point and 0.5 ml of reagent was applied to the surface of a piece of engineered plastic. Again the effect on the plastic surface was monitored and any changes recorded. the surfaces were visually inspected for discolouration, swelling, cracking or disintegration (dissolving).

2. Assessment of Threaded Parts: Some of the materials were machined into threaded parts (6-32" or ¼-28") to enable assessment of the plastics in the presence of flowing and in some instances heated reagents. In these examples, fluids were pumped through the plastics by syringe pump and the wetted parts visually inspected for chemical attack; discolouration, swelling, cracking or disintegration (dissolving).

The results of the surface tests and threaded parts tests are given in Table 3 below. Depending on the amount of chemical attack on the surface or threaded parts, the following indications were given with 1 = No chemical attack; 2 = Slight surface attack; 3 = Significant surface damage and 4 = Dissolves.

The test types used are indicated as follows:

* = the assessment of a threaded part when heated to 5 ºC below the boiling point of the reagent.

+ = the assessment of a threaded part at room temperature.

" = result of a surface test, when the material was heated to 5 ºC below the boiling point of the reagent. ^ = result of a surface test, when the material was at room temperature.

Table 3. Results of Surface tests and threaded parts test:

Chemical/Engineering Plastic Tested	TFAA	TFMSA	BF_3 Etherate
PEEK	1+	4+	1*
Techtron-PPS HPV	1*	2*	1^
Techtron PPS	1^	2"	1^
Techtron CM-PSGF	2^	2"	1^
Symalit PVDF 1000	1+	1+	1^
Fluorosint 500	1*	1^	1*

Conclusions:

[0038] As can be seen from Table 3 above, a reinforced polytetrafluoroethylene, as exemplified by Fluorosint 500 shows a superior chemical resistance to trifluoroacetic acid (TFAA), trifluoromethane sulfonic acid (TFMSA) and boron trifluoride etherate

[0039] (BF_3 etherate) as compared to other engineering plastics. Not only does the reinforced polytetrafluoroethylene show a good chemical resistance at room temperature, but also at higher temperatures, which are typically temperatures as used in chemical reactions that may be executed in the micro-fluidic system of the invention. This makes

[0040] reinforced polytetrafluoroethylene an excellent choice of material for the wetted parts in a micro-fluidic system.

Claims

1. Micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system, wherein the second material comprises a reinforced polytetrafluoroethylene.

2. Micro-fluidic system according to claim 1, wherein the second element is a valve, a sealing element, a ferrule, a nut, an element in the back pressure regulator, a luer connector, a union or a holder part.

3. Micro-fluidic system according to claim 1 or claim 2, wherein the reinforced polytetrafluoroethylene is polytetrafluoroethylene reinforced with a filler that is chemically compatible with polytetrafluoroethylene.

4. Micro-fluidic system according to claim 3, wherein the filler is mica, preferably synthetic fluorinated mica.

5. Micro-fluidic system according to any one of claims 1-4, wherein the amount of polytetrafluoroethylene in the second material of the micro-fluidic system is at least 60wt% based on the second material.

6. Micro-fluidic system according to any one of claims 1-5, wherein the reinforced polytetrafluoroethylene has a tensile modulus of at least 1400MPa as measured on a machined piece using ASTM D638-10, at 23°C, on a type V specimen of 4 mm thickness at 1 mm/min testing speed.

7. Element suitable for use as the second element in a micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system,

wherein the second material of the second element comprises a reinforced polytetrafluoroethylene.

8. Use of the element according to claim 7 in a micro-fluidic system comprising

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system.

9. Use of a reinforced polytetrafluoroethylene in a second element of a micro-fluidic system, wherein the micro-fluidic system comprises

- a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm and
- a second element of a second material in communication with the channel and which is contacted by the fluid materials during operation of the micro-fluidic system.

10. Kit of parts comprising the element of claim 7 and a first element of a first material comprising a channel comprising at least one inlet and at least one outlet for transporting fluids, wherein the channel has at least one cross-sectional dimension in the range from 0.05 to 10mm.

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EUROPEAN SEARCH REPORT

Application Number
EP 12 15 4899

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The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
Munich	21 May 2012	Smith-Hewitt, Laura

CATEGORY OF CITED DOCUMENTS

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