Claims

1. A method for loading a crystallization device comprising multiple receptacles with a pre-defined amount of at least one matrix-forming compound capable of forming a crystallization matrix for a membrane protein, comprising the following steps:

   a) Modifying the state of aggregation of said at least one matrix-forming compound to a fluidic state which allows dispensing said at least one matrix-forming compound, and
   b) dispensing a defined amount of said at least one matrix-forming compound into at least one receptacle of the crystallization device, wherein said dispensed matrix-forming compound solidifies within said receptacle.

2. The method according to claim 1, wherein the state of aggregation of said at least one matrix-forming compound is modified by modifying the temperature, preferably by heating.

3. The method according to claim 1 or 2, wherein said process is automated by using a robotic system comprising a dispensing unit.

4. The method according to at least one of the claims 1 to 3, wherein said matrix-forming compound has at least one of the following characteristics:
   a) It is capable of forming a meso phase; and/or
   b) It is capable of forming a cubic phase; and/or
   c) It is capable of forming a sponge phase; and/or
   d) It is a lipidic compound; and/or
   e) It is amphiphilic; and/or
   f) It comprises a saturated or unsaturated fatty-acid chain.
   g) It is an alcohol derivative from a fatty acid.

5. The method according to at least one of the claims 1 to 4, wherein said matrix-forming compound capable of forming a crystallization matrix for a membrane protein has at least one of the following characteristics:

   a) it is mixed with an additive thereby forming an additive composition;

   b) said matrix-forming compound or said additive composition consists of or comprises at least one compound selected from the group consisting of

   i) Fatty acids, alcohol derivatives from fatty acids, monoglycerides, diglycerides, lipids and their derivatives, preferably the corresponding compounds that have

their acid group(s) replaced by a hydroxyl or thiol or ether or thioether group or ω-hydroxyalkenes or their ethers or homologous thiols or thioethers; monoacylglycerols, preferably cis monounsaturated monoacylglycerols, more preferably monoolein (C18: c9), monopalmitolein (C16: c9) and monovacennin (C18: c7); medium-chain length alkyl glycosides; polyalkylenglycols, polyethylenglycols, diacylglycerophospholipids, monoacylglycerophospholipids and derivatives thereof capable of forming a crystallization matrix for a biopolymer; and/or

ii) polyketides, saccharolipids, prenol lipids, sterol lipids, sphingolipids, glycerophospholipids and glycerolipids and/or derivates of lipids, in particular phosphatidylcholine (PC), in particular DOPC, phosphatidylethanolamine, in particular DOPE, phosphatidylserine, in particular DOPS, cardiolipin, lysophosphatidylcholine, 2-monoolein, oleamide, cholesterol, cell membrane components, and natural or synthetic compounds stabilizing the membrane protein in the crystallization matrix.

6. A method for manufacturing a crystallization device comprising multiple receptacles with a pre-defined amount of at least one matrix-forming compound capable of forming a crystallization matrix for a membrane protein, wherein the method according to one of the claims 1 to 5 is performed.

7. A crystallization device comprising multiple receptacles, wherein at least some of said receptacles comprise a defined homogeneous amount of at least one solid matrix-forming compound capable of forming a crystallization matrix for a membrane protein.

8. A crystallization device according to claim 7, wherein said matrix-forming compound has not yet formed a crystallisation matrix.

9. The crystallization device according to claim 7 or 8, wherein said matrix-forming compound capable of forming a crystallization matrix for a membrane protein has at least one of the following characteristics:

a) it is mixed with an additive thereby forming an additive composition;

b) said matrix-forming compound or said additive composition consists of or comprises at least one compound selected from the group consisting of

i) Fatty acids, alcohol derivatives from fatty acids, monoglycerides, diglycerides, lipids and their derivatives, preferably the corresponding compounds that have their acid group(s) replaced by a hydroxyl or thiol or ether or thioether group or ω-hydroxyalkenes or their ethers or homologous thiols or thioethers; monoa-

cylglycerols, preferably cis monounsaturated monoacylglycerols, more preferably monoolein (C18: c9), monopalmitolein (C16: c9) and monovacennin (C18: c7); medium-chain length alkyl glycosides; polyalkylenglycols, polyethylenglycols, diacylglycerophospholipids, monoacylglycerophospholipids and derivatives thereof capable of forming a crystallization matrix for a biopolymer; and/or

ii) polyketides, saccharolipids, prenol lipids, sterol lipids, sphingolipids, glycerophospholipids and glycerolipids and/or derivates of lipids, in particular phosphatidylcholine (PC), in particular DOPC, phosphatidylethanolamine, in particular DOPE, phosphatidylserine, in particular DOPS, cardiolipin, lysophosphatidylcholine, 2-monoolein, oleamide, cholesterol, cell membrane components, and natural or synthetic compounds stabilizing the membrane protein in the crystallization matrix.

10. The use of a crystallization device according to claims 7 to 9 or a crystallization device produced according to the method defined in claims 1 to 6 in a method of crystallizing biopolymers, in particular membrane proteins.

11. A method of crystallizing biopolymers, wherein a defined amount of at least one matrix-forming compound capable of forming a crystallization matrix for a membrane protein contained in at least one receptacle of a crystallization device according to one of the claims 7 to 9 or a crystallization device manufactured according to one of the method of claim 1 to 6 is contacted with a liquid to form a crystallization matrix.

12. The method of claim 11, wherein said liquid comprises water, one or more additives and/or the biopolymer to be crystallized.

13. The method according to claim 11 or 12, wherein the crystallization matrix is contacted with a precipitating solution.

14. The method according to one of the claims 10 to 13, wherein the crystallization device comprises at least one receptacle for receiving the at least one matrix-forming compound capable of forming a crystallization matrix for a membrane protein and at least one reservoir which is in communication with said at least one receptacle and wherein a precipitation solution is preferably dispensed into the reservoir.

15. The method according to claim 14, wherein the precipitation solution in the reservoir is covered with a cover, preferably a film which prevents evaporation.

Claims

1. A method for loading a crystallization device comprising multiple receptacles with a pre-defined amount of at least one amphiphilic matrix-forming compound capable of forming a crystallization matrix for a membrane protein, comprising the following steps:

   a) modifying the state of aggregation of said at least one amphiphilic matrix-forming compound from a solid to a fluidic state which allows dispensing said at least one matrix-forming compound, and
   b) dispensing a defined amount of said at least one matrix-forming compound into at least one receptacle of the crystallization device, wherein said dispensed matrix-forming compound solidifies within said receptacle, wherein the crystallization matrix is not formed prior to the dispensing step and wherein the matrix-forming compound is not mixed with the membrane protein to be crystallized prior to the dispensing step.

2. The method according to claim 1, wherein the state of aggregation of said at least one matrix-forming compound is modified by modifying the temperature.

3. The method according to claim 1, wherein the state of aggregation of said at least one matrix-forming compound is modified by heating.

4. The method according to any one of claims 1 to 3, wherein said process is automated by using a robotic system comprising a dispensing unit.

5. The method according to any one of claims 1 to 4, wherein said matrix-forming compound has at least one of the following characteristics:
   a) it is capable of forming a meso phase; and/or
   b) it is capable of forming a cubic phase; and/or
   c) it is capable of forming a sponge phase; and/or
   d) it is a lipidic compound; and/or
   e) it comprises a saturated or unsaturated fatty-acid chain; and/or
   f) it is an alcohol derivative from a fatty acid.

6. The method according to any one of claims 1 to 5, wherein said matrix-forming compound capable of forming a crystallization matrix for a membrane protein has at least one of the following characteristics:

   a) it is mixed with an additive thereby forming an additive composition;

b) said matrix-forming compound or said additive composition consists of or comprises at least one compound selected from the group consisting of

i) fatty acids, alcohol derivatives from fatty acids, monoglycerides, diglycerides, lipids and their derivatives; monoacylglycerols; medium-chain length alkyl glycosides; diacylglycerophospholipids, monoacylglycerophospholipids and derivatives thereof capable of forming a crystallization matrix for a biopolymer; and/or

ii) polyketides, saccharolipids, prenol lipids, sterol lipids, sphingolipids, glycerophospholipids and glycerolipids and/or derivates of lipids, phosphatidylethanolamine, phosphatidylserine, cardiolipin, lyso-phosphatidylcholine, 2-monoolein, oleamide, cholesterol, cell membrane components, and natural or synthetic compounds stabilizing the membrane protein in the crystallization matrix;

c) said matrix-forming compound consists of or comprises cis monounsaturated monoacylglycerols;

d) said matrix-forming compound consists of or comprises at least one compound selected from the group consisting of monoolein (C18: c9), monopalmitolein (C16: c9) and monovacennin (C18: c7);

e) said additive consists of or comprises at least one compound selected from the group consisting of phosphatidylcholine (PC), DOPC, DOPE, and DOPS.

7. A method for manufacturing a crystallization device comprising multiple receptacles with a pre-defined amount of at least one amphiphilic matrix-forming compound capable of forming a crystallization matrix for a membrane protein, wherein the method according to any one of claims 1 to 6 is performed.

8. A crystallization device comprising multiple receptacles, wherein at least some of said receptacles comprise a defined homogeneous amount of at least one solid amphiphilic matrix-forming compound capable of forming a crystallization matrix for a membrane protein, wherein said matrix-forming compound has not yet formed a crystallisation matrix.

9. The crystallization device according to claim 8, wherein said matrix-forming compound capable of forming a crystallization matrix for a membrane protein has at least one of the following characteristics:

a) it is mixed with an additive thereby forming an additive composition;

b) said matrix-forming compound or said additive composition consists of or comprises at least one compound selected from the group consisting of

i) fatty acids, alcohol derivatives from fatty acids, monoglycerides, diglycerides, lipids and their derivatives; monoacylglycerols; medium-chain length alkyl glycosides; diacylglycerophospholipids, monoacylglycerophospholipids and derivatives thereof capable of forming a crystallization matrix for a biopolymer; and/or

ii) polyketides, saccharolipids, prenol lipids, sterol lipids, sphingolipids, glycerophospholipids and glycerolipids and/or derivates of lipids, phosphatidylethanolamine, phosphatidylserine, cardiolipin, lyso-phosphatidylcholine, 2-monoolein, oleamide, cholesterol, cell membrane components, and natural or synthetic compounds stabilizing the membrane protein in the crystallization matrix;

c) said matrix-forming compound consists of or comprises cis monounsaturated monoacylglycerols;

d) said matrix-forming compound consists of or comprises at least one compound selected from the group consisting of monoolein (C18: c9), monopalmitolein (C16: c9) and monovacennin (C18: c7);

e) said additive consists of or comprises at least one compound selected from the group consisting of phosphatidylcholine (PC), DOPC, DOPE, and DOPS.

10. The use of a crystallization device according to claim 8 or 9 or a crystallization device loaded according to the method of any one of claims 1 to 6 or produced according to the method of claim 7 in a method of crystallizing biopolymers.

11. A method of crystallizing biopolymers, wherein a defined amount of at least one amphiphilic matrix-forming compound capable of forming a crystallization matrix for a membrane protein contained in at least one receptacle of a crystallization device according to claim 8 or 9 or a crystallization device loaded according to the method of any one of claims 1 to 6 or manufactured according to the method of claim 7 is contacted with a liquid to form a crystallization matrix.

12. The method of claim 11, wherein said liquid comprises water, one or more additives and/or the biopolymer to be crystallized.

13. The method according to claim 11 or 12, wherein the crystallization matrix is contacted with a precipitating solution.

14. The method according to any one of claims 10 to 13, wherein the crystallization device comprises at least one receptacle for receiving the at least one matrix-forming compound capable of forming a crystallization matrix for a membrane protein and at least one reservoir which is in communication with said at least one receptacle.

15. The method according to claim 14, wherein a precipitation solution is dispensed into the reservoir.

16. The method according to claim 15, wherein the precipitation solution in the reservoir is covered with a cover.

17. The method according to claim 16, wherein the cover is a film which prevents evaporation.

18. The use of claim 10 or the method of any one of claims 11 to 17, wherein the biopolymer is a membrane protein.