Electronic Supplementary Material (ESI) for Polymer Chemistry.

Supporting Information

Radical Polymerization Reactions for Amplified Biodetection Signals

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Table S1. Operation conditions and specifications of polymerization-based biodetection methods in literature.

#	Polymerization	Analyte type[a]	Binding mode[b]	Detection method	Rinsing solvent /buffer[c]	Amplification time	Linear dynamic range (limit of detection)	Ref.
1	ATRP	ssDNA	sandwich	visual detection	MeOH	2 h 20 m	not applicable (1 nM)	22
2	ATRP	ssDNA	sandwich	visual detection	MeOH, water	2 h 5 m	not applicable (1 μM)	23
3	ATRP	rabbit IgG	sandwich	UV-Vis spectroscopy	MeOH	6 h	3.3 pM-166.7 pM (0.2 pM)	24
4	AGET ATRP	ssDNA	sandwich	ellipsometry	DMSO, MeOH	2 h 10 m	1 nM-100 nM (1 nM)	31
5	AGET ATRP	ssDNA	sandwich	visual detection	DMSO, MeOH	2 h 10 m	not applicable (10 nM)	31
6	AGET ATRP	human IgG	sandwich	contact angle measurement	MeOH, water	7 m	6.7 pM-670 nM (0.9 pM)	32
7	AGET ATRP	human IgG	sandwich	visual detection	MeOH, water	10 m	not applicable (67 pM)	32
8	AGET ATRP	ssDNA	sandwich	electrochemistry	MeOH, acetone	24 h	100 pM-1 uM (15 pM)	34
9	AGET ATRP	ovalbumin	half-sandwich	electrochemistry	acetone	22 h 30 m	2.3 pM-11.7 nM (1.6 pM)	34
10	AGET ATRP	PSA	sandwich	chemiluminescence	acetone	12 h	180 fM-700pM (140 fM)	35
11	AGET ATRP	PSA	sandwich	electrochemistry	acetone	12 h	180 fM-700pM (46 fM)	35
12	AGET ATRP	CEA	sandwich	electrochemiluminescence	acetone	7 h	5.6 fM-5.6 nM (2.8 fM)	36
13	AGET ATRP	PSA	sandwich	electrochemistry	acetone	12 h	35 fM-1.4 nM (4.9 fM)	37
14	AGET ATRP	CEA	sandwich	electrochemistry	acetone	12 h	2.8 fM-220 pM (0.56 fM)	37
15	AGET ATRP	CEA	sandwich	electrochemistry	acetone	12 h	56 fM-560 pM (56 fM)	38
16	AGET ATRP	AFP	sandwich	electrochemistry	acetone	12 h	140 fM-1.4 nM (140 fM)	38
17	AGET ATRP	CA125	sandwich	electrochemistry	acetone	12 h	0.05-100 ng/mL (0.05 ng/mL)	38
18	AGET ATRP	CA153	sandwich	electrochemistry	acetone	12 h	0.05-100 ng/mL (0.05 ng/mL)	38
19	eATRP	ssDNA	sandwich	electrochemistry	EtOH, DMF, water	30 m	100 aM-100 pM (72 aM)	41
20	eATRP	dsDNA	sandwich	electrochemistry	EtOH, DMF, water	1 h	1.0 fM-1.0 nM (0.47 fM)	42
21	eATRP	PKA	sandwich	electrochemistry	EtOH, DMF, water	30 m	0-140 mU/mL (1.63 mU/mL)	43
22	eATRP	ssDNA	sandwich	electrochemistry	EtOH, water	3h 30 m	10 aM-10 pM (4.7 aM)	44
23	Fluorogenic ATRP	Streptavidin	half-sandwich	fluorescence	water	24 h	not applicable (0.55 nM)	46
24	Biocatalytic ATRP	hemozoin	not applicable	UV-Vis spectroscopy	aqueous buffer	4 h	not applicable (4.7 nM)	56
25	Biocatalytic ATRP	hemoglobin	not applicable	UV-Vis spectroscopy	aqueous buffer	2 h	not applicable (100 nM)	59

26	RAFT	ssDNA	sandwich	ellipsometry	MeOH	6 h	1.0 fM-1.0 uM (1.0 fM)	25
27	RAFT	ssDNA	sandwich	ellipsometry	water	2 h (at least)	10 pM-100 nM (2.8 pM)	62
28	RAFT	ssDNA	sandwich	electrochemistry	EtOH, water	1 h 30 m	10 aM-10 pM (3.2 aM)	63
29	RAFT	PKA	sandwich	electrochemistry	DMF, water	1 h 30 m	0-140 mU/mL (1.05 mU/mL)	64
30	eRAFT	ssDNA	sandwich	electrochemistry	DMF, water	1 h 30 m	10 aM-10 pM (4.1 aM)	68
31	eRAFT	ssDNA	sandwich	electrochemistry	EtOH, water	4 h 30 m	10 aM-1 pM (5.4 aM)	114
32	EFRP	TGF-β	half-sandwich	fluorescence	water	4 h	not applicable (6.2 nM)	79
33	ATRP-RFRP	streptavidin	half-sandwich	ellipsometry	water	6 h	91 pM-9.1 nM (91 pM)	83
34	ATRP-RFRP	ssDNA	half-sandwich	ellipsometry	water	6 h	1 nM-100 nM (1 nM)	83
35	RFRP	mutant p53 DNA	sandwich	ellipsometry	water	2 h	1 nM-100 nM (0.5 nM)	84
36	RFRP	mutant p53 DNA	sandwich	ellipsometry	water	40 m	5 pM-10 nM (5 pM)	85
37	RFRP	mutant p53 DNA	sandwich	visual detection	water	40 m	not applicable (5 pM)	85
38	UV-initiated FRP	biotin	half-sandwich	visual detection	aqueous buffer	10 m	not applicable (0.005 biotin/μm^2)	34
39	Vis-initiated FRP	mutant p53 DNA	sandwich	ellipsometry	water	30 m	500 pM-50 nM (500 pM)	96
40	Vis-initiated FRP	biotinylated antibody	half-sandwich	fluorescence	water	30 m	not applicable (10 pM)	97
41	Vis-initiated FRP	biotinylated antibody	half-sandwich	fluorescence	water	30 m	not applicable (0.16 biotin/μm^2)	98
42	Vis-initiated FRP	Biotin	half-sandwich	visual detection	water	35 s	not applicable (15 biotin/μm^2)	100
43	Vis-initiated FRP	*Pf*HRP2	sandwich	visual detection	water	1m 20 s	not applicable (5.8 nM)	101
44	Vis-initiated FRP	mouse IgG	half-sandwich	visual detection	water	55 s	not applicable (70 pM)	115
45	Vis-initiated FRP	*Pf*HRP2	sandwich	visual detection	water	1m 20 s	not applicable (6.9 nM)	102
46	Vis-initiated FRP	MMP-8	sandwich	visual detection	water	2 m	not applicable (15.4 nM)	103
47	Vis-initiated FRP	MMP-9	sandwich	visual detection	water	2 m	not applicable (2.7 nM)	103
48	Vis-initiated FRP	*Pf*HRP2	sandwich	visual detection	water	1m 25 s	not applicable (13 nM)	104
49	Vis-initiated FRP	streptavidin	sandwich	visual detection	water	1m 10 s	not applicable (0.3 nM)	108

a) ssDNA: single-stranded DNA. dsDNA: double-stranded DNA. IgG: Immunoglobulin G. PSA: Prostate specific antigen. CEA: Carcinoembryonic antigen. AFP: Alpha-fetoprotein. CA125: Cancer antigen 125. CA153: Carbohydrate antigen 153. PKA: Protein kinase. iRBCs: *P. falciparum*-infected red blood cells. TFG-β: Transforming growth factor-beta. *Pf*HRP2: *P. falciparum* histidine-rich protein 2. MMP-8: Matrix metalloproteinase-8. MMP-9: Matrix metalloproteinase-9.

b) Sandwich: DNA or protein binding assays where target molecules are stuck between capture binders and detection binders. Half-sandwich: a model DNA or protein binding assays where one-step binding events immobilized initiator-coupled target DNA or protein.

c) MeOH: Methanol. DMSO: Dimethyl sulfoxide. EtOH: Ethanol. DMF: Dimethylformamide. NaOH: Sodium hydroxide.

Table S2. Required equipment and deoxygenation conditions for polymerization-based biodetection methods in literature.

#	Polymerization	Equipment for initiation	Purging*	Sealed*	Ref.	#	Polymerization	Equipment for initiation	Purging*	Sealed*	Ref.
1	ATRP	X	O	O	22	**26**	RAFT	hot plate	O	O	25
2	ATRP	X	O	O	23	**27**	RAFT	hot plate	O	O	62
3	ATRP	X	O	O	24	**28**	RAFT	hot plate	O	O	63
4	AGET ATRP	X	X	O	31	**29**	RAFT	hot plate	O	O	64
5	AGET ATRP	X	X	O	31	**30**	eRAFT	EC cell*	O	O	68
6	AGET ATRP	X	X	O	32	**31**	eRAFT	EC cell*	O	O	114
7	AGET ATRP	X	X	O	32	**32**	EFRP	X	X	X	79
8	AGET ATRP	X	X	O	34	**33**	ATRP-RFRP	X	O	O	83
9	AGET ATRP	X	X	O	34	**34**	ATRP-RFRP	X	O	O	83
10	AGET ATRP	X	X	O	35	**35**	RFRP	X	O	O	84
11	AGET ATRP	X	X	O	35	**36**	RFRP	X	X	X	85
12	AGET ATRP	X	X	O	36	**37**	RFRP	X	X	X	85
13	AGET ATRP	X	X	O	37	**38**	UV-initiated FRP	UV-lamp	O	O	34
14	AGET ATRP	X	X	O	37	**39**	Vis-initiated FRP	LED*	O	O	96
15	AGET ATRP	X	X	O	38	**40**	Vis-initiated FRP	LED*	O	O	97
16	AGET ATRP	X	X	O	38	**41**	Vis-initiated FRP	LED*	O	O	98
17	AGET ATRP	X	X	O	38	**42**	Vis-initiated FRP	LED*	X	X	100
18	AGET ATRP	X	X	O	38	**43**	Vis-initiated FRP	LED*	X	X	101
19	eATRP	EC cell*	X	O	41	**44**	Vis-initiated FRP	LED*	X	X	115
20	eATRP	EC cell*	X	O	42	**45**	Vis-initiated FRP	LED*	X	X	102
21	eATRP	EC cell*	X	O	43	**46**	Vis-initiated FRP	LED*	X	X	103
22	eATRP	EC cell*	X	O	44	**47**	Vis-initiated FRP	LED*	X	X	103
23	Fluorogenic ATRP	X	O	O	46	**48**	Vis-initiated FRP	LED*	X	X	104
24	Biocatalytic ATRP	hot plate	X	O	56	**49**	Vis-initiated FRP	LED*	X	X	108
25	Biocatalytic ATRP	hot plate	X	O	59						

* EC cell: Electrochemical cell. Hot plate includes any temperature controllers. LED: Light-emitting diode. Purging: Inert gas purging. Sealed: Sealed reactors. O: Required. X: Not required.

The same entry number (#) in Table S1 and Table S2 represents the same biodetection method.

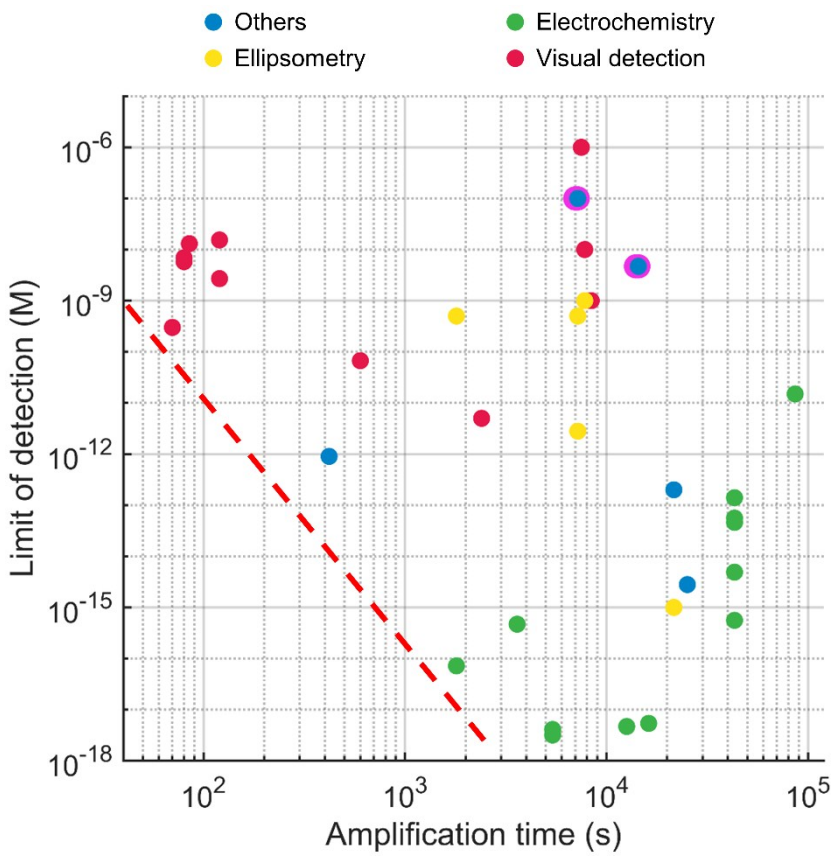

Figure S1. Reported limit of detection (M) and amplification time (s) of polymerization-based biodetection methods in literature. Colored dots represent different types of detection methods. The red dotted line indicates the lower bound, under which the amplification time and limit of detection of biosensors are not achieved yet, but potentially more practical. This plot considers only sandwich DNA or protein binding assays where target molecules are immobilized between capture binders and detection binders, which excludes half-sandwich assays. As an exception, solution-phase assays of hemozoin and hemoglobin (pink outline) are included. Amplification time includes time for inert gas purging if required, polymerization, and coupling signaling molecules. Rinsing time before and after polymerization is not considered. Extracted from **Table S1** in Supplementary Information.

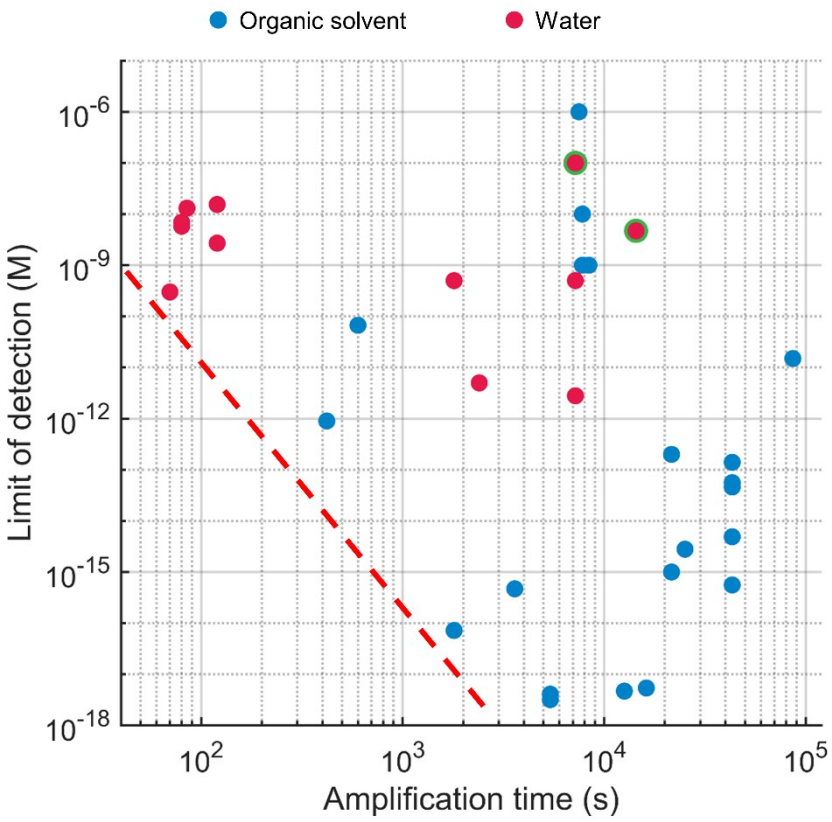

Figure S2. Reported limit of detection (M) and amplification time (s) of polymerization-based biodetection methods in literature. Colored dots represent rinsing solvents or buffer solutions. The red dotted line indicates the lower bound, under which the amplification time and limit of detection of biosensors are not achieved yet, but potentially more practical. This plot considers only sandwich DNA or protein binding assays where target molecules are immobilized between capture binders and detection binders, which excludes half-sandwich assays. As an exception, solution-phase assays of hemozoin and hemoglobin (green outline) are included. Amplification time includes time for inert gas purging if required, polymerization, and coupling signaling molecules. Rinsing time before and after polymerization is not considered. Extracted from **Table S1** in Supplementary Information.