Electronic Supplementary Information

A rapid and simple electrochemical detection of the free drug concentration in human serum using boron-doped diamond electrodes

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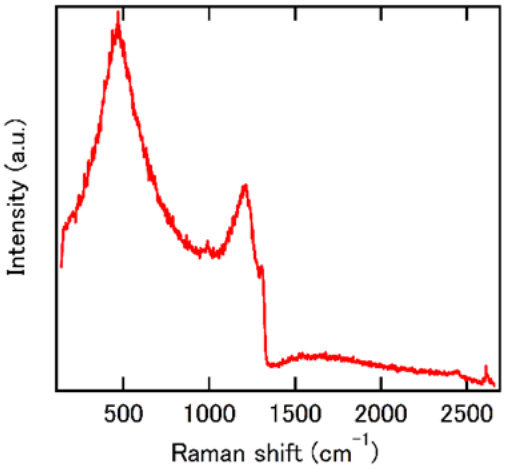
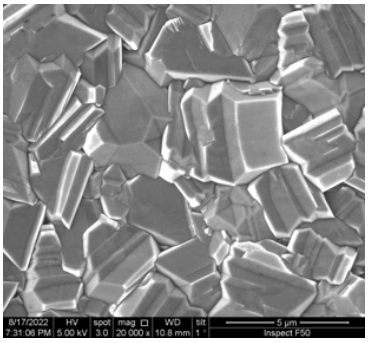


Figure S1. Raman spectrum of BDD.

(A)



(B)

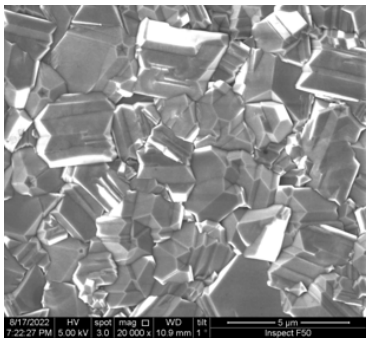


Figure S2. SEM image of BDD electrode. (A)BDD-A, (B)BDD-B

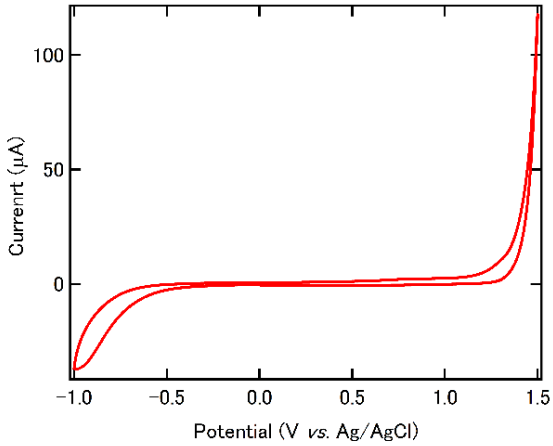


Figure S3. Cyclic voltammogram of 0.1 M PB (pH 7.4) using BDD. Start potential: 0 V *vs.* Ag/AgCl; Scan range: −1.0 V to 1.5 V; Scan rate: 100 mV s^{-1}

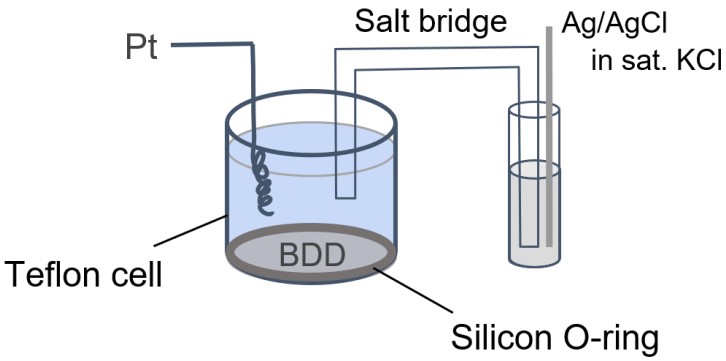


Figure S4. Illustrated outline of 3 electrode systems. A silicone O-ring is sandwiched between the cell and the BDD).

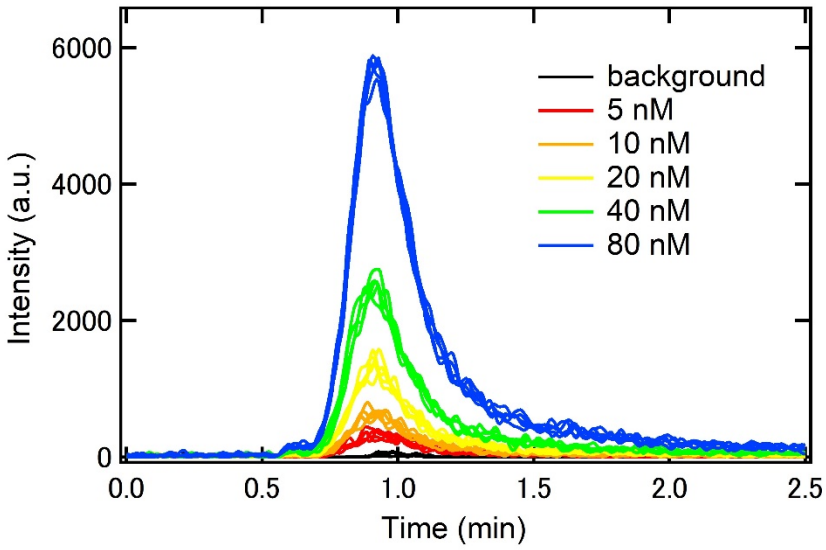


Figure S5. LC/MS/MS chromatograms of doxorubicin. Concentration range: 0, 5, 10, 20, 40, 80 nM, QC: 5, 20, 80 nM, m/z=397.05.

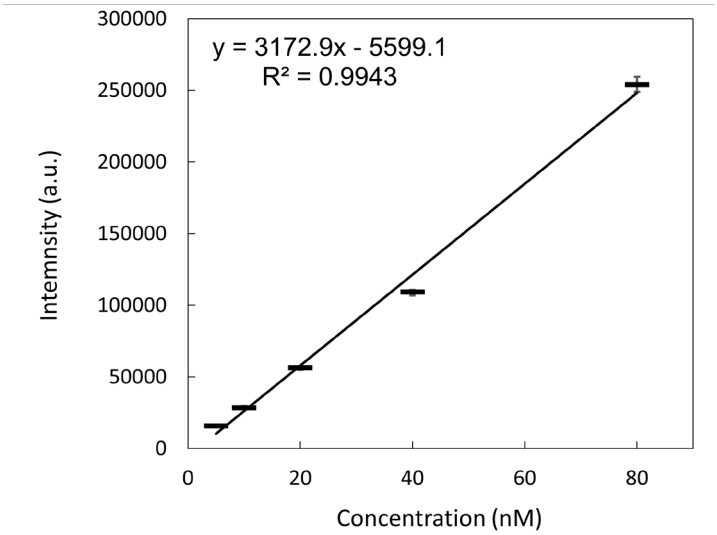


Figure S6. Calibration curve of doxorubicin using LC/MS/MS. LOD=0.188 nM (LOD = 3.3 sd of background area / slope), mean ± s.e.m., n = 5.

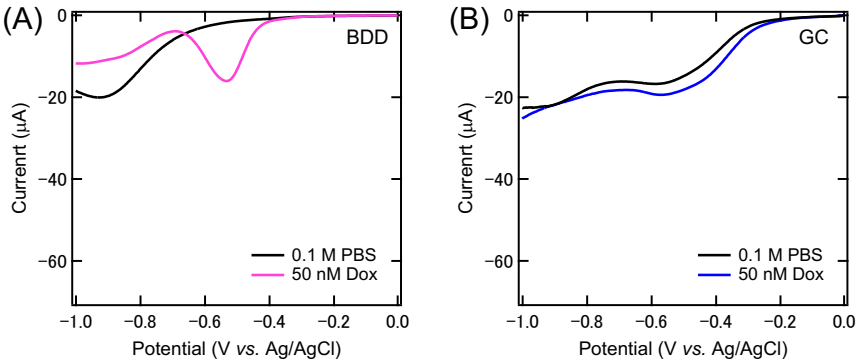


Fig. S7. Linear sweep voltammograms of doxorubicin in 0.1 M PB (pH 7.4) by BDD and GC with the 1 min N2 bubbling. (A) BDD, in the absence (black line) and the presence of 50 nM doxorubicin (DOX, magenta line). (B) GC, in the absence (black line) and the presence of 50 nM doxorubicin (DOX, blue line).

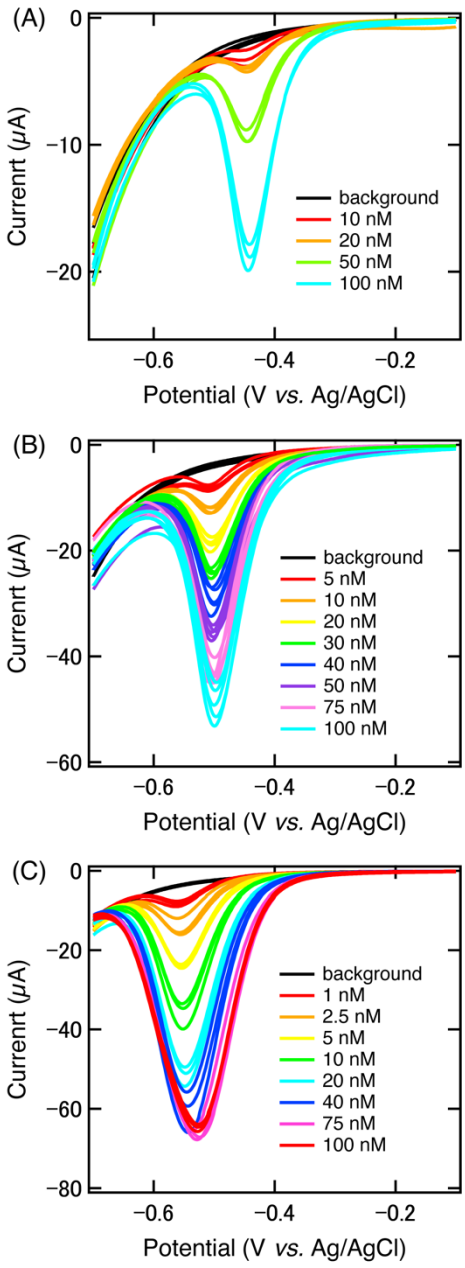


Figure S8. Linear sweep voltammogram of doxorubicin at three different pH.

(A) pH 5.1 (10, 20, 50, 100 nM in 0.1 M acetate buffer, n = 3); (B) pH 6.0 (5, 10, 20, 30, 40, 50, 75, 100 nM doxorubicin in 0.1 M PB, n = 5); (C) pH 7.4 (1, 2.5, 5, 10, 20, 40, 75, 100 nM doxorubicin in 0.1 M PB, n = 3), Scan rate: 100 mV s^{-1}.

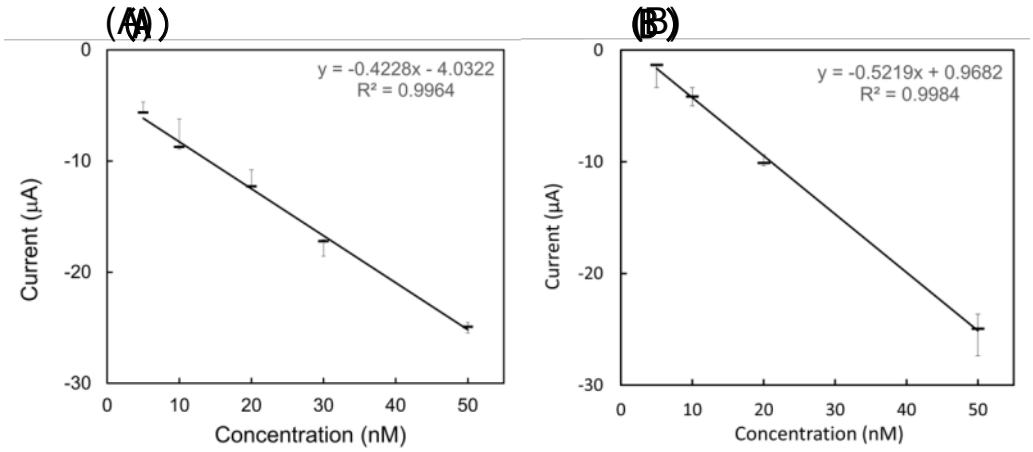


Figure S9. Calibration curves of doxorubicin in 0.1 M PB (pH 6.0) at each electrode using LSV. Measurements were performed just before the unbound concentration measurements. (A) BDD-A, (B) BDD-B, mean ± s.e.m., n = 3.

Table S1. Optimised parameters for mass spectrometric analysis.

Parameter	Doxorubicin
Ionization method	ESI (positive)
Nebulizing gas flow	3 L/min
Heating gas flow	10 L/min
Drying gas flow	10 L/min
Interface temperature	300 ℃
DL temperature	250 ℃
Block heater temperature	400 ℃
CID gas pressure	270 kPa
Interface voltage	+4 kV
Q1 Pre Bias	−26.0 V
Collision energy	−15.0 V
Q3 Pre Bias	−20.0 V

Table S2. Average current (μA), SD (μA) and CV (%) values for each calibration measurement using BDD-A and B

	BDD-A			**BDD-B**		
Added (nM)	Average (μA)	SD (μA)	CV (%)	Average (μA)	SD (μA)	CV (%)
5	-9.4	0.47	5.0	-8.1	0.96	11.9
10	-12.5	1.24	9.9	-10.9	0.67	6.1
20	-16.1	0.71	4.4	-16.9	0.41	2.4
30	-20.1	0.68	3.2	—	—	—
50	-28.7	0.38	1.3	-31.7	1.56	4.9

Table S3. Comparison of electrochemical measurement results of doxorubicin with various electrodes

Material for sensing	**Technique**	**Detection range /μM**	**LOD /nM**	**Sample**	**Ref.**
AgNPs-CDs-rGO/GCE	DPV	0.01~2.5	2	Human serum	[1]
Nano-TiO_2/nafion composite film modified GCE	LSV	0.005~2	1	Plasma	[2]
Thin film of poly-arginine modified GCE	DPV	0.069~1.08 0.1~3.45	69 103	Whole plasma Whole blood	[3]
MWCNT/$CoFe_2O_4$ nanoparticles modified CPE	DPV	5×10^{-5}~1.15	0.01	Human blood serum, urine	[4]
PAMT@AuNPs@rGO/GCE	DPV	3×10^{-5}~0.03, 0.03~30	0.009	Blood serum	[5]
VMSF/ErGO layer on GCE	DPV	0.001~20	0.77	Human whole blood	[6]
MCS/rGO/GCE	DPV	0.01~10	1.5	Human serum	[7]
AuNRDs/1T-MoS_2 nanosheets /SPE	AdsDPV	0.01~9.5	2.5	Human blood serum	[8]

$_{L}$-GSH-MoS_2-CYS/GCE	DPV	0.1~78.3, 98.3~1218	31	–	[9]
FeV/SCNFs/GCE	CV	0.02~542.5	5.2	Blood serum, human urine	[10]
Graphene quantum dots/GCE	DPV	0.018~3.6	0.016	Human plasma	[11]
Au/N-prGO-CS electrode	DPV	0.01~15	10	Human plasma	[12]
DRN-aptamer-modified electrode	EIS	0.031~0.125	28	–	[13]
PT/*β*-CD/GQD modified Au electrode	DPV	0.086~3.45	12	Human plasma	[14]
Poly(Azure B)-DNA composite modified GCE	DPV	1×10^{-4}~0.1	0.07	Human serum	[15]
BNNS-$NiCo_2O_4$/SPE	DPV	0.01~600	9.4	Injection solution, biological specimens	[16]
Fe_3O_4@Pt nanoparticles/ MWCNT/CPE	DPV	0.05~70	1	Urine sample	[17]
N-doped carbon nanoonions/ GCE	DPV	2×10^{-4}~10	0.06	Serum sample	[18]
NiHCF/Ni-Al-LDH modified gold electrode	DPV	0.01~6.2	1.9	Biological sample, human blood serum	[19]
GCE-AgNPs/poly(chitosan)	DPV	0.103~8.6	103	Human bio-fluids, B16F10 cell lysates	[20]
VMSF/chemically pretreated- GCE	DPV	5×10^{-4}~23	0.2	Human whole blood	[21]
rGO/AuNPs/polypyrrole/GCE	DPV	0.02~25000	20	–	[22]
SNPs@MOF/BNSs-Fc/GCE	Ratiometric SWV	0.01~10	2	Human serum	[23]
BDD	LSV	0.001~0.1	0.14	Human serum	This work

Abbreviations: AgNPs, silver nanoparticles; CDs, carbon dots; rGO, reduced graphene oxide; GCE, glassy carbon electrode; DPV, differential pulse voltammetry; LSV, linear sweep voltammetry; CPE, carbon nanotube paste electrode; MWCNT, multi-walled carbon nanotubes; PAMT, poly(2-amino-5-mercapto-1,3,4-thiadiazole); VMSF, vertically-ordered mesoporous silica-nanochannel film; ErGO, electrochemically reduced graphene oxide; MCS, mesoporous carbon nanospheres; AuNRDs, gold nanorods; AdsDPV, adsorptive stripping differential pulse voltammetry; SPE, screen-printed electrode; $_{L}$-GSH, $_{L}$-glutathione; CYS, cystamine; CV, cyclic voltammetry; SCNFs, sulfur-doped carbon nanofiber; FeV, iron vanadate; Au/N-prGO-CS electrode, chitosan and nitrogen- doped porous reduced graphene oxide onto gold electrode; EIS, electrochemical impedance spectroscopy; DRN- aptamer, daunorubicin-binding aptamer; GQD, graphene quantum dots; PT/*β*-CD, poly(taurine-β-cyclodextrins); BNNS, bird nest-like nano-structure; MB, methylene blue; NiHCF, nickel hexacyanoferrate; Ni-Al-LDH, Ni-Al layered double hydroxides; SWV, square wave voltammetry; LSV, linear sweep voltammetry. Adapted with permission from Elsevier B.V.: Microchemical Journal (Yang et al. 2022), Copyright 2022.

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