

Claims

1. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer comprises an anticoagulant entity, comprising the steps of:
 - i) treating a surface of the solid object with a cationic polymer;
 - ii) treating the surface with an anionic polymer;
 - iii) optionally repeating steps i) and ii) one or more times;
 - iv) treating the surface with a cationic polymer; and
 - v) treating the outermost layer of cationic polymer with an anticoagulant entity, thereby to covalently attach the anticoagulant entity to the outermost layer of cationic polymer;wherein,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of >4 µeq/g;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
2. A process for the manufacture of a solid object according to claim 1, wherein the anionic polymer is dextran sulfate.
3. A process for the manufacture of a solid object according to claim 1 or claim 2, wherein the anionic polymer is characterized by having a total molecular weight of 750 kDa-10,000 kDa, such as 1,000 kDa-10,000 kDa.
4. A process for the manufacture of a solid object according to any one of claims 1 to 3, wherein the total molecular weight of the anionic polymer is measured according to Evaluation Method G.
5. A process for the manufacture of a solid object according to any one of claims 1 to 4, wherein the anionic polymer is characterized by having a solution charge density of between >4 µeq/g and 7 µeq/g, such as between >5 µeq/g and 7 µeq/g.
6. A process for the manufacture of a solid object according to any one of claims 1 to 5, wherein step ii) is carried out at a salt concentration of 0.25 M-4.0 M, such as 0.25 M-3.0 M.
7. A process for the manufacture of a solid object according to any one of claims 1 to 6, wherein the salt is an inorganic salt.
8. A process for the manufacture of a solid object according to claim 7, wherein the salt is an inorganic sodium salt.

9. A process for the manufacture of a solid object according to claim 8, wherein the salt is selected from the group consisting of sodium chloride, sodium sulfate, sodium hydrogen phosphate and sodium phosphate.
10. A process for the manufacture of a solid object according to claim 9, wherein the salt is sodium chloride.
11. A process for the manufacture of a solid object according to any one of claims 1 to 10, wherein step iii) is not optional.
12. A process for the manufacture of a solid object according to claim 11, wherein in step iii), steps i) and ii) are repeated between 1 and 10 times, such 1, 2, 3, 4, 5 or 6 times.
13. A process for the manufacture of a solid object according to any one of claims 1 to 12, wherein the cationic polymer of step i) is the same as the cationic polymer of step iv).
14. A process for the manufacture of a solid object according to any one of claims 1 to 13, wherein the cationic polymer of step i) is a polyamine, which is optionally cross-linked.
15. A process for the manufacture of a solid object according to any one of claims 1 to 14, wherein the cationic polymer of step iv) is a polyamine, which is optionally cross-linked.
16. A process for the manufacture of a solid object according to any one of claims 1 to 15, additionally comprising a pre-treatment step before step i).
17. A process for the manufacture of a solid object according to any one of claims 1 to 16, additionally comprising a step between step i) and step ii), between step ii) and step iii), between step iii) and step iv) or between step iv) and step v).
18. A process for the manufacture of a solid object according to any one of claims 1 to 17, wherein the anticoagulant entity is a heparin moiety.
19. A process for the manufacture of a solid object according to claim 18, wherein the heparin moiety is an end-point attached heparin moiety.
20. A process for the manufacture of a solid object according to claim 19, wherein the end-point attached heparin moiety is connected through its reducing end.
21. A process for the manufacture of a solid object according to claim 18, wherein the anticoagulant entity is a full length heparin.
22. A process for the manufacture of a solid object according to any one of claims 1 to 21, wherein the anticoagulant entity is covalently attached via a linker.

23. A process for the manufacture of a solid object according to claim 22, wherein the linker comprises a secondary amine.
24. A process for the manufacture of a solid object according to claim 22, wherein the linker comprises a secondary amide.
25. A process for the manufacture of a solid object according to claim 22, wherein the linker comprises a 1,2,3-triazole.
26. A process for the manufacture of a solid object according to claim 22, wherein the linker comprises a thioether.
27. A process for the manufacture of a solid object according to any one of claims 1 to 26, wherein the solid object is a medical device, an analytical device, a separation device or a membrane.
28. A process for the manufacture of a solid object according to claim 27, wherein the solid object is a thromboresistant medical device.
29. A process for the manufacture of a solid object according to claim 27, wherein the solid object is an extracorporeal medical device.
30. A process for the manufacture of a solid object according to claim 28, wherein the solid object is an intracorporeal medical device.
31. A process for the manufacture of a solid object according to claim 30, wherein the intracorporeal medical device is a stent or a stent-graft.
32. A process for the manufacture of a solid object according to any one of claims 1 to 31, wherein the solid object has anticoagulant entity activity of at least 1 pmol/cm² of surface e.g. at least 2 pmol/cm² of surface, at least 3 pmol/cm² of surface, at least 4 pmol/cm² of surface, or at least 5 pmol/cm² of surface for binding of ATIII, suitably measured according Evaluation Method B.
33. A process for the manufacture of a solid object according to any one of claims 1 to 32, wherein the solid object has blood contact performance of at least 80% preserved platelets, e.g. at least 85% preserved platelets, e.g. at least 90% preserved platelets, suitably measured according Evaluation Method E.
34. A process for the manufacture of a solid object according to any one of claims 1 to 33, wherein the solid object has an F1+2 value of <10,000 pmol/L, less than 7,500 pmol/L,

less than 5,000 pmol/L or less than 4,000 pmol/L, suitably measured according Evaluation Method F.

35. A process for the manufacture of a solid object according to any one of claims 1 to 34, wherein the anticoagulant entity is a heparin moiety, and wherein the solid object has heparin concentration of at least 1 $\mu\text{g}/\text{cm}^2$, e.g. at least 2 $\mu\text{g}/\text{cm}^2$, at least 4 $\mu\text{g}/\text{cm}^2$, at least 5 $\mu\text{g}/\text{cm}^2$, or at least 6 $\mu\text{g}/\text{cm}^2$, suitably measured according Evaluation Method A.
36. A process for the manufacture of a solid object according to any one of claims 1 to 35, wherein the solid object has a zeta potential profile suitably measured according to Evaluation Method D characterised by an isoelectric point (IEP) below pH 3, a global minimum of the curve below pH 5 and a delta value i.e. the difference between the zeta potential at the global minimum and the zeta potential at pH 9 of at least 20 mV.
37. A process for the manufacture of a solid object according to any one of claims 1 to 36, wherein the anionic polymer is a polymer comprising groups selected from $-\text{CO}_2^-$, $-\text{SO}_3^-$, $-\text{PO}_3\text{H}^-$ and $-\text{PO}_3^{2-}$.
38. A process for the manufacture of a solid object according to claim 37, wherein the anionic polymer is a polymer comprising $-\text{SO}_3^-$ groups.
39. A process for the manufacture of a solid object according to claim 38, wherein the sulfur content of the anionic polymer is between 10% and 25% by weight of the anionic polymer.
40. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer comprises an anticoagulant entity, comprising the steps of:
 - i) treating a surface of the solid object with a cationic polymer;
 - ii) treating the surface with an anionic polymer;
 - iii) optionally repeating steps i) and ii) one or more times;
 - iv) treating the surface with a cationic polymer; and
 - v) treating the outermost layer of cationic polymer with an anticoagulant entity, thereby to covalently attach the anticoagulant entity to the outermost layer of cationic polymer;wherein,
the anionic polymer is a polymer comprising $-\text{SO}_3^-$ groups,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.

41. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer comprises an anticoagulant entity, comprising the steps of:
- i) treating a surface of the solid object with a cationic polymer;
 - ii) treating the surface with an anionic polymer;
 - iii) optionally repeating steps i) and ii) one or more times;
 - iv) treating the surface with a cationic polymer; and
 - v) treating the outermost layer of cationic polymer with an anticoagulant entity, thereby to covalently attach the anticoagulant entity to the outermost layer of cationic polymer;
- wherein,
the anionic polymer is characterized by having a total molecular weight of 650 kDa-10,000 kDa;
the anionic polymer is dextran sulfate;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
42. A process for the manufacture of a solid object according to either claim 40 or 41, wherein the anticoagulant entity is a heparin moiety.
43. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising cationic polymer to which is covalently bound an anticoagulant entity;
and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of $>4 \mu\text{eq/g}$.
44. A solid object according to claim 43, wherein the anionic polymer is characterized by having a total molecular weight of 650 kDa-1,000 kDa.
45. A solid object according to claim 43, wherein the anionic polymer is characterized by having a total molecular weight of 1,000 kDa-4,500 kDa.
46. A solid object according to claim 43, wherein the anionic polymer is characterized by having a total molecular weight of 4,500 kDa-7,000 kDa.
47. A solid object according to claim 43, wherein the anionic polymer is characterized by having a total molecular weight of 7,000 kDa-10,000 kDa.
48. A solid object according to any one of claims 43 to 47, wherein the anionic polymer is applied to the surface at a salt concentration of 0.25 M-5.0 M, such as 0.25 M-4.0 M or 0.25 M-3.0 M.

49. A solid object according to claim 48, wherein the anionic polymer is a polymer comprising groups selected from -CO_2^- , -SO_3^- , $\text{-PO}_3\text{H}^-$ and -PO_3^{2-} .
50. A solid object according to claim 49, wherein the anionic polymer is a polymer comprising -SO_3^- groups.
51. A solid object according to claim 50, wherein the sulfur content of the anionic polymer is between 10% and 25% by weight of the anionic polymer.
52. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising cationic polymer to which is covalently bound an anticoagulant entity; the anionic polymer is a polymer comprising -SO_3^- groups and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer.
53. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising cationic polymer, comprising the steps of:
- treating a surface of the solid object with a cationic polymer;
 - treating the surface with an anionic polymer;
 - optionally repeating steps i) and ii) one or more times; and
 - treating the surface with a cationic polymer;
- wherein,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of $>4 \mu\text{eq/g}$;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
54. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising cationic polymer, comprising the steps of:
- treating a surface of the solid object with a cationic polymer;
 - treating the surface with an anionic polymer;
 - optionally repeating steps i) and ii) one or more times; and
 - treating the surface with a cationic polymer;
- wherein,
the anionic polymer is a polymer comprising -SO_3^- groups,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.

55. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising cationic polymer, comprising the steps of:
- treating a surface of the solid object with a cationic polymer;
 - treating the surface with an anionic polymer;
 - optionally repeating steps i) and ii) one or more times; and
 - treating the surface with a cationic polymer;
- wherein,
the anionic polymer is characterized by having a total molecular weight of 650 kDa-10,000 kDa;
the anionic polymer is dextran sulfate;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
56. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising cationic polymer;
and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of $>4 \mu\text{eq/g}$.
57. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising cationic polymer; the anionic polymer is a polymer comprising $-\text{SO}_3^-$ groups and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer.
58. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising anionic polymer, comprising the steps of:
- treating a surface of the solid object with a cationic polymer;
 - treating the surface with an anionic polymer;
 - optionally repeating steps i) and ii) one or more times;
- wherein,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of $>4 \mu\text{eq/g}$;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
59. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising anionic polymer, comprising the steps of:
- treating a surface of the solid object with a cationic polymer;
 - treating the surface with an anionic polymer;

- iii) optionally repeating steps i) and ii) one or more times;
wherein,
the anionic polymer is a polymer comprising -SO_3^- groups,
the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
60. A process for the manufacture of a solid object having a surface comprising a layered coating of cationic and anionic polymer wherein the outer coating layer is a layer comprising anionic polymer, comprising the steps of:
i) treating a surface of the solid object with a cationic polymer;
ii) treating the surface with an anionic polymer;
iii) optionally repeating steps i) and ii) one or more times;
wherein,
the anionic polymer is characterized by having a total molecular weight of 650 kDa-10,000 kDa;
the anionic polymer is dextran sulfate;
and wherein,
step ii) is carried out at a salt concentration of 0.25 M-5.0 M.
61. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising anionic polymer; and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a solution charge density of $>4 \mu\text{eq/g}$.
62. A solid object having a surface comprising a layered coating of cationic and anionic polymer, wherein the outer coating layer is a layer comprising anionic polymer; the anionic polymer is a polymer comprising -SO_3^- groups and wherein the anionic polymer is characterized by having (a) a total molecular weight of 650 kDa-10,000 kDa; and (b) a sulfur content between 10% and 25% by weight of the anionic polymer.