

Patent Claims

1. Micro flow filtration system for performing a fluidic process, such as concentrating of components contained in a fluid sample or for exchanging the solvent of the sample fluid, the system ~~(1)~~ comprising:
- a fluid channel ~~(2)~~ having two ends ~~(10, 11)~~ and being formed by conduits ~~(4, 5)~~ allowing a bidirectional flow of the fluid sample through the channel ~~(2)~~;
 - a tangential flow filtration module ~~(3)~~ (TFF-module) having a first fluid port ~~(14)~~, a second fluid port ~~(15)~~, a permeate outlet ~~(16)~~ and a semi-permeable membrane ~~(17)~~ capable of separating the fluid sample into a retentate stream flowing through one of the ports ~~(14, 15)~~ and a permeate stream upon passage of the fluid of the sample through the semipermeable membrane ~~(17)~~ and through the permeate outlet ~~(16)~~;
 - at least two pairs ~~(8, 9)~~ of piston pumps ~~(6)~~ having each two piston pumps ~~(6)~~, each piston pump having a piston swept volume forming a reservoir ~~(18, 19)~~ being able to contain a fluid, the piston pumps ~~(6)~~ being capable to drive a fluid flow;
 - the volume of the piston pumps ~~(6)~~ of one pair ~~(8)~~ of piston pumps ~~(8a, 8b)~~ is larger than the volume of the piston pumps ~~(6)~~ of the other pair ~~(9)~~ of piston pumps ~~(9a, 9b)~~,
 - a control unit for controlling the piston pumps ~~(6)~~,
- wherein
- the TFF-module ~~(3)~~ is located in the fluid channel ~~(2)~~ so that one conduit ~~(4)~~ is connected to the first fluid port ~~(14)~~ and the other conduit ~~(5)~~ is connected to the second fluid port ~~(15)~~ to allow a fluid flowing through the channel ~~(2)~~ to pass through the TFF-module ~~(3)~~;
 - at each of the ends ~~(10, 11)~~ of the channel ~~(2)~~ one piston pump ~~(6)~~ of each pair ~~(8, 9)~~ of piston pumps is arranged in such a manner that the piston pumps ~~6~~ are fluidically connected, wherein all piston pumps are arranged on the same side of the semipermeable membrane of the TFF-module;
 - the control unit is arranged and adapted to control driving of the pis-

- ton pumps of each pair ~~(8, 9)~~ of piston pumps ~~(6)~~ synchronously and/or to control the switching and/or the switching time for switching from one pair ~~(8)~~ of piston pumps ~~(8a, 8b)~~ to the other pair ~~(9)~~ of piston pumps ~~(9a, 9b)~~ and
- 5 - the system is arranged and adapted such that the control unit defines a regulation that during the fluidic process at least for a period of time only one of the pairs ~~(8, 9)~~ of piston pumps ~~(6)~~ is used to drive the fluid flow through the fluid channel ~~(2)~~.
2. Micro flow filtration system according to claim 1, characterized in that the
- 10 piston pumps ~~(6)~~ at the end of the fluid channel ~~(2)~~ are fluidically connected in parallel.
3. Micro flow filtration system according to claim 1, characterized in that
- the piston pumps ~~(6)~~ at the end of the fluid channel ~~(2)~~ are fluidically connected in series and
- 15 - ~~preferably~~ at least two of the piston pumps ~~(6)~~ located at one end of the fluid channel ~~(2)~~ are combined in an integrated piston pump ~~(60)~~ having at least two piston pump chambers ~~(61, 62)~~ fluidically serial connected and having at least two pistons ~~(63, 64)~~ arranged in such a manner that at least one piston being able to move
- 20 in at least two piston pump chambers ~~(61, 62)~~ and being able to drive the fluid out of at least one of the at least two piston pump chambers ~~(61, 62)~~.
4. Micro flow filtration system according to claim 3, characterized in that the integrated piston pump ~~(60)~~ comprises an integrated piston ~~(65)~~ having
- 25 at least a primary piston ~~(63)~~ and a secondary piston ~~(64)~~ which are ~~preferably~~ coupled to another, wherein the primary piston ~~(63)~~ and a secondary piston ~~(64)~~ are able to move synchronously in at least one chamber ~~(61, 62)~~ and ~~preferably~~ at the end of the movement path in a chamber ~~(61)~~ the secondary piston ~~(64)~~ being able to move further in
- 30 another chamber ~~(62)~~ of the integrated piston pump ~~(60)~~.
5. Micro flow filtration system according to any one of the preceding claims, characterized in that the volume of the piston pumps ~~(6)~~ of the first pair

~~(8)~~ of piston pumps ~~(8a, 8b)~~ is at least three times larger than the volume of the piston pumps ~~(6)~~ of the second pair ~~(9)~~ of piston pumps ~~(9a, 9b)~~, preferably.

5 6. Micro flow filtration system according to any one of the preceding claims, characterized in that the volume of the piston pumps of the first pair of piston pumps is at least five times larger than the volume of the piston pumps of the second pair of piston pumps, further preferably.

10 7. Micro flow filtration system according to any one of the preceding claims, characterized in that the volume of the piston pumps of the first pair of piston pumps is at least ten times larger than the volume of the piston pumps of the second pair of piston pumps, particularly preferably.

15 8. Micro flow filtration system according to any one of the preceding claims, characterized in that the volume of the piston pumps of the first pair of piston pumps is at least 25 times larger than the volume of the piston pumps of the second pair of piston pumps, also particularly preferably.

20 ~~6-9.~~ Micro flow filtration system according to any one of the preceding claims, characterized in that the volume of the piston pumps of the first pair of piston pumps is at least 100 times larger than the volume of the piston pumps of the second pair of piston pumps.

~~6-10.~~ Micro flow filtration system according to any one of the preceding claims, characterized in that the system ~~(1)~~ comprises a balance ~~(24)~~ for weighting the permeate withdrawn from the TFF-module ~~(3)~~.

25 ~~7-11.~~ Micro flow filtration system according to any one of the preceding claims, characterized in that the system ~~(1)~~ comprises in the fluid channel or in the TFF-module ~~(3)~~ at least one pressure sensor ~~(22, 23, 24)~~ for monitoring and measuring the pressure in the system ~~(1)~~, preferably at least two or more pressure sensors ~~(22, 23, 24)~~ located on opposite sides of the TFF-module ~~(3)~~ which can be used to determine the trans-
30 membrane pressure across the semipermeable membrane ~~(17)~~.

- 8.12. Micro flow filtration system according to any one of the preceding claims, characterized in that the system (1) comprises an optical measuring device (26) for acquiring the concentration of the components contained in the fluid sample, wherein the optical measuring device (26) preferably comprises a cuvette (30) integrated in the fluid channel (2).
- 9.13. Micro flow filtration system according to any one of the preceding claims, characterized in that the control unit (80) is adapted to synchronize the stroke of the pistons of the piston pumps (6) of the same pair (8, 9) of piston pumps (6) such that the piston swept volume of the piston pumps (6) is synchronously adapted.
- 10.14. Micro flow filtration system according to any one of the preceding claims, characterized in that the control unit (80) controls the piston pumps (6) of one pair (8, 9) of piston pumps (6) in such a manner that the fluid flows back and forth through the TFF-module (3) from one piston pump (6) to the other piston pump (6) of one pair (8, 9) of piston pumps (6).
- 11.15. Flow filtration method for concentrating a component contained in a fluid sample using a tangential flow filtration module (3), the method comprising the following steps:
- providing a micro flow filtration system (1) preferably according to any one of the preceding claims comprising
 - a fluid channel (2) having two ends (10, 11) and being formed by two conduits (4, 5) allowing a bidirectional flow of the fluid sample through the channel (2);
 - a tangential flow filtration module (3) having a first fluid port (14), a second fluid port (15), a permeate outlet (16) and a semipermeable membrane (17) capable of separating the fluid sample;
 - at least two pairs (8, 9) of piston pumps (6), each piston pump (6) forming a reservoir (18, 19) being able to contain a fluid;
 - a control unit (80) for controlling movement of the pistons of the piston pumps (6);
- wherein
- the TFF-module (3) is located in the fluid channel (2) so that one

- conduit (4) is connected to the first fluid port (14) and the other conduit 5 is connected to the second fluid port (15);
- at each of the ends (10, 11) of the channel (2) one piston pump (6) of each pair (8, 9) of piston pumps (6) is arranged in such a manner that the piston pumps (6) are connected fluidically, wherein all piston pumps are arranged on the same side of the semipermeable membrane of the TFF-module;
 - the piston pumps (6) of a first pair (8) of piston pumps have a larger volume than the piston pumps (6) of a second pair (9) of piston pumps (6);
 - the control unit (80) is arranged and adapted to control of moving the pistons of the piston pumps of each pair (8, 9) of piston pumps synchronously and/or to control the switching and/or the switching time for switching from one pair (8) of piston pumps (8a, 8b) to the other pair (9) of piston pumps (9a, 9b),
 - filling at least one piston pump (6) of the first pair (8) of piston pumps with a fluid;
 - moving the piston of the first piston pump (8a) of the first pair (8) of piston pumps controlled by the control unit (80) in a first direction to reduce the piston swept volume to drive the fluid sample from the first piston pump (8a) through the fluid channel (2) and to pass the TFF-module (3) thereby increasing the concentration of the components in the fluid sample in the system (1) and withdrawing an amount of fluid in a permeate stream;
 - moving the piston of the second piston pump (8b) of the first pair (8) of piston pumps controlled by the control unit (80) in the first direction to enhance the piston swept volume to allow fluid to enter the piston pump (8b) after passage through the fluid channel (2);
 - moving the piston of the second piston pump (8b) and the piston of the first piston pump (8a) of the first pair (8) of piston pumps controlled by the control unit (80) in a second direction opposite to the first direction to drive back the fluid sample from the second piston pump (8b) through the TFF-module (3) into the first piston pump (8a);
 - determining if the volume of the fluid sample in the system (1) has been reduced below a predetermined value or if an predetermined

time interval after starting of the process has been reached;

- repeating the steps of moving the first and second piston pumps ~~(8a, 8b)~~ of the first pair of piston pumps ~~(8)~~ controlled by the control unit ~~(80)~~ in the first and second direction until the predetermined value or the predetermined time interval has been reached, thereby driving the fluid back and forth through the TFF-module ~~(3)~~; and
- if the volume of the fluid sample in the system ~~(4)~~ has been reduced below the predetermined value or if the predetermined time interval after starting of the process has been reached, using the piston pumps ~~(9a, 9b)~~ of the second pair ~~(9)~~ of piston pumps according to the steps above thereby establishing a continuous bidirectional flow of fluid in the channel ~~(2)~~.

~~12.16.~~ Flow filtration method according to the preceding claim, characterized in that moving the piston pumps ~~(8, 9)~~ of the first pair ~~(8)~~ of piston pumps and of the second pair ~~(9)~~ of piston pumps is controlled by the control unit ~~(80)~~ in such a manner that the fluid is driven with a constant pressure through the TFF-module ~~(3)~~.

17. Flow filtration method according to claim ~~11-15~~ or ~~12.16~~, characterized in that the volume of the piston pumps ~~(6)~~ of one pair ~~(8)~~ of piston pumps ~~(8a, 8b)~~ is at least three times larger than the volume of the piston pumps of another pair of piston pumps.

18. Flow filtration method according to claim 15 or 16, characterized in that the volume of the piston pumps of one pair of piston pumps is, further preferably at least five times larger than the volume of the piston pumps of another pair of piston pumps.

19. Flow filtration method according to claim 15 or 16, characterized in that the volume of the piston pumps of one pair of piston pumps is, particularly preferably at least 25 times larger than the volume of the piston pumps of another pair of piston pumps.

~~13.20.~~ Flow filtration method according to claim 15 or 16, characterized in that the volume of the piston pumps of one pair of piston pumps is, also

particularly ~~preferably~~ at least 100 times larger than the volume of the piston pumps ~~(6)~~ of another ~~pair (9)~~ of piston pumps ~~(9a, 9b)~~.

5 ~~44-21.~~ Flow filtration method according to any one of the claims ~~44-15~~ to ~~43-20~~, characterized in that the volume of the fluid sample in the system ~~(1)~~ is determined by weighting the permeate withdrawn from the TFF-module ~~(3)~~, ~~preferably~~ using a balance ~~(21)~~.

~~45-22.~~ Flow filtration method according to any one of the claims ~~44-15~~ to ~~44-21~~, characterized in that the volume of the fluid sample in the system is determined by measuring or determining the piston stroke length

10 ~~46-23.~~ Micro flow filtration system or flow filtration method according to any one of the preceding claims, characterized in that the piston pumps ~~(6)~~ are motor driven and ~~preferably~~ the system ~~(1)~~ comprises for each piston pump ~~(6)~~ or piston pump pair ~~(8, 9)~~ a motor ~~(12)~~ for driving the piston pump ~~(6)~~.

15 ~~47-24.~~ Flow filtration method according to any one of the claims ~~44-15~~ to ~~46-23~~, characterized in controlling the flow from the first piston pump ~~(8a, 9a)~~ to the second piston pump ~~(8b, 9b)~~ of a pair ~~(8, 9)~~ of piston pumps by monitoring the actual pressure of the fluid in the system ~~(1)~~ ~~preferably~~ the transmembrane pressure.

20 ~~48-25.~~ Flow filtration method according to any one of the claims ~~44-15~~ to ~~47-24~~, characterized in

25 - controlling the flow from a first piston pump to a second piston pump of a pair ~~(8, 9)~~ of piston pumps by an incrementally driven motor, ~~preferably~~ a stepping motor ~~(12)~~ to drive the piston pumps ~~(6)~~ and controlling the increments moved by the motor ~~(12)~~.