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(54) FLUID PREHEATING

(75) Inventor: **Tony Ziegler**, Bergzabern (DE)

Correspondence Address:
Paul D. Greeley
Ohlandt, Greeley, Ruggiero & Perle, L.L.P.
10th Floor
One Landmark Square
Stamford, CT 06901-2682 (US)

(73) Assignee: **Agilent Technologies, Inc.**

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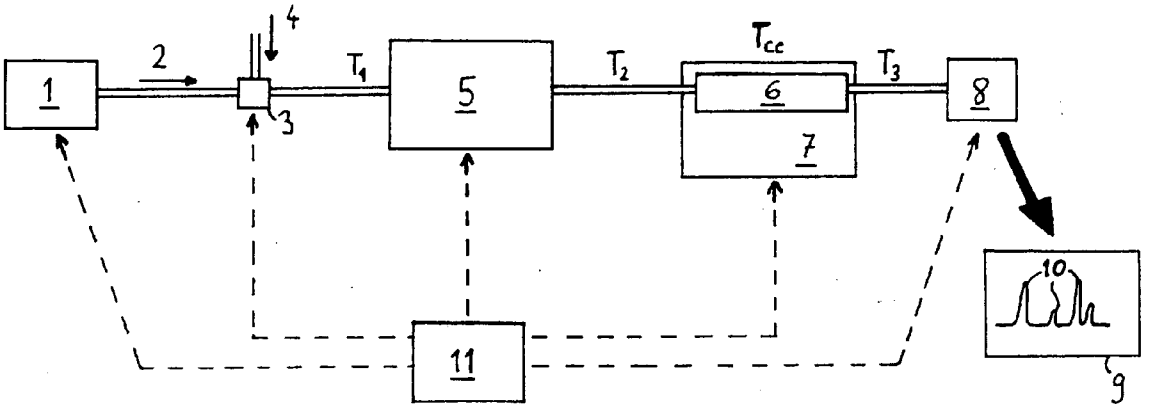
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(57) **ABSTRACT**

A heating system for preheating a fluid. The heating system comprises a heating unit with a heating flow path; wherein the heating unit is adapted to be operated at a first temperature and to provide a heat transfer between the heating unit and the fluid passing through the heating flow path, with the heat transfer not being sufficient for heating up the fluid passing through the heating flow path to the first temperature.



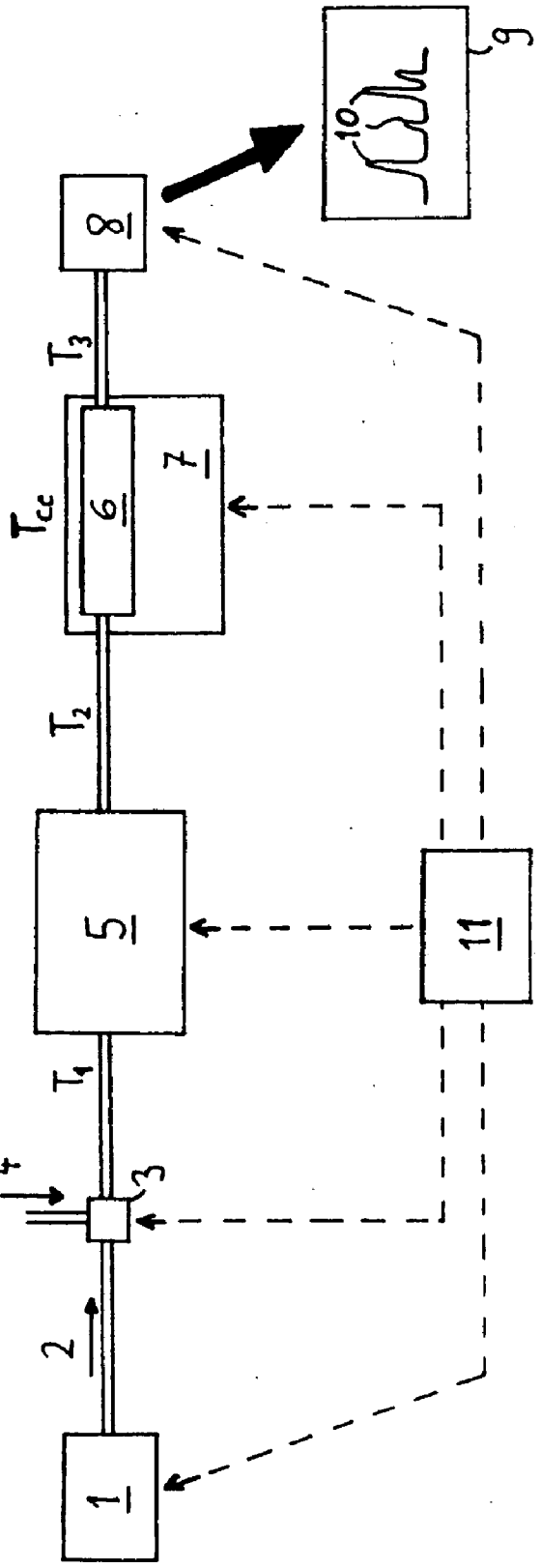


Fig. 1

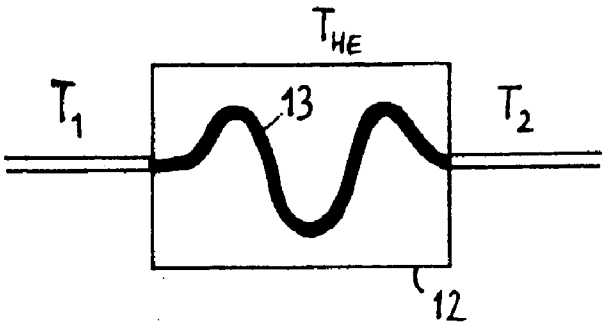


Fig. 2

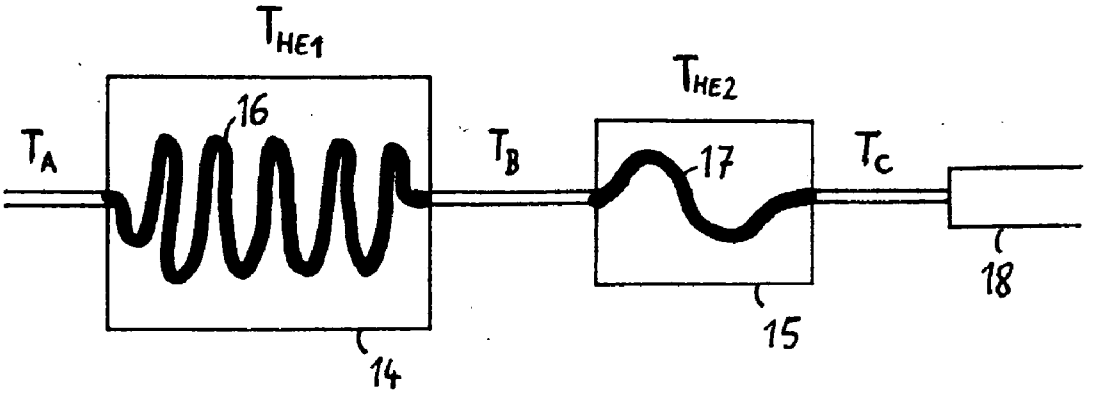


Fig. 3

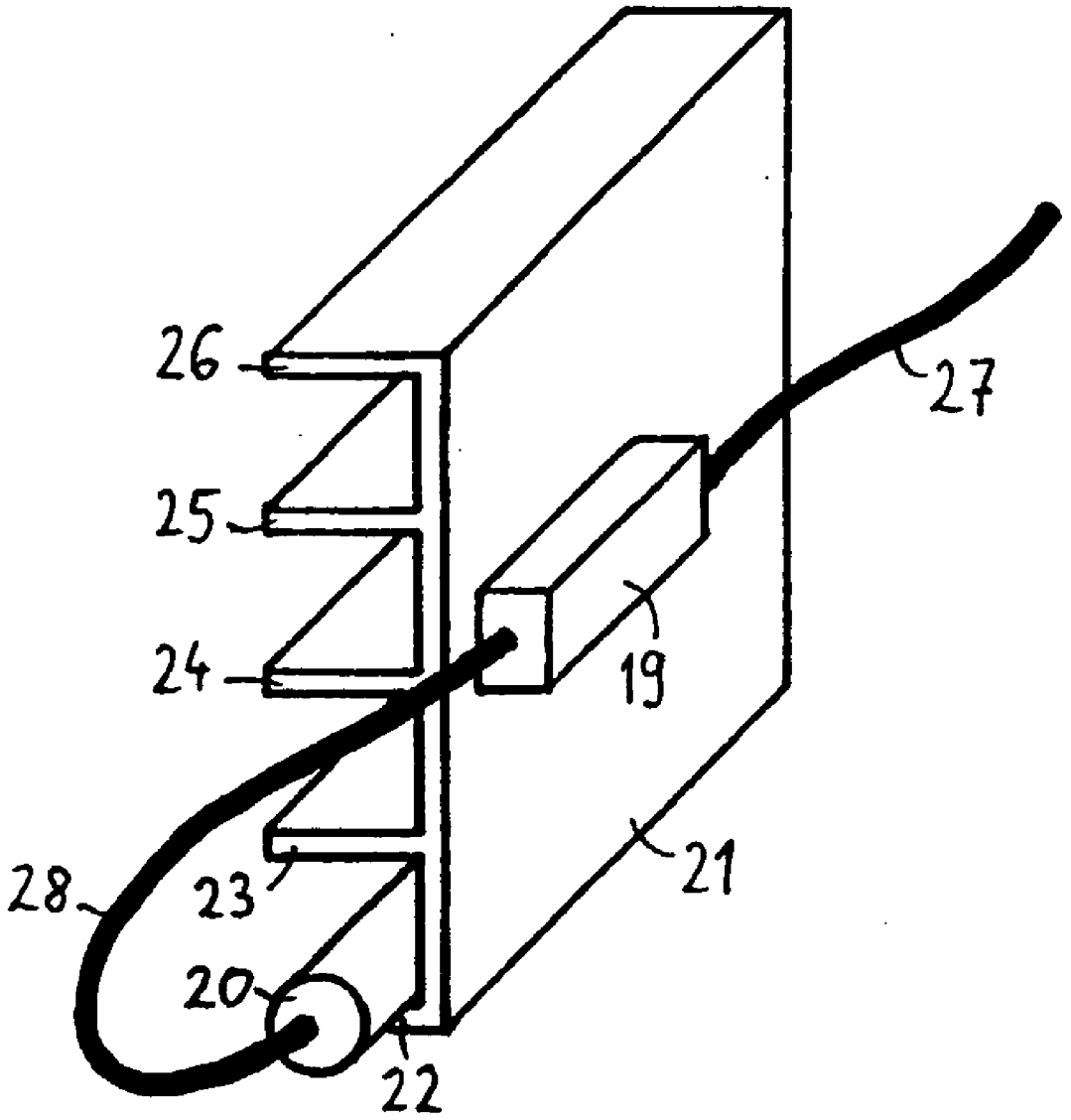


Fig. 4

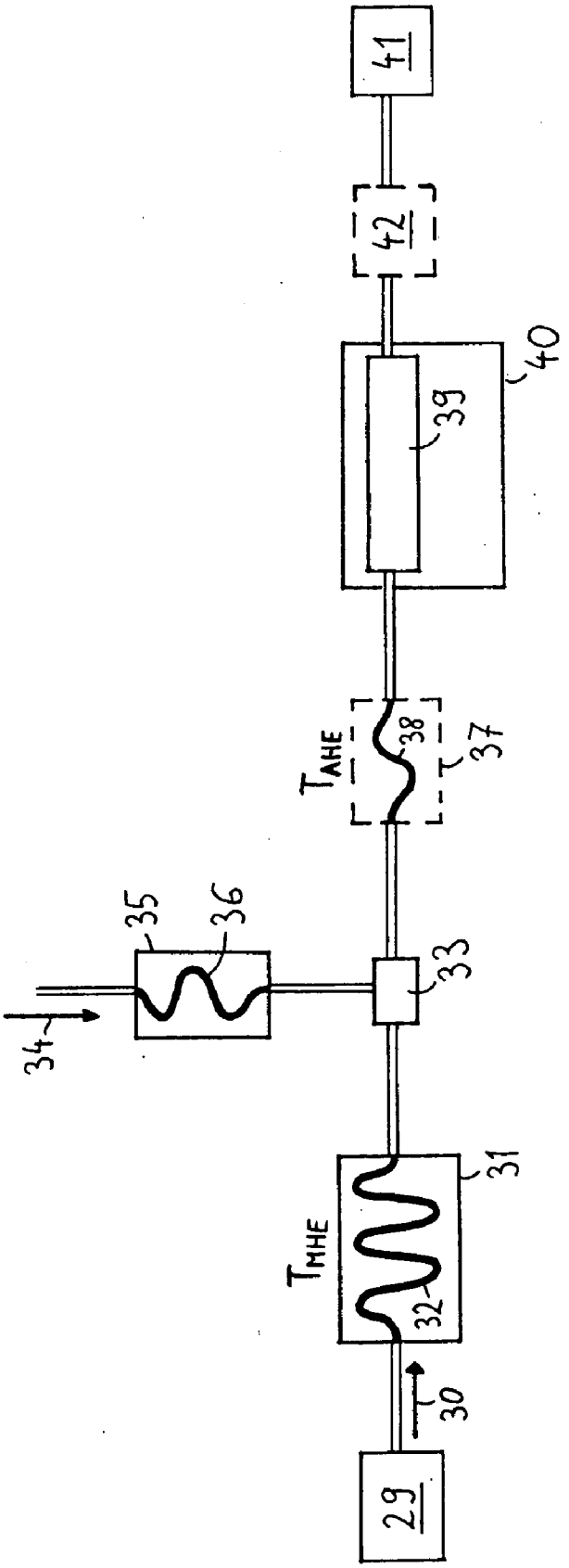


Fig. 5

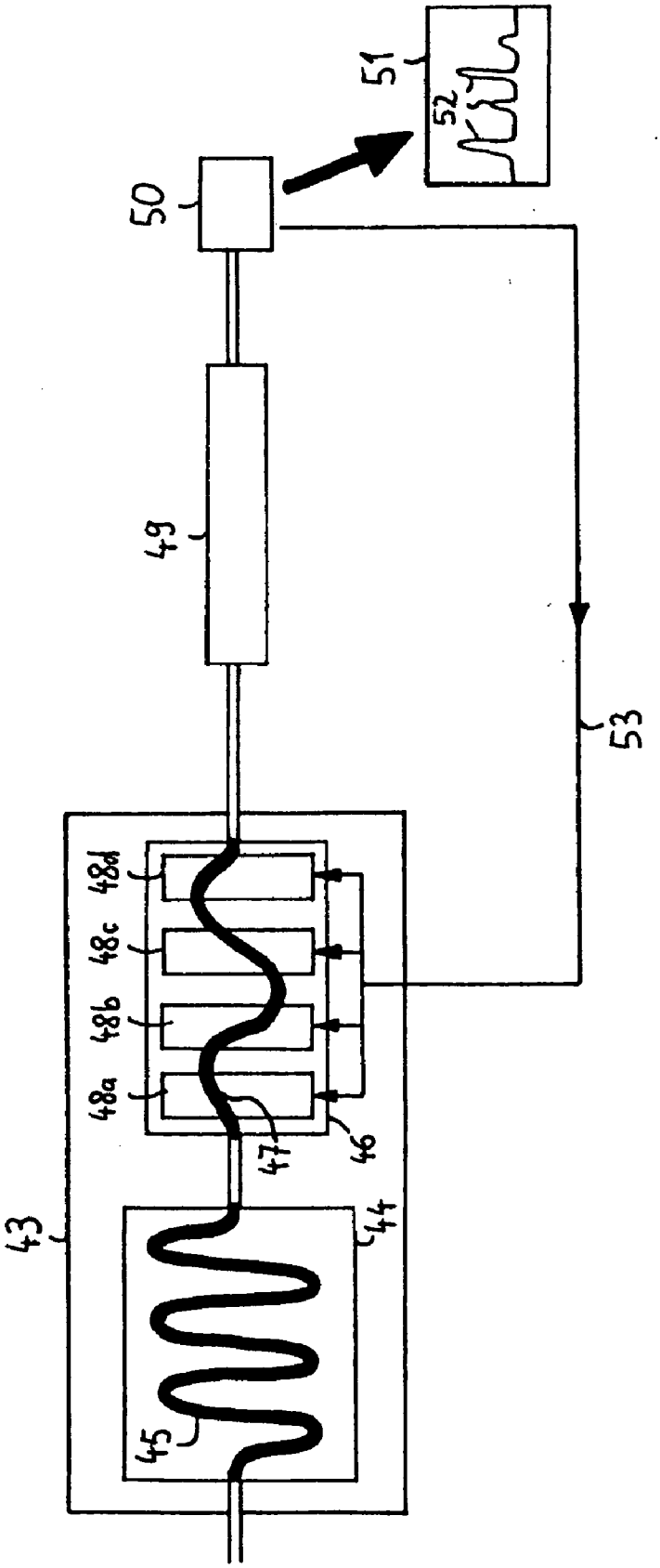


Fig. 6

FLUID PREHEATING

BACKGROUND ART

[0001] 1. Field of the Invention

[0002] The present invention relates to fluid preheating.

[0003] 2. Discussion of the Background Art

[0004] U.S. Pat. No. 5,238,557 describes an apparatus for controlling the temperature of a mobile phase in a fluid chromatographic system which comprises both an ingoing capillary connected to an inlet of a column and an outgoing capillary connected to an outlet of the column. A portion of the ingoing capillary and a portion of the outgoing capillary are arranged in thermal contact with each other to form a contact region wherein heat exchange can occur. In preferred embodiments, liquid leaving the column at an elevated temperature loses a portion of its heat, thus avoiding or at least substantially reducing the transfer of heat to the detector. At the same time, liquid flowing to the column is pre-heated by the liquid leaving the column so that the heating power required for bringing the mobile phase to the desired temperature is reduced as compared with prior art devices.

[0005] European Patent Application EP 0716302 describes a method for thermally stabilizing two columns for liquid chromatography. The method comprises the following steps: operating the first column at a first temperature which is different from the operating temperature of the second column, and transferring the sample contained in the first column to the second column by operation of switching means arranged between the two columns. In an embodiment of the invention, the first column is a pre-column and the pre-column is operated, during an enrichment phase, at a first temperature lower than an operating temperature of the separation column, in order to maintain a sample at a first temperature. The sample contained in the pre-column is heated, after completion of the enrichment phase, to a second temperature higher than the operating temperature of the separation column, then the sample contained in the pre-column is transferred to the separation column and then the sample is cooled to the operating temperature of the separation column.

SUMMARY OF THE INVENTION

[0006] It is an object of the invention to provide an improved preheating of a fluid.

[0007] A heating system according to embodiments of the present invention comprises a heating unit with a heating flow path. The heating unit is adapted to be operated at a first temperature and to provide a heat transfer between the heating unit and the fluid passing through the heating flow path, with the heat transfer not being sufficient for heating up the fluid passing through the heating flow path to the first temperature.

[0008] The heating unit and the heating flow path are implemented in a way that the fluid passing through the heating flow path is not heated up to the temperature the heating unit itself is kept at. The heating unit is purposely designed such that the a mount of heat transferred from the heating unit to the fluid does not suffice for bringing the fluid to the temperature of the heating unit. For this reason, the temperature of the fluid appearing at the outlet of the heating flow path remains below the temperature the heating unit is kept at.

[0009] In prior art solutions, it has always been tried to provide a "good" heat exchanger with heating capabilities that are sufficiently large for heating up the fluid to the heating unit's temperature. It has never been considered to purposely design a heating unit with insufficient heating capabilities. However, it has been found that, when preheating a fluid, insufficient heating might yield superior results.

[0010] In a preferred embodiment of the invention, the heating system is used for preheating a fluid before the fluid is supplied to a separation system adapted for separating compounds of a fluid sample. The separation system might e.g. be used for acquiring a peak pattern indicating the composition of the fluid sample, with each of the peaks being related to a certain compound of the fluid sample. By utilizing a heating system according to an embodiment of the present invention, the precision of the separation process is improved. It has been verified experimentally that insufficient heating of the fluid supplied to a separation system leads to an improved quality of the acquired peak pattern. In particular, it has been found that the peak's heights are increased and the peak's half widths are reduced when employing a heating system according to an embodiment of the present invention. Insufficient heating improves the sensitivity of sample analysis. Even tiny amounts of a certain sample compound may be detected.

[0011] According to a preferred embodiment, the temperature of the fluid obtained at the heating flow path's outlet is lower than the first temperature, which is the temperature the heating unit is kept at. Because of the insufficient heating capabilities of the heating unit, the fluid does not attain the first temperature when traveling through the heating flow path.

[0012] A heating system according to an embodiment of the present invention may e.g. be realized by reducing the heating power of the heating unit. Additionally or alternatively, the length of the heating flow path may be reduced until the heat transfer from the heating unit to the fluid becomes sufficiently small. In order to further reduce the heat exchange between the heating unit and the fluid, the number of turns of the heating flow path may be reduced. Another possibility for reducing the heat transfer is to increase the velocity of the fluid passing through the heating unit.

[0013] In a preferred embodiment, the temperature of the fluid at the heating unit's outlet depends on the thermal properties of the fluid. In particular, the temperature increase of the fluid travelling through the heating flow path might e.g. depend on the heat capacitance of the fluid, and on the fluid's thermal conductivity. For example, the higher the fluid's heat capacitance, the more heat will be required for increasing the temperature by one degree Celsius. In case of a fluid having a large heat capacitance like e.g. water, a given heat transfer will lead to a relatively small increase of the fluid's temperature. In case of an organic solvent like e.g. methanol or acetonitrile, a heat transfer of similar magnitude might cause a much larger increase of the fluid's temperature.

[0014] In a further preferred embodiment, a variation of the fluid's composition gives rise to a corresponding tem-

perature variation of the fluid at the outlet of the heating flow path. A variation of the fluid's composition induces a corresponding variation of the fluid's thermal properties. This variation of the fluid's thermal properties gives rise to a corresponding temperature variation of the fluid obtained at the outlet of the heating flow path. Hence, the temperature of the fluid at the heating flow path's outlet might e.g. float in accordance with the fluid's composition.

[0015] In a preferred embodiment of the invention, the heating system is implemented as a two-stage heating system comprising a main heating unit with a main heating flow path and an auxiliary heating unit with an auxiliary heating flow path. The main heating unit is located upstream of the auxiliary heating unit, with the outlet of the main heating flow path being fluidically coupled with the inlet of the auxiliary heating flow path. The main heating unit is kept at a second temperature, whereas the auxiliary heating unit is kept at the first temperature, with the first temperature being higher than the second temperature.

[0016] The main heating unit provides sufficient heating capabilities for heating up a fluid passing through the main heating flow path to the second temperature the main heating unit is kept at. In contrast, the auxiliary heating unit is a heating unit according to an embodiment of the present invention, which is purposely realized in a way that the heat transfer between the auxiliary heating unit and the fluid is not sufficient for bringing the fluid to the first temperature the auxiliary heating unit is kept at. The main heating unit is implemented as a conventional heating unit. Thus, the main heating unit provides a basic level of heating, and there are no temperature variations of the fluid at the main heating unit's outlet. The auxiliary h eating u nit receives the fluid at the second temperature and provides for some additional heating, with the heating capabilities of the auxiliary heating unit not being sufficient for heating up the fluid to the first temperature the auxiliary heating unit is kept at.

[0017] By implementing a two-stage heating process, the advantages of a heating unit according to embodiments of the present invention may be utilized while providing for reliable overall heating. By utilizing a two-stage heating process, the quality of peak patterns acquired in a separation process may be improved. In particular, the heights of the peaks may be increased and/or the peaks' half widths may be reduced.

[0018] In a preferred embodiment, the main heating unit is implemented such that the fluid passing through the main heating flow path is heated up to the second temperature. For example, the main heating flow path might be sufficiently long, and/or the heating power of the main heating unit may be sufficiently large for heating up the fluid passing through the main heating flow path to the second temperature.

[0019] In a preferred embodiment, the heating system comprises a sample injection unit located between the main heating unit and the auxiliary heating unit, with the sample injection unit being adapted for injecting a fluid sample into the fluid passing through the heating system. In this embodiment, the fluid sample is not conveyed through the main heating unit. The fluid sample only has to pass through the auxiliary heating unit. As a consequence, the dispersion of a sample plug is kept small, the half width of the acquired peaks is reduced, and a peak pattern of improved resolution is obtained.

[0020] According to a further preferred embodiment, the heating system further comprises a sample heating unit adapted for preheating the fluid sample before the fluid sample is provided to the sample injection unit.

[0021] According to a further preferred embodiment, one or more of the heating flow paths are realized as heat transfer capillaries. The capillaries' inner diameter might e.g. lie in the range between 0.05 mm and 0.30 mm.

[0022] According to a preferred embodiment, a heating unit may be made of at least one of the following materials: cast iron, cast copper, cast aluminium, cast bronze.

[0023] A separation system according to embodiments of the present invention comprises a heating unit for preheating a fluid, with the heating unit comprising a heating flow path. The heating unit is adapted to be operated at a first temperature and to provide a heat transfer between the heating unit and the fluid passing through the heating flow path, with the heat transfer not being sufficient for heating up the fluid passing through the heating flow path to the first temperature. The separation system further comprises a separation column adapted for separating compounds of a fluid sample, with the heating flow path's outlet being fluidically coupled with the separation column's inlet.

[0024] According to a preferred embodiment, the separation system might further comprise a fluid delivery unit, preferably a pump, located upstream of the heating unit, with the fluid delivery unit being adapted for conveying the fluid through the separation system. In a further embodiment, the separation system might comprise a sample injection unit located upstream of the heating unit. Via the sample injection unit, fluid sample may be injected into the mobile phase. In case the heating unit comprises both a main heating unit and an auxiliary heating unit, the injection unit may either be located upstream of the main heating unit or between main heating unit and auxiliary heating unit. In yet another embodiment, the separation system comprises a detection unit located downstream of the separation column, with the detection unit being capable of detecting compounds of the fluid sample. According to yet another embodiment, the separation system further comprises a control unit adapted for controlling operation of at least some of the above-mentioned functional units.

[0025] According to a preferred embodiment, the composition of the mobile phase is kept constant during sample analysis. In this embodiment, the retention time of a certain compound is mainly determined by the interaction of said compound with the stationary phase of the separation column.

[0026] In an alternative embodiment, the composition of the mobile phase is varied during the separation process. For example, the elution strength of the mobile phase might be continuously increased as a function of time by varying the solvent composition of the mobile phase according to a gradient. For example, in order to continuously increase the elution strength of the composite solvent, the percentage of organic solvent might be slowly increased as a function of time.

[0027] According to a preferred embodiment, the variation of the composite solvent's composition causes a corresponding temperature variation of the fluid obtained at the outlet of the heating flow path. For example, by varying solvent

composition as a function of time, the composite solvent's thermal properties (in particular the composite solvent's thermal capacitance) might vary correspondingly. The temperature increase of the fluid passing through the heating unit depends on the fluid's thermal properties. For this reason, the temperature increase of the fluid obtained at the heating unit's outlet also varies in accordance with solvent composition.

[0028] Preferably, the separation system might e.g. be one of: a liquid chromatography system, an electrophoresis system, an electrochromatography system.

[0029] In a preferred embodiment, the separation system comprises a thermostated column compartment adapted for keeping the separation column at a predefined temperature.

[0030] In a further preferred embodiment, the temperature of the thermostated column compartment is approximately equal to the first temperature the heating unit is operated at. Further preferably, the thermostated column compartment is thermally coupled with the heating unit.

[0031] According to a preferred embodiment, the heating power of the heating unit is regulated in dependence on a feedback signal.

[0032] According to a further preferred embodiment, the heating unit comprises a plurality of switchable heater modules that may be activated in dependence on a feedback signal. By varying the number of active heater modules, the heating power of the heating unit may be varied until an optimum amount of heating is found.

[0033] In a preferred embodiment, the feedback signal indicates the temperature of the fluid at the outlet of the heating unit.

[0034] In an alternatively preferred embodiment, the feedback signal indicates a quality of peak patterns acquired with the separation system. A feedback signal indicating the peak pattern's quality may e.g. be used for regulating the heating power of the heating unit in a closed-loop control operation. The quality of the obtained peak patterns may e.g. be optimised by regulating the number of active heater modules. By utilizing a closed loop control, this optimisation process may be carried out automatically without human intervention.

[0035] A method for preheating a fluid according to embodiments of the present invention comprises: conveying the fluid through a heating unit, the heating unit being kept at a first temperature, with the heat transfer during the fluid's passage through the heating unit not being sufficient for bringing the fluid's temperature to the first temperature; and supplying the fluid to a separation system.

[0036] In a preferred embodiment, the method further comprises adjusting the heating unit's heating power in dependence on at least one of: a type of separation system, a type of solvent, a slope of a solvent gradient, a flow rate of the fluid.

[0037] 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 for regulating the heating power of the heating unit in a closed-loop control operation.

BRIEF DESCRIPTION OF THE DRAWINGS

[0038] 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).

[0039] FIG. **1** shows a separation system comprising a heating unit;

[0040] FIG. **2** depicts a single-stage heating unit;

[0041] FIG. **3** shows a dual-stage heating unit;

[0042] FIG. **4** shows a thermostated column compartment that is thermally coupled with a heat exchanger;

[0043] FIG. **5** shows a heating unit with a sample injection unit located downstream of the main heat exchanger; and

[0044] FIG. **6** illustrates how the amount of heating can be regulated using a closed-loop control.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

[0045] FIG. **1** gives an overview of a separation system adapted for separating compounds of a given sample. The separation system comprises a fluid delivery unit **1**, e.g. a pump, for supplying a flow of eluent **2** to a sample injection unit **3**. At the sample injection unit **3**, a volume of fluid sample **4** may be injected. Both the eluent and the sample are supplied to a heating system **5**. During the passage through the heating flow path of the heating system, the eluent and the sample are heated up. The eluent and the sample are supplied to a separation column **6** that is filled with a stationary phase. The separation system further comprises a thermostated column compartment **7** adapted for keeping the separation column **6** at a pre-defined temperature. The separation column **6** might e.g. be kept at a temperature of about 80° Celsius. Due to the interaction between the sample compounds and the packing material, the sample compounds appear at the separation column's outlet at different points of time. The separation column's outlet is fluidically coupled with a detection unit **8**. The detection unit **8** might e.g. be a fluorescence detection unit. Alternatively, the detection unit **8** might be adapted for detecting an intensity of light transmitted through a detection cell. Further alternatively, the detection unit **8** might be adapted for detecting an electrical property of the fluid. Optionally, the separation system might further comprise a cooling unit located between the separation column's outlet and the detection unit, in order to bring the fluid to a temperature suitable for detection.

[0046] When traversing the separation column **6**, the sample compounds interact with the packing material in the separation column **6**. For each of the sample's compounds, the time required for passing through the separation column **6** depends on the interaction between the respective compound and the separation column's stationary phase. Hence, the sample's various compounds become separated and

arrive at the detection unit **8** at different points of time. At the detection unit **8**, a respective property of the fluid is detected as a function of time, and a characteristic peak pattern **9** is obtained. Each of the peaks **10** of the peak pattern **9** corresponds to a certain compound contained in the sample **4**.

[**0047**] The separation system might further comprise a control unit **11** adapted for controlling operation of one or more of: the fluid delivery unit **1**, the sample injection unit **3**, the heating system **5**, the thermostated column compartment **7**, the detection unit **8**. The separation system shown in FIG. **1** may be operated in different modes of operation. In the so-called gradient mode, the eluent **2** is composed of at least two different solvents, with solvent composition being varied as a function of time. For example, the eluent **2** may be composed of water and an organic solvent (like e.g. acetonitrile), with the amount of organic solvent being increased in accordance with a predefined gradient. Thus, an increase of the elution strength is accomplished. In dependence on the elution strength of the composite solvent, sample compounds are washed out consecutively.

[**0048**] Alternatively, the separation system may be operated in a so-called isocratic mode. In isocratic mode, the composition of eluent **2** is kept constant, and accordingly, elution strength is not varied as a function of time. Hence, the retention time of a certain sample compound is solely determined by its interaction with the separation column's stationary phase.

[**0049**] In a preferred embodiment, the separation system is a liquid chromatography system. Alternatively, the separation system might be an electrophoresis system or an electrochromatography system.

[**0050**] The heating system **5** shown in FIG. **1** is adapted for preheating both the eluent and the sample. While passing through the heating system **5**, the fluid is heated up from an initial temperature T_1 to a temperature T_2. Fluid a t a temperature T_2 is supplied to the separation column **6**. The thermostated column compartment **7** is constantly kept at a temperature T_{CC}, which might e.g. be equal to about 80° Celsius. During the passage through the separation column **6**, the fluid's temperature further increases, with the fluid's temperature T_3 at the separation column's outlet being higher than the temperature T_2. The magnitude of the temperature increase of the fluid passing though the separation column depends on the type of column used. Large temperature increases might e.g. occur in narrow bore columns at high flow rates. The increase of fluid temperature is due to friction between the mobile phase and the stationary phase. The increase of the fluid's temperature inside the column depends on the flow rate and the fluid's composition.

[**0051**] It has been found that for obtaining a peak pattern **9** of high resolution, the heating system **5** should be implemented such that the temperature T_2 at the heating system's outlet is slightly below the temperature T_{CC} of the thermostated column compartment **7**. Furthermore, it has been found that non-sufficient heating capabilities of the heating system **5** seem to be advantageous in terms of the quality of the acquired peak patterns.

[**0052**] FIG. **2** shows a heating system **5** according to an embodiment of the present invention. The heating system comprises a heat exchanger **12**, with a heating capillary **13** extending through the heat exchanger **12**. The heating capillary **13** may be arranged in a number of turns. Preferably, the heating capillary **13** is made of stainless steel. The heating capillary **13** might be 10-15 cm long and its inner diameter might be in the range between 0.05 and 0.3 mm. The heat exchanger **12** may be made of one of the following materials: cast iron, cast copper, cast aluminum, cast bronze or bronze alloy. The heat exchanger **12** is constantly kept at a temperature T_{HE}.

[**0053**] In heating systems of the prior art, it has always been tried to provide a voluminous heat exchanger with sufficient heating capabilities for heating up the fluid to the temperature the heat exchanger itself is kept at. However, experimental results suggest that employing a rather small heat exchanger with reduced heating capabilities improves the quality of the acquired peak patterns. A small heat exchanger does not provide the heating capabilities necessary for heating up the fluid to the temperature the heat exchanger itself is kept at. However, such an incomplete heat transfer seems to be the reason for an improved quality of the obtained peak patterns. In particular, the peaks' heights are increased, the peaks' half widths are reduced, and the overall resolution of the peak pattern is improved.

[**0054**] The heat transfer between the heat exchanger **12** and the fluid passing through the heating capillary **13** depends on the volume of the heat exchanger, on the heating power, on the total length of the heating capillary, on the heating capillary's inner diameter, on the capillary's wall thickness, on the fluid's velocity (which determines the fluid's staying time), etc. In order to purposely reduce the heat transfer between the heat exchanger **12** and the fluid, one might e.g. reduce the dimensions of the heat exchanger **12**, reduce the length of the heating capillary **13**, reduce the number of turns of the heating capillary **13**, reduce the heating power of the heat exchanger **12**, increase the fluid's velocity, etc. As a consequence, the heat transfer from the heat exchanger **12** to the fluid passing through the heating capillary **13** will no longer suffice for bringing the fluid's temperature to the temperature T_{HE} of the heat exchanger. Therefore, the temperature T_2 of the fluid obtained at the heat exchanger's outlet will remain below the temperature T_{HE} of the heat exchanger.

[**0055**] Both in gradient mode and in isocratic mode, a heating system according to embodiments of the present invention allows acquiring peak patterns of improved quality. In gradient mode, the eluent's composition is continuously varied as a function of time. The percentage of organic solvent is continuously increased and correspondingly, the amount of water is reduced. The specific heat of water is much higher than the specific heat of the most common organic solvents. Hence, during gradient operation, the specific heat of the composite solvent declines, which means that the amount of heat required for heating up the composite solvent gets smaller and smaller. In turn, a fixed amount of heat causes a more pronounced temperature increase. When employing a heat exchanger of the type shown in FIG. **2** in gradient mode, the temperature T_2 of the composite solvent rises with increasing percentage of organic solvent. Hence, the gradient in solvent composition leads to a corresponding temperature gradient of the composite solvent obtained at the heat exchanger's outlet.

[**0056**] In FIG. **2**, a heating system with a single heating stage has been shown. In an alternative embodiment shown

in FIG. **3**, the heating system comprises a main heating stage with a main heat exchanger **14** and an auxiliary heating stage with an auxiliary heat exchanger **15**. The main heat exchanger **14** comprises a heating flow path **16**, and the auxiliary heat exchanger **15** comprises a heating flow path **17**.

[**0057**] Fluid at a temperature TA is supplied to the main heat exchanger **14**, which is kept at a temperature T_{HE1}. The main heat exchanger **14** is a rather bulky heat exchanger, and the heating flow path **16** of the main heat exchanger **14** is sufficiently long for heating up the fluid to the temperature T_{HE1} of the main heat exchanger **14**. Hence, the temperature T_B of the fluid at the main heat exchanger's outlet is approximately equal to T_{HE1}.

[**0058**] The outlet of the main heat exchanger **14** is fluidically coupled with the inlet of the auxiliary heat exchanger **15**. The auxiliary heat exchanger **15** is kept at a temperature T_{HE2}, with T_{HE2} being larger than T_{HE1}. In applications in the field of liquid chromatography or electrophoresis, the main heat exchanger's temperature T_{HE1} might e.g. be about 70° Celsius and the temperature T_{HE2} of the auxiliary heat exchanger might e.g. be about 80° Celsius. According to embodiments of the present invention, the auxiliary heat exchanger **15** of the auxiliary heating stage is implemented such that its heating capabilities are not sufficient for heating up fluid passing through the heating flow path **17** to the temperature T_{HE2} of the auxiliary heat exchanger **15**. Accordingly, the temperature T_C of the fluid at the auxiliary heat exchanger's outlet is smaller than the temperature T_{HE2} the auxiliary heat exchanger **15** is kept at. The fluid obtained at the outlet of the auxiliary heat exchanger **15** might e.g. be supplied to a separation column **18**.

[**0059**] The auxiliary heat exchanger **15** should be designed such that the heat transfer during the fluid's passage through the auxiliary heating flow path **17** is not sufficient for heating up the fluid to the temperature T_{HE2}. This can be accomplished by reducing the dimensions of the auxiliary heat exchanger **15**, by reducing the heating power, by shortening the length of the heating flow path **17**, etc.

[**0060**] FIG. **4** shows a separation system according to an embodiment of the present invention. The separation system comprises a heat exchanger **19** with reduced heating capabilities, a separation column **20**, and a thermostated column compartment **21** adapted for heating both the heat exchanger **19** and the separation column **20**. The column compartment **21** comprises a base plate and a plurality of fins **22** to **26**. The heat exchanger **19** is fixed to the rear side of the base plate, whereby a heat-conductive paste might be used for establishing a thermal contact between the thermostated column compartment **21** and the heat exchanger **19**. Both the thermostated column compartment **21** and the heat exchanger **19** are constantly kept at a temperature T_{CC}, which might e.g. be equal to about 80° Celsius. Eluent and fluid sample are supplied to the heat exchanger **19** via a capillary **27**.

[**0061**] The heat exchanger **19** is a heat exchanger according to an embodiment of the present invention. Because of the limited heating capabilities of the heat exchanger **19**, the temperature of the fluid passing through the heat exchanger **19** does not attain the temperature T_{CC}. After passing through the heat exchanger **19**, the fluid is supplied, via a capillary **28**, to the inlet of separation column **20**. Hence, the temperature of the fluid supplied to the separation column **20** is smaller than the temperature T_{CC} the separation column itself is kept at. This temperature difference is supposed to have a positive effect on the accuracy of the obtained results.

[**0062**] FIG. **5** shows a separation system according to another embodiment of the present invention. The separation system comprises a fluid delivery unit **29** adapted for supplying a flow of eluent **30** to a main heat exchanger **31**. The main heat exchanger **31** is kept at a temperature T_{MHE}. While passing through the main heating flow path **32** of the main heat exchanger **31**, the eluent is heated up. The main heating flow path **32** is sufficiently long for heating up the eluent to the temperature T_{MHE}. Hence, a flow of eluent at a temperature T_{MHE} is supplied to an injection unit **33**.

[**0063**] Furthermore, a volume of fluid sample **34** may be provided to the injection unit **33**. In a preferred embodiment, the sample supply flow path comprises a sample heating unit **35** with a heating flow path **36**. During its passage through the heating flow path **36**, the fluid sample is heated up. At the injection unit **33**, the sample is injected into the flow of eluent.

[**0064**] Both eluent and fluid sample are supplied to an auxiliary heat exchanger **37**, which is kept at a temperature T_{AHE}. The auxiliary heat exchanger **37** comprises an auxiliary heating flow path **38**. According to embodiments of the present invention, the auxiliary heating flow path is not sufficiently long for providing a complete heat transfer, and hence, the temperature of the fluid at the outlet of the auxiliary heat exchanger **37** is lower than the temperature T_{AHE}. The outlet of the auxiliary heat exchanger **37** is fluidically coupled with the inlet of a separation column **39**. The separation column **39** is contained in a thermostated column compartment **40** adapted for keeping the separation column **39** at a pre-defined temperature. When traversing the separation column **39**, the sample compounds interact with the separation column's stationary phase and become separated. The separation column's outlet is fluidically coupled with a detection unit **41**. At the detection unit **41**, the sample's various compounds are detected as a function of time. Optionally, the separation flow path might further comprise a cooling unit **42** located between the separation column **39** and the detection unit **41**. Before being supplied to the detection unit **41**, the fluid is cooled down to a suitable temperature.

[**0065**] In the embodiment of FIG. **5**, the injection unit **33** is located downstream of the main heat exchanger **31**. Hence, a fluid sample **34** supplied to the separation system does not pass through the main heating flow path **32** of the main heat exchanger **31** before being supplied to the separation column **39**. The fluid sample **34** only has to pass through the heating flow path **36** of the sample heating unit **35** and the auxiliary heating flow path **38** of the auxiliary heat exchanger **37**, which are both quite short. In the embodiment of FIG. **5**, sample dispersion is kept small, and as a consequence, the width of the bands obtained at the separation column's outlet is reduced. Hence, the reduced dispersion leads to a reduction of the half width of the acquired peaks. The quality of the peak patterns acquired by the detection unit **41** is improved, and sample peak patterns of improved resolution are obtained.

[**0066**] For accomplishing a sufficient amount of heating, it might not even be necessary to provide both a sample heating unit **35** and an auxiliary heat exchanger **37**. Accord-

ing to a preferred embodiment, the separation system might only comprise a sample heating unit **35**, but no auxiliary heat exchanger **37**. In this embodiment, only the sample heating unit **35** is responsible for heating up the fluid sample. In yet another preferred embodiment, the separation system might comprise an auxiliary heat exchanger **37**, but no sample heating unit **35**. According to this embodiment, the fluid sample is heated up while passing through the auxiliary heat exchanger **37**, and before being supplied to the separation column **39**.

[**0067**] FIG. **6** shows a further embodiment of a heating system **43** comprising a main heat exchanger **44** with a heating flow path **45** and an auxiliary heat exchanger **46** with a heating flow path **47**. The main heat exchanger **44** is kept at a temperature T_{HE1}, and the auxiliary heat exchanger **46** is kept at a temperature T_{HE2}, with T_{HE2} being above T_{HE1}. The auxiliary heat exchanger **46** comprises a plurality of switchable heating modules **48***a*, **48***b*, **48***c*, **48***d*, which may be switched on and off independently. Thus, it is possible to vary the total heating power of the auxiliary heat exchanger **46**. Additionally or alternatively, the heating power of the auxiliary heat exchanger **46** may be regulated by varying the heating current flowing through one or more of the heating modules **48***a*, **48***b*, **48***c*, **48***d*. The outlet of the auxiliary heat exchanger **46** is fluidically coupled with the inlet of a separation column **49**. During their passage through the separation column **49**, the various compounds of a fluid sample get separated. The separation column's outlet is fluidically coupled with a detection unit **50**, the detection unit **50** being adapted for determining a detection signal as a function of time. Thus, a peak pattern **51** is obtained, with each of the peaks **52** corresponding to a certain compound of the sample of interest.

[**0068**] In the embodiment shown in FIG. **6**, the quality of the acquired peak pattern **51** is used for determining an optimum amount of heating, and for activating or deactivating a corresponding number of the heating modules **48***a* to **48***d*. By analyzing at least one of the peaks' heights and half widths, a measure indicating the quality of the peak pattern may be derived. This measure of the peak pattern's quality may be used for deriving a feedback signal **53** indicating which ones of the heating modules **48***a* to **48***d* should be activated or deactivated.

[**0069**] In the following, an example of the heating system's operation is given. Initially, the heating modules **48***a* and **48***b* might be active, while the heating modules **48***c* and **48***d* are switched off. Now, the detection unit **50** might increase the amount of heating by activating the heating module **48***c* and observing the peak pattern's quality in dependence on this modification. If the quality of the peak pattern improves, the heating module **48***c* will remain active. If the quality of the obtained peak pattern decreases, the additional heating module **48***c* will be switched off and the detection unit **50** will start reducing the amount of heating. For example, the detection unit **50** might modify the feedback signal **53** in a way that the heating modules **48***b* to **48***d* are switched off, whereas heating module **48***a* remains active. If the quality of the peak pattern is improved, the heating module **48***b* will remain deactivated.

[**0070**] The closed loop control shown in FIG. **6** is capable of adjusting the amount of heating in a way that peak patterns of optimum quality are obtained. When employing different solvents having different thermal properties, it might be useful to readjust the proper amount of heating individually for each of the solvents. Furthermore, when the separation system shown in FIG. **6** is used in gradient operation, it might be useful to readjust the amount of heating in accordance with the variation of solvent composition.

What is claimed is:

1. A heating system for preheating a fluid, comprising:

a heating unit with a heating flow path;

wherein the heating unit is adapted to be operated at a first temperature and to provide a heat transfer between the heating unit and the fluid passing through the heating flow path, with the heat transfer not being sufficient for heating up the fluid passing through the heating flow path to the first temperature.

2. The heating system of claim 1, wherein the heating flow path's outlet is fluidically coupled with a separation system, the separation system being adapted for separating compounds of a fluid sample.

3. The heating system of claim 1, further comprising at least one feature selected from the group consisting of:

the heating unit is implemented such that the fluid's temperature after passing through the heating unit's heating flow path is lower than the first temperature;

the heating power of the heating unit is not sufficiently large and/or the heating unit's heating flow path is not sufficiently long for bringing the temperature of the fluid passing through the heating flow path to the first temperature;

the temperature of the fluid at the heating flow path's outlet depends on the thermal properties of the fluid passing through the heating unit's heating flow path; and

a variation of the fluid's composition gives rise to a variation of the fluid's thermal properties and to a corresponding variation of the fluid's temperature at the heating flow path's outlet.

4. The heating system of claim 1, wherein the heating unit is an auxiliary heating unit with an auxiliary heating flow path,

wherein the heating system further comprises a main heating unit with a main heating flow path;

the main heating flow path's outlet being fluidically coupled with the auxiliary heating flow path's inlet, and

wherein the main heating unit is adapted to be operated at a second temperature being lower than the first temperature and to provide a heat transfer between the main heating unit and a fluid passing through the main heating flow path, with the heat transfer being sufficient for heating up the fluid passing through the main heating flow path to the second temperature.

5. The heating system of claim 4, further comprising at least one feature selected from the group consisting of:

the main heating unit is located upstream of the auxiliary heating unit;

the main heating unit is implemented such that the fluid's temperature attains the second temperature when passing through the main heating unit's main heating flow path;

the heating power of the main heating unit is sufficiently large, and the main heating unit's main heating flow path is sufficiently long for bringing the temperature of the fluid passing through the main heating flow path to the second temperature;

the heating system comprises a sample injection unit located between the main heating unit and the auxiliary heating unit, with the sample injection unit being adapted for injecting a fluid sample into the fluid passing through the heating system; and

the heating system comprises a sample heating unit adapted for preheating the fluid sample before the fluid sample is provided to the sample injection unit.

6. The heating system of claim 1, further comprising at least one feature selected from the group consisting of:

the main heating flow path is implemented as a first heat transfer capillary;

the auxiliary heating flow path is implemented as a second heat transfer capillary;

the capillaries' inner diameter lies in the range between 0.05 mm and 0.30 mm;

the heating unit is made of at least one of: cast iron, copper, aluminium, bronze; and

the heating unit comprises a plurality of switchable heater modules.

7. A separation system comprising:

a heating unit for preheating a fluid, the heating unit comprising a heating flow path, wherein the heating unit is adapted to be operated at a first temperature and to provide a heat transfer between the heating unit and the fluid passing through the heating flow path, with the heat transfer not being sufficient for heating up the fluid passing through the heating flow path to the first temperature; and

a separation column adapted for separating compounds of a fluid sample, with the heating flow path's outlet being fluidically coupled with the separation column's inlet.

8. The separation system of claim 8, further comprising at least feature selected from the group consisting of:

a fluid delivery unit, preferably a pump, located upstream of the heating unit and being adapted for moving the fluid in the separation system;

a sample injection unit located upstream of the heating unit and being adapted for injecting the fluid sample into a mobile phase of the separation system;

a detector located downstream of the separation column and being adapted for detecting separated compounds of the fluid sample; and

a controller adapted for controlling operation of the separation system.

9. The separation system of claim 8, further comprising at least one feature selected from the group consisting of:

the fluid conveyed through the heating unit is a solvent, and the solvent's composition is kept constant during sample analysis;

the fluid conveyed through the heating unit is a composite solvent, and the solvent's composition is varied according to a gradient during sample analysis;

the fluid conveyed through the heating unit is a composite solvent, and a variation of the composite solvent's composition gives rise to a corresponding temperature variation of the composite solvent supplied to the separation system;

the temperature of the fluid further increases when passing through the separation column;

the separation system is one of: a liquid chromatography system, an electrophoresis system, an electrochromatography system;

the separation system comprises a thermostated column compartment adapted for keeping the separation column at a predefined temperature;

the temperature the thermostated column compartment is kept at is approximately equal to the first temperature; and

the thermostated column compartment is thermally coupled with the heating unit.

10. The separation system of claim 8, further comprising at least one feature selected from the group consisting of:

the heating unit's heating power is varied in dependence on a feedback signal;

the heating unit comprises a plurality of switchable heater modules that may be activated in dependence on a feedback signal;

the feedback signal indicates the temperature of the fluid at the outlet of the heating unit;

the feedback signal indicates a quality of peak patterns acquired with the separation system; and

the heating unit's heating power is controlled in a closed-loop control operation.

11. The separation system of claim 8, wherein the heating unit is auxiliary heating unit with an auxiliary heating flow path,

wherein the heating system further comprises a main heating unit with a main heating flow path;

the main heating flow path's outlet being fluidically coupled with the auxiliary heating flow path's inlet, and

wherein the main heating unit is adapted to be operated at a second temperature being lower than the first temperature and to provide a heat transfer between the main heating unit and a fluid passing through the main heating flow path, with the heat transfer being sufficient for heating up the fluid passing through the main heating flow path to the second temperature.

12. The separation system of claim 13, further comprising at least one feature selected from the group consisting of:

a sample injection unit located between the main heating unit and the auxiliary heating unit, the sample injection unit being adapted for injecting the fluid sample into a mobile phase of the separation system; and

a sample heating unit adapted for preheating the fluid sample before the fluid sample is provided to the sample injection unit.

13. A method for preheating a fluid, the method comprising:

conveying the fluid through a heating unit, the heating unit being kept at a first temperature, with the heat transfer during the fluid's passage through the heating unit not being sufficient for bringing the fluid's temperature to the first temperature; and

supplying the fluid to a separation system.

14. The method of claim 15, wherein composition of the fluid conveyed through the heating unit is varied according to a gradient.

15. The method of claim 15, wherein composition of the fluid conveyed through the heating unit is kept constant.

16. The method of claim 15, wherein the heating unit is an auxiliary heating unit with an auxiliary heating flow path,

the method further comprising:

conveying the fluid through a main heating unit before supplying the fluid to the auxiliary heating unit, the main heating unit being kept at a second temperature, the second temperature being lower than the first temperature, with the heat transfer during the fluid's passage through the main heating unit being sufficient for bringing the fluid's temperature to the second temperature.

17. The method of claim 15, further comprising:

adjusting the heating unit's heating power in dependence on at least one of: a type of separation system, a type of solvent, a slope of a solvent gradient, a flow rate of the fluid.

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