Supplementary Information—Review

Possibilities and Challenges for Quantitative Optical Sensing of Hydrogen Peroxide

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Table S1. Hydrogen peroxide concentrations found in natural waters.

Keywords	Found Concentration	Reference
(Open Ocean) Seawater		
Surface waters east of New Zealand. Method: Flow injection analysis (FIA) with chemiluminescent detection. Maximum concentrations were found at ~10 m depth.	Convergence zone: 78.9 nM Subtropical waters: 70.8 nM Subantarctic water: 68.4 nM	[1]
Surface water sampled between Osaka, Japan to Honolulu, Hawaii (May–June 2002). Method: FIA with luminol chemiluminescence.	10–250 nM	[2]
Open ocean seawater collected at 500 m depth (Pacific Ocean, east of New Zealand; 46°38′ S 178° 32′ E, subtropical convergence zone) (February 2005, 7:45 a.m.) Max. concentrations found at ~10 m depth. Method: FIA with acridinium ester and 0.1 M carbonate buffer, pH 11.3).	Surface water: 8.5–138.5 nM Average at 500 m: 0.779 nM	[3]
Time periods: Mediterranean Sea (August 2015), South Pacific (October 2015), South Atlantic Ocean (November- December 2015) Method: FIA; Co(II) catalyzed oxidation of luminol. All results exhibited lower concentrations beneath the limit of detection. Values shown are only possible H_2O_2 ranges.	Offshore > 1000 m depth: 0.25 ± 0.27 nM (Mediterranean, Balearics-Algeria) 0.90 ± 1.2 nM (S Atlantic, Angola Basin) 2.9 ± 2.2 nM (Mediterranean, Corsica-France) 0.55 ± 1.3 nM (Mediterranean, Sardinia-Sicily)	[4]

Surface waters from Western Seto Inland Sea and the estuary of the Phta-gawa River (7% river input), June 1990 and 1991. Method: FIA with potassium hydrogen phthalate, ethylenediaminetetraacetic acid disodium salt (EDTA) and p-hydroxyphenyl acetic acid (POPHAA) with 2 pupurogallin units peroxidase, type II.	Max. 400 nM (summer, 12:00–2:00 p.m.) 60–140 nM (winter)	[5]
Rain Water		
Sampled October 2003; 10:20 a.m. on the roof of the chemistry building of the University of Otago. Method: FIA with acridinium ester and 0.01 M carbonate buffer (pH 11.3).	6.34 μM	[3]
Sampled between July 2001–January 2006; downtown Sao Paulo City, Brazil. Samples were filtered (0.22μM pore size cellulose acetate membrane) and analyzed within 15 minutes of collection, to avoid decomposition. Method: FIA based on one-electron oxidation of phenol by H_2O_2 catalyzed by peroxidase. The resulting phenoxy radical reacts with 4-aminoantipyridine and H_2O_2.	0.5–78 μM Average: 14 μM	[6]
Sampling time: March–April 1988 by wet only sampling. Analysis: FIA based on bis-(2,4,6-trichloronphenyl)oxalate (TCPO), perylene as sensitizer, borate buffer (0.08 M) and acetone as solvent.	0.9–6.8 ppmw (Bahia, Brasil) 0.1–2.2 ppmw (Dortmund, Germany; summertime)	[7]
Method: standard addition of scopoletin to a pH 7 buffered sample, addition of a horseradish peroxidase (HRP) / phenol mixture, which catalyzes the oxidation of scopoletin by H_2O_2.	14–75 μM (Miami, Florida) 21 μM (Bahama Islands)	[8]
Sampling at nonurban sites of **peroxides** in the eastern US. Method: FIA; fluorescence detection of p-hydroxyphenyl acetic acid formed by the reaction of POHPAA with peroxide at pH 8.5 together with HRP. The difference in fluorescence before and after addition of catalase is used for H_2O_2 determination.	Median values: < 10 μM (rain sample, precipitating cloud water sample and non-precipitating cloud water samples)	[9]
Method: *N*,*N*-diethyl-*p*-phenylenediamine (DPD) is oxidized using a peroxide catalyzed reaction, resulting in a colored radical cation, which can be measured using a photometer.	1.4–5.3 μM (September 1994, Christchurch, NZ) 7.3 nM (December, 1994, Christchurch, NZ) 1.3 μM (October, 1994, West Melton, NZ) 27.2 μM (November 1994, Lake Hochstetter, NZ) 3.9 μM (December 1994, Ngatimoti / Nelson, NZ)	[10]

Method: FIA; chemiluminescence reaction where Co(II) works as ion catalyst for the oxidation of alkaline luminol (in a H_3BO_3 buffer at pH 9.5) in the presence of H_2O_2. The method was applied as standard addition method.	1.08 nM (December, Turkey)	[11]
Snow Water		
Method: FIA; chemiluminescence reaction where Co(II) works as ion catalyst for the oxidation of alkaline luminol (in a H_3BO_3 buffer at pH 9.5) in the presence of H_2O_2. The method was applied as standard addition method.	130 μM (March, Turkey)	[11]
Antarctic station (Georg von Neumayer, 70 ° 37'S/08°22'W) in December 1989–January 1990; Ekström shelf ice, 8 km from ice edge. Snow pits showed H_2O_2 maxima between 70–140 cm depth (summer snow). No seasonal variation in H_2O_2 was observed below 2 m. Method: snow was melted and the chemiluminescence reaction with peroxyoxalate analyzed.	86 ppbw–485 ppbw (precipitating snow) 54–167 ppbw (surface snow, 3 cm depth) Up to ~200 ppbw (snow pits; down to 2 m)	[12]
Snow waters were collected in January 2000, in Beijing, China. Method: Chemiluminescent reaction of 7-(4,6-dichloro-1,3,5-triazinylamino)-4-methylcoumarin (DTMC) with H_2O_2; enhanced by addition of cation surfactants, buffered at pH 11–11.6.	170–560 nM	[13]
River Water		
Surface water samples from freshwater stream Leith, Dunedin, NZ (November 2003, at 1:45 p.m.). Method: FIA using acridinium ester, 0.01 M carbonate buffer (pH 11.3).	283 nM	[3]
Surface water sample taken from the Volga River Area, Russia. Method referred to in paper: scopoletin and HRP type II.	1.3–3.2 μM	[14]
Lake Water		
Samples taken from surface waters of Gölbaşi Lake, Turkey. Method: FIA; chemiluminescence reaction where Co^{2+} works as ion catalyst for the oxidation of alkaline luminol (in a H_3BO_3 buffer at pH 9.5) in the presence of H_2O_2. The method was applied as standard addition method.	1.51 mM	[11]
Lake surface water samples. Method: scopoletin and HRP on a fluorimeter. H_2O_2 was determined using a standard addition method. 40 lakes, sampled twice in July and once in August 2004, within an hour of solar noon, Mackenzie Delta, Western Canadian Arctic.	Peak value 4.0 μM (near solstice) < 1.0 μM (late July–August)	[15]
Lake water samples (top 2-3 m) were taken from Lake Erie and H_2O_2 concentrations correlated to cyanobacterial bloom dynamics. Sampling time, May– October 2014. Method: Amplex Red on a	47 ± 16 nM to 1570 ± 16 nM (average: 371 ± 17 nM)	

UPLC.		
Geothermal Springs		
Site: High-temperature (68–80 °C), acidic (pH 3–3.5) geothermal springs, Yellowstone National Park. Method: FIA with acridinium ester and 0.01 M carbonate buffer (pH 11.3).	~1 μM (high dissolved sulfide content) 2–3 μM (oxygenated water)	[16]

Table S2. Hydrogen peroxide concentrations found in the human body.

Keywords	Found concentration	Reference
Oral Bacteria		
H_2O_2 production was observed when testing three different bacteria; *Streptococcus sanguis* I and II (sanguis and oralis), and *Strep. mitior* (mitis biotype I). Method: electrochemically.	2.2–9.8 mM (aerobic growth) 1.1–3.9 mM (anaerobic growth)	[19]
Urine–Freshly Voided		
Urine, freshly voided. Samples were taken from healthy humans. Method: Three different assays were used. I) 2-oxoglutarate decarboxylation, II) ferrous oxidation-xylenol orange (FOX) and III) an O_2-electrode.	I) 38.5 ± 46.3 μM (range: 11–173 μM), II) 36.5 μM, III) 33.7 μM,	[20]
Method: ferrous oxidation-xylenol orange (FOX).	15 ± 9.8 μM (healthy), 56.3 ± 3.9 μM (cancer patients)	[21]
Exhaled Air		
Method: Assay, HRP, potassium citrate buffer and 3,3',5,5' tetramethyl benzidine.	Healthy: not detectable	[22]
Method: Assay, HRP, potassium citrate buffer and 3,3',5,5' tetramethyl benzidine.	0.26 ± 0.04 μM (healthy) 0.87 ± 0.01 μM (lung disease, bronchiectasis)	[23]
Exhaled air was measured in smokers. Method: Assay, HRP, POPHAA.	Common cold: 0.2 μM (symptomatic) and 0.09 μM (recovered) Healthy Control: 0.08 - 0.1 μM	[24]
Test subjects were breathing 15 minutes through mouthpiece with and without inhalation filter. Method: Assay, HRP, POPHAA and H_2O_2 form 2,2′-dihydroxybiphenyl-5,5′-diacetate. Read-out via plate reader.	Chronic obstructive pulmonary disease (COPD) patients: 2.774 μM (ambient air) 0.780 μM (without filter) 0.420 μM (with filter) Healthy control: 4.282 μM (ambient air) 0.748 μM (without filter) 0.454 μM (with filter)	[25]

Blood Plasma		
Method: HPLC followed by chemiluminescent reaction of isoluminol, H_2O_2 and microperoxidase.	< 0.25 μM	[26,27]
Method: a radioisotopic technique where peroxide decarboxylates I- ^{14}C- alpha-ketoacids is used. The $^{14}CO_2$ is detected.	13–57 μM	[28]
Method: electrochemical and spectrophotometric (HRP and H_2O_2 mediated oxidation of phenol red).	3.16 ± 0.14 μM (hypertensive) 2.50 ± 0.16 μM (normotensive)	[29]
Whole blood was drawn into heparin containing vials. The plasma was separated via centrifugation. Method: HRP, phenol and 4-aminoantipyrine in pH 6.9 phosphate buffer.	Initial exercise test: 7.15 ± 0.74 μM (before test) to 9.09 ± 1.04 μM (3 min after test) Exercise test after 3 week endurance training: 6.31 ± 1.05 μM (before test) to 5.85 ± 1.08 μM (after test)	[30]
Blood was taken after fasting overnight. Plasma was removed via centrifugation. Samples were frozen (test showed no significant difference in peroxide production between fresh and frozen plasma). Catalase was inhibited using sodium azide. Method: electrochemical with modified Clark electrode.	3.358 ± 0.145 μM (hypertensive) 3.000 ± 0.087 μM (normotensive) (Plasma peroxide production: Men > Women; and White (European descent) > Black (sub-Saharan African descent)	[31]
Method: Assay, plasma-incubation with 4-aminoantipyrine / phenol reagent in the presence of HRP.	Before insulin treatment: 82.1 ± 31.4 μM (Type 1 diabetes) 61.7 ± 39.1 μM (Type 2 diabetes) 21.3 ± 9.0 μM (control) After insulin treatment: 54.2 ± 29.3 μM (Type 1 diabetes) 44.7 ± 25.2 μM (Type 2 diabetes)	[32]
Test subjects were non-smokers, without a history in diabetes mellitus or hypertension. Method: ferrous oxidation-xylenol orange (FOX).	66.9 ± 10.9 μM (preeclampsia) 50.1 ± 5.6 μM (normal pregnancy)	[33]
Red Blood Cells		

Production of hydrogen peroxide by red blood cell. Catalase was inhibited using 3-amino-1,2,4-triazole (aminotriazole). H_2O_2 production could be indirectly determined via the catalase inhibition.	1.36 ± 0.2 μM/h (generation rate) 0.2 nM (steady state)	[34]
Whole Blood		
Method: a radioisotopic technique where peroxide decarboxylates I- ^{14}C- alpha-ketoacids is used. The $^{14}CO_2$ is detected.	114–577 μM	[28]
Eyes		
Method: *2,6-dichloroindophenol procedure according to [35]. The dye is reduced by ascorbate in a sodium phosphate buffer; and re-oxidized to the blue leuco-2,6-dichloropheno-indophenol dye in the presence of H_2O_2 and peroxidase [36]. Another study, however, concluded that this method is unsuitable for aqueous humor, as it is dependent on the ascorbic acid concentration (ascorbic acid is also present in the aqueous humor) [37].	Aqueous humor from cataract patients : 10–660 μM* Marfan's syndrome patients: > 3000 μM* Control group: 14–31 μM (mean: 24 ± 7 μM)* Different secondary sources; non-accessible** Cataract patients: 18 μM* 33–364 μM (mean: 189 ± 88)** <10 μM** Cataract–diabetic patients: 36 μM*	[38]

Table S3. Hydrogen peroxide concentrations in other biological samples.

Keywords	Found Concentrations	Reference
Corals		
Coral: *Stylophora pistillata.* The coral was stirred in a beaker to induce H_2O_2 release. Method: HRP with POHPAA in pH 8.8 TRIS buffer.	Max. accumulated release: ~1600 nM (feeding batch experiment) ~400 nM–40 μM (estimated in DBL) 200 nM (measured 0.2 cm outside DBL)	[39]
Coral: *Stylophora pistillata*. H_2O_2 release due to bacterial contact. Method: HRP with POHPAA in pH 8.8 TRIS buffer.	~20 μM in DBL	[40]
Animal Cells		
Peritoneal exudate cells (PEC) were harvested from guinea pigs, established as macrophage monolayer and different stimuli (phorbol myristate acetate (PMA), opsonized zymosan, concanavalin A (Con A), wheat germ agglutinin (WGA), N-formyl-methionylleucyl-phenylalanine (FMLP) and A23187) for H_2O_2 production added. Method: HRP type II in a potassium phosphate buffer at pH 7 and phenol red.	[nmol per mg macrophage protein per 30 min] 1.6 ± 0.9 101 ± 39.5 (2 nM PMA) 192.6 ± 33.8 (20 nM PMA) 37.5 ± 5.7 (0.5 mg/mL opsonized zymosan) 22.1 ± 4.2 (50 μg/mL, ConA) 30.0 ± 8.5 (50 μg/mL WGA) 22.6 ± 5.1 (1 μM FMLP) 10.5 (10 μM A23187)	[41]
Algae		
Symbiodinium spp. H_2O_2 release as response to heat stress. Method: Amplex Red® assay. HRP, pH 7.4 phosphate buffer and Amplex Red® reagent.	Release rate: 0.25–0.9 pmol/cell to 1.0–2.64 pmol/cell Increase under stress heat: 25–400 %	[42]
Algae samples were collected at Forsmark, Swedish east coast at the southern end of the Gulf of Bothnia. The algae were sampled at different temperatures in the field and irradiated at 600 μmol photons m^{-2} s^{-1} for 6 h. The concentration given is μmol per g ash free dry weight per	*Pleurosira laevis* (Diatom) 1.5 ± 0.4 μmol (T = 17 °C) *Fucus vesiculosus* (Brown algae)	[43]

hour. Method: HRP, phosphate buffer pH 7 and luminol in MOPS buffer pH 7.6.	1.8 ± 0.6 μmol (T = 12 °C) *Cladophora glomerata* (Green algae) 3.0 ± 0.3 μmol (T = 17 °C) 2.8 ± 0.9 μmol (T = 23 °C) *Entermorpha ahlneriana* (Green algae) 22 ± 18 μmol (T = 17 °C) 64 ± 60 μmol (T = 23 °C) *Entermorpha flexuosa* (Green algae) 5.6 ± 3.1 (T= 23 °C) *Entermorpha intestinalis* (Green algae) 10 ± 5 μmol (T = 15 °C) 26 ± 1 μmol (T = 17 °C)	
Algae: *Ulva rigida* (Chlorophyta), collected from Taliarte, east coast of Gran Canaria; August 1993. Measured at an irradiation of 700 μmol photons m^{-2} s^{-1}. Method: HRP, phosphate buffer pH 7.0 and luminol in MOPS buffer pH 7.0.	1.2 μmol g FW h^{-1} (pH 8.2) < 5 nmol g FW^{-1} h^{-1} (pH 6.5; non detectable) 5.0 μmol g FW^{-1} h^{-1} (pH 9.0)	[44]
Algae: *Anacystis nidulans* (Blue algae). Method: scopoletin fluorescence assay (scopoletin, peroxidase, $KMnO_4$). No production found in *Anabaetia cylindrica*, *Agmtienellum quadrutplicatumti*, and *Chlorella pyrenoidosa*.	0.4 μmol H_2O_2 mg^{-1} Chl^{-1} min^{-1}	[45]
Algae: *Oscillatoria boryana* (Cyanobacterium). Incubation under 80 μE m^{-2} s^{-1}. Measurement with 4-aminoantioyrine and phenol.	27.48–81 mmol mg^{-1} $Chl.h^{-1}$ (20–80 mE m^{-2} s^{-1}) 97–108 mmol mg^{-1} $Chl.h^{-1}$ (160–240 mE m^{-2} s^{-1}) 100 mM (enhancer riboflavin; 12 x higher than control)	[46]
Algae: *Symbiodinium* (Pyrrhophyta) irradiated with 100–1000 μmol photons m^{-2} s^{-1}. Method: HRP, Amplex Red®, sodium phosphate buffer, pH 7.4.	Production: up to 2 pmol/cell (24 h, 26 °C) < 0.3 pmol / cell (1 h, 100 PAR) < 4 pmol / cell (1h, 1000 PAR)	[47]
Recombinant Microsomal Enzyme		

Sample: recombinant microsomal enzymes. Method: HRP and Amplex Red®.	[nmol H_2O_2 per minute, per mg of protein] Liver microsomes control rat: 2.62 ± 0.19 Recombinant human NADPH-cytochrome P450 reductase: 0.91 ± 0.22 Supermix (recombinant NADPH-cytochrome P450 reductase plus mixture of recombinant cytochrome P450s): 3.78 ± 0.30	[48]

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