University of São Paulo
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Trends and Opportunities in Bioanalytical Techniques: From the Human Biomonitoring to the Age of Exposome

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2018

VI ESCBIO

Human biomonitoring

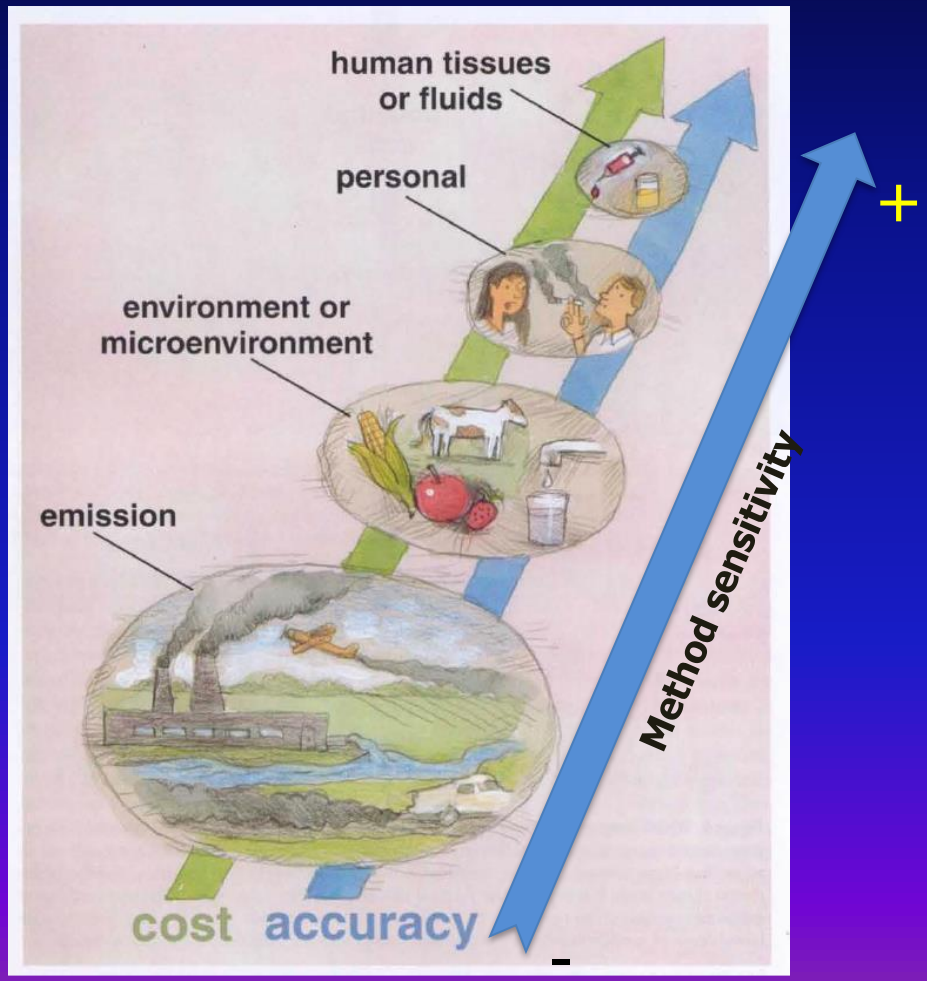
Biomonitoring is defined as one method for assessing human exposure to chemicals (TARGET) by measuring them or their metabolites in human tissues or specimens, such as blood or urine (CDC 2005).

Why?

-Establishing baseline values for specific groups
-Identifying populations at risk (high exposure to toxic elements and deficiency of Essentials)
-Supporting the prioritization of government actions (public policies)

In addition to providing information on the nutritional and toxicological conditions of a given population, several biomonitoring studies attempt to correlate the concentration of some chemicals or metabolites found in the body with several outcomes.

From Source to Exposure Sensitivity, Cost and Accuracy



Human biomonitoring

(Target Analytes)

Table 1. Some examples of the compounds and metabolites evaluated in HB studies.

Chemical compound	Matrix	Method	References
Essential and toxic elements	WB and urine	ICP-MS	LI et al., 2014a
Bisphenols (BP)	WB and urine	LC-MS/MS	KOLATOROVA SOSVOROVA et al., 201
Other phenols	Urine	LC-MS/MS	YE et al., 2005
HPAs´ metabolites	Urine	GC-MS/MS LC-MS/MS	LI et al., 2014b; RAPONI et al., 2016
Polychlorinated biphenyls and dibenzodioxins (PCB e PCDD)	WB and urine	GC-MS/MS	ZHANG et al., 2017
Phthalate metabolites	Urine	LC-MS/MS	ROCHA et al., 2017
Perfluorinated substances (PFOS)	WB and urine	UPLC-MS/MS	ZHANG et al., 2014
Metabolites of organophosphate pesticides	Urine	LC-MS/MS	REEMTSMA, LINGOTT, ROEGLER, 201
Metabolites of aromatic amines	Urine	LC-MS/MS	HOLLAND et al., 2004
Parabens	WB and urine	LC-MS/MS	FREDERIKSEN, JØRGENSEN, ANDERSSON, 2010; KOLATOROVA SOSVOROVA et al., 2017
Triclosan (TCS) and triclocarban (TCC) and their metabolites	Urine	LC-MS/MS	PROVENCHER et al., 2014

***WB (whole blood)**

Human biomonitoring
Target analytes

List of Priorities-ATSDR

CDC-NHANES

In each survey period, the reported chemicals or their metabolites were measured in blood, serum, and urine samples from random subsamples of the National Health and Nutrition Survey (NHANES)

Chemicals included in the *National Exposure Report* have been selected on the basis of:

- **Scientific data that suggested exposure in the U.S. population;**
- **Seriousness of health effects known, or thought to result from some levels of exposure;**
- **Need to assess the efficacy of public health actions to reduce exposure to a chemical;**
- **Availability of an analytical method that is accurate, precise, sensitive, specific, and rapid;**
- **Availability of adequate blood or urine samples from the National Health and Nutrition Examination Survey (NHANES) survey;**
- **Analytical cost to perform the analysis;**

Human biomonitoring

List of Priorities-ATSDR

ATSDR's Substance Priority List

What is the Substance Priority List (SPL)?

2017 Substance Priority List

Click here to view the ATSDR 2017 Substance Priority List

The Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) section 104 (i), as amended by the Superfund Amendments and Reauthorization Act (SARA), requires ATSDR and the EPA to prepare a list, in order of priority, of substances that are most commonly found at facilities on the National Priorities List (NPL) and which are determined to pose the most significant potential threat to human health due to their known or suspected toxicity and potential for human exposure at these NPL sites. CERCLA also requires this list to be revised periodically to reflect additional information on hazardous substances. In CERCLA, it is called the priority list of hazardous substances that will be candidates for toxicological profiles.

This substance priority list is revised and published on a 2-year basis, with a yearly informal review and revision. (No list was published in 2009 while ATSDR transitioned to a new agency science database.) Each substance on the list is a candidate to become the subject of a toxicological profile prepared by ATSDR. The listing algorithm prioritizes substances based on frequency of occurrence at NPL sites, toxicity, and potential for human exposure to the substances found at NPL sites.

It should be noted that this priority list is not a list of "most toxic" substances, but rather a prioritization of substances based on a combination of their frequency, toxicity, and potential for human exposure at NPL sites.

Human biomonitoring

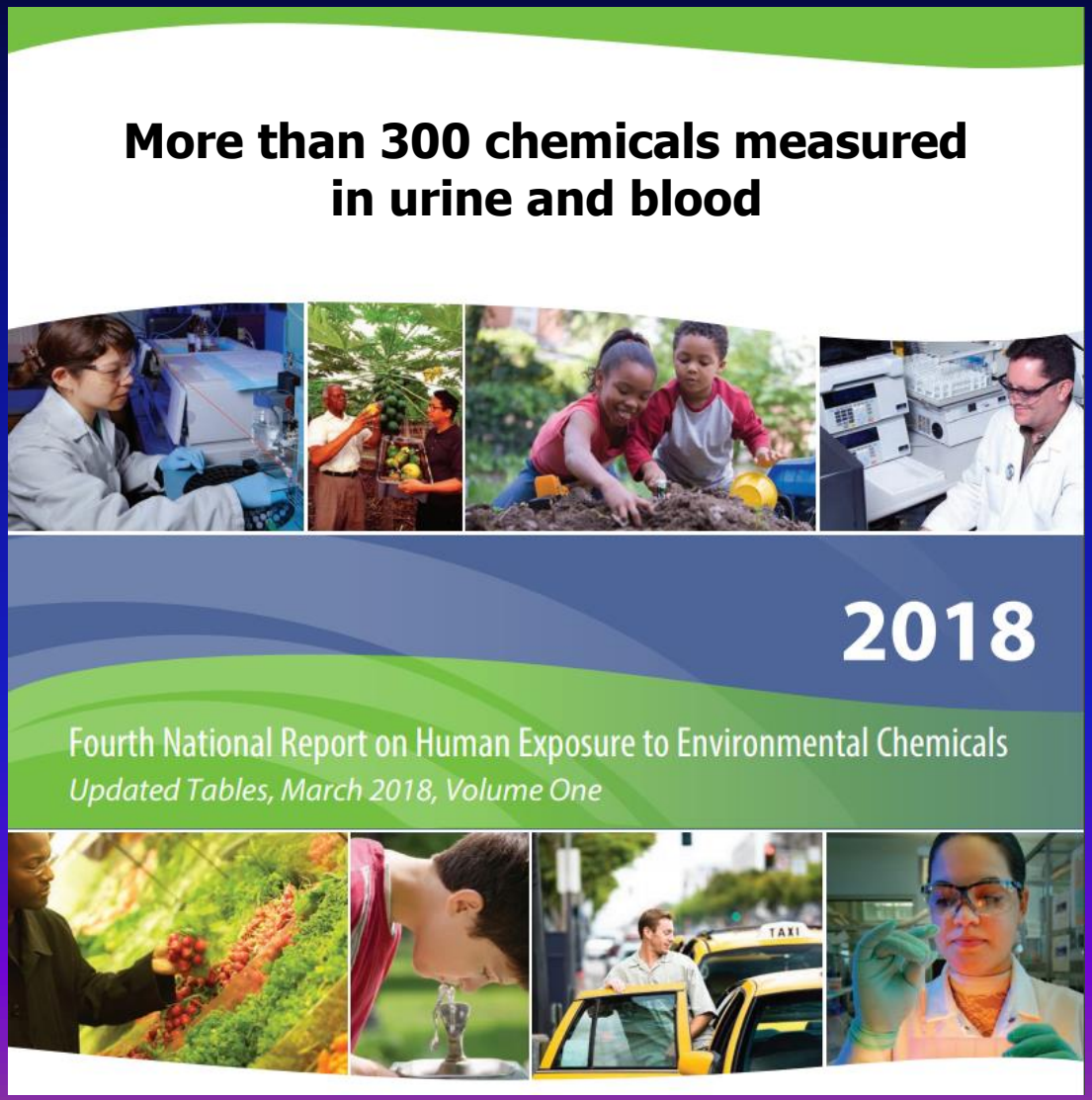
List of Priorities-ATSDR (CDC)

The ATSDR 2017 Substance Priority List

Hide/Show Table

2017 Rank	Substance Name	Total Points	CAS RN
1	ARSENIC	1674	7440-38-2
2	LEAD	1531	7439-92-1
3	MERCURY	1458	7439-97-6
4	VINYL CHLORIDE	1358	75-01-4
5	POLYCHLORINATED BIPHENYLS	1345	1336-36-3
6	BENZENE	1329	71-43-2
7	CADMIUM	1320	7440-43-9
8	BENZO(A)PYRENE	1306	50-32-8
9	POLYCYCLIC AROMATIC HYDROCARBONS	1279	130498-29-2
10	BENZO(B)FLUORANTHENE	1251	205-99-2
11	CHLOROFORM	1203	67-66-3
12	AROCLOR 1260	1191	11096-82-5
13	DDT, P,P'-	1183	50-29-3
14	AROCLOR 1254	1172	11097-69-1
15	DIBENZO(A,H)ANTHRACENE	1156	53-70-3
16	TRICHLOROETHYLENE	1155	79-01-6
17	CHROMIUM, HEXAVALENT	1148	18540-29-9

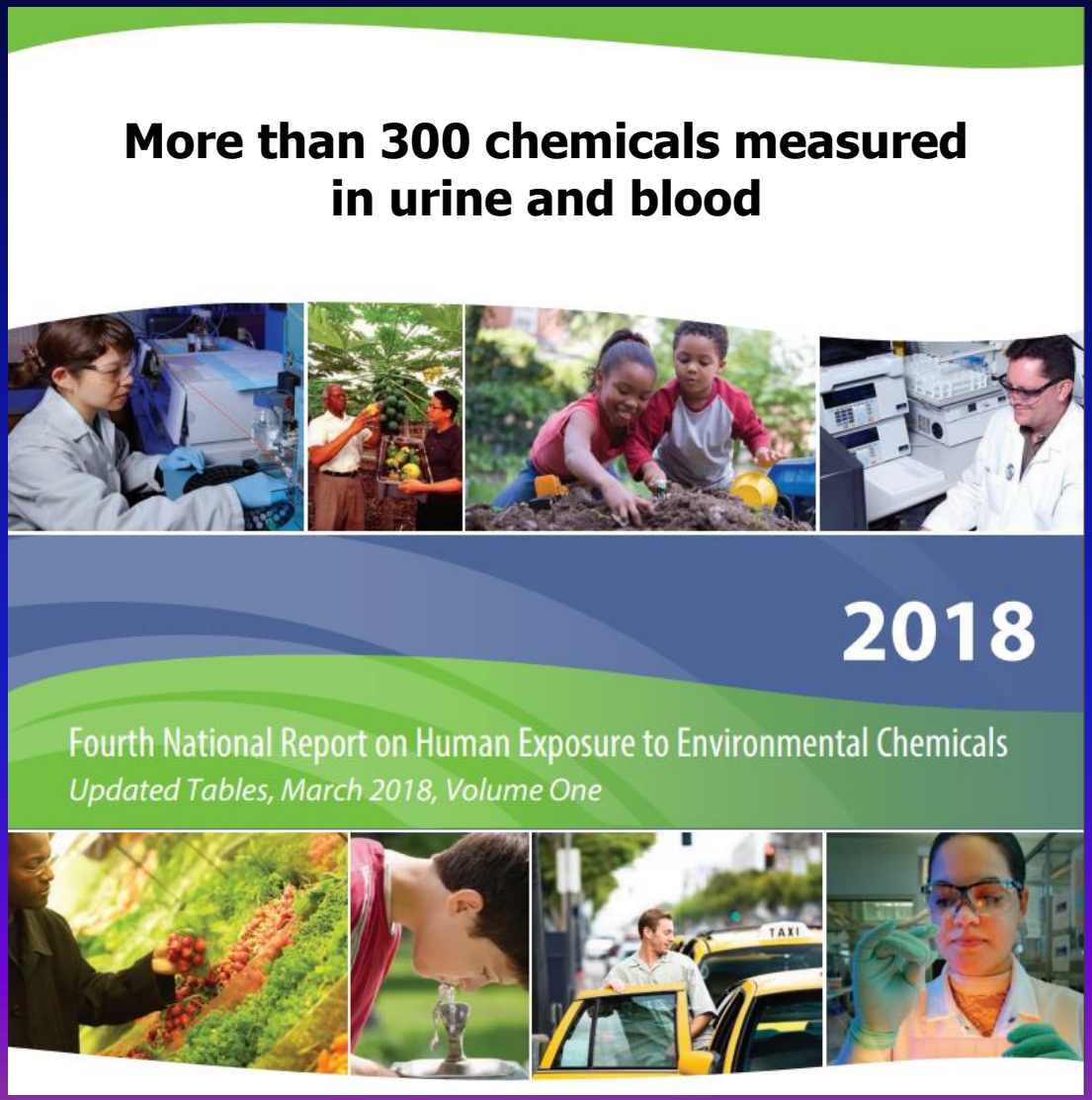
Human biomonitoring
USA



New chemical data (2018)

- BPF, BPS in urine
- Flame retardants in urine
- Cobalt, chromium in blood (40+yrs)
- DiBP, DBP metabolites in urine
- Heterocyclic amines in urine
- VOCs in blood (10 new)

Human biomonitoring
USA



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- VOCs in blood (10 new)

Intake below the estimated average requirement

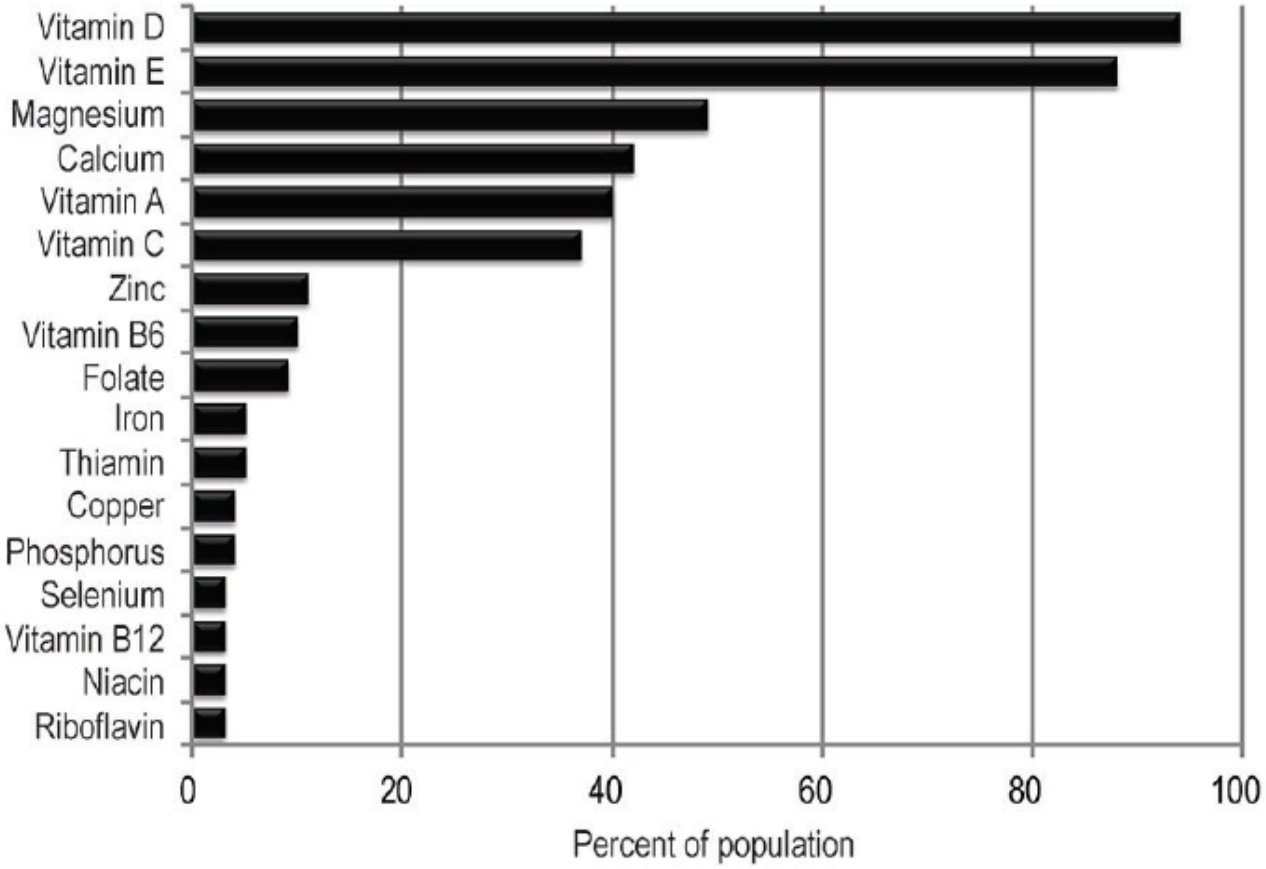


FIGURE 1-1 Percentage of U.S. population with usual intakes below the Estimated Average Requirement. NOTE: Mean intake is estimated directly from the day 1 dietary recall. It does not include nondietary sources, such as skin synthesis of vitamin D. Based on data from What We Eat in America, NHANES 2007-2010.
SOURCE: USDA and HHS, 2015 (Figure D1.1).

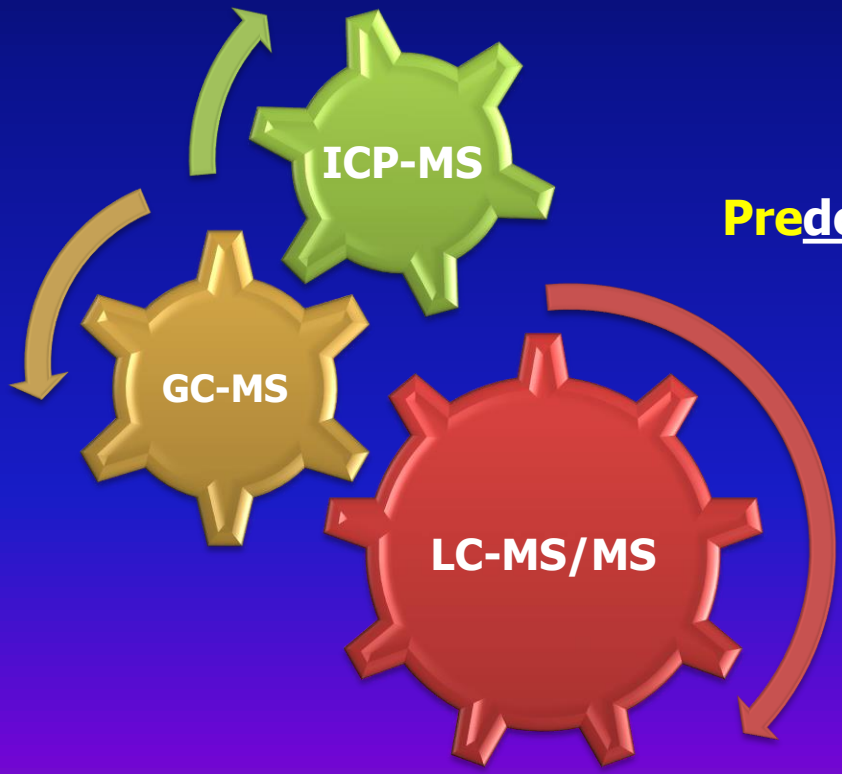
Human biomonitoring
(representative matrices)

Where??
The knowledge of Kinetics is very important

- **Whole Blood**
- Plasma/Serum
- **Urine**
- Saliva
- Hair
- Nail
- Feces
- Adipose tissue

Human biomonitoring

How?



Predominance of three techniques (mass spectrometry)

Advances in Analytical Instrumentation and HBS

Advances in analytical methods allow us to measure lower and lower levels of environmental chemicals in people

CDC Safety Level Pb in Blood (µg/dL)

70
60
50
40
30
20
10
0

Delves-cup FAAS

40 µg/dL

30 µg/dL

GF AAS

25 µg/dL

ICP-MS

10 µg/dL

5.0 µg/dL

Venous blood
(7 mL)

Pediatric

Capillary blood
(200 µL)

A drop

SPECTROCHIMICA ACTA PART B

Spectrochimica Acta Part B 62 (2007) 992–1003

www.elsevier.com/locate/sab

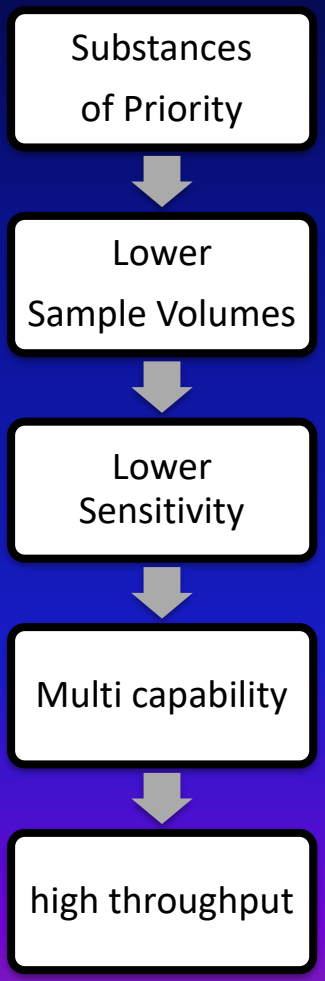
Viewpoint

Atomic spectrometry and trends in clinical laboratory medicine☆

Patrick J. Parsons [a,b,*], Fernando Barbosa Jr. [c]

1965 1970 1975 1980 1985 1990 1995 2000

Analytical Advances for HBS
Trends: All measured in a Sample Spot



Are you thinking in method development for human biomonitoring studies?

Talanta 154 (2016) 511–519

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

A fast method for bisphenol A and six analogues (S, F, Z, P, AF, AP) determination in urine samples based on dispersive liquid-liquid microextraction and liquid chromatography-tandem mass spectrometry

Bruno Alves Rocha [a], Bruno Ruiz Brandão da Costa [a], Nayara Cristina Perez de Albuquerque [b], Anderson Rodrigo Moraes de Oliveira [b], Juliana Maria Oliveira Souza [a], Maha Al-Tameemi [c], Andres Dobal Campiglia [c], Fernando Barbosa Jr. [a,*]

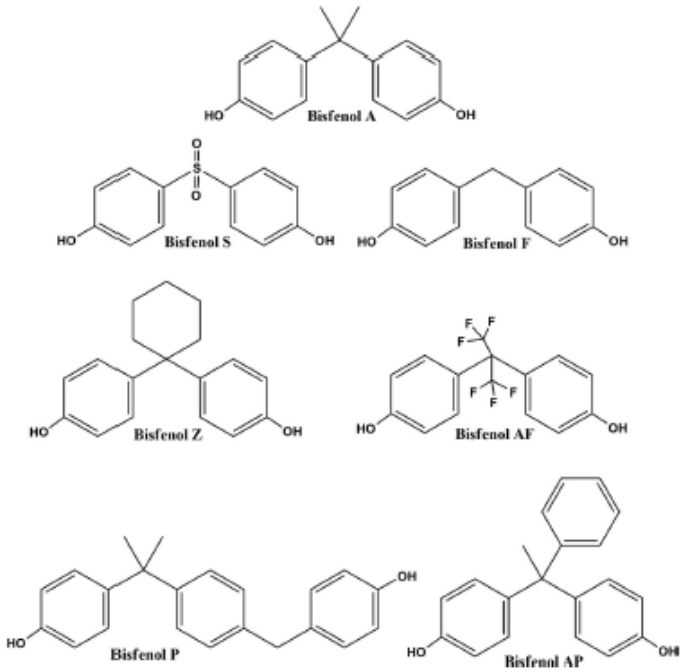


Fig. 1. Chemical structures of bisphenol A and analogues.

Table 5
The mean concentrations and detection rates of urinary bisphenol A (ng mL^{-1}).

Country	AM[a]	GM[b]	Detection rate (%)	Reference
Brazil	2.8	1.9	92	This study
China	3.8	1.1	94	[48]
Vietnam	3.3	1.4	94	[48]
India	2.0	1.6	94	[48]
Kuwait	4.1	1.2	94	[48]
Japan	2.0	0.8	94	[48]
Korea	3.5	2.0	94	[48]
USA	–	0.7	97	[49]
USA	–	0.7	95	[50]
USA	–	2.6	93	[51]
6 European member states	–	1.8	91	[52]

[a] Arithmetic mean;
[b] Geometric mean.

Talanta 183 (2018) 94–101

Contents lists available at ScienceDirect

Talanta

journal homepage: www.elsevier.com/locate/talanta

A fast and simple air-assisted liquid-liquid microextraction procedure for the simultaneous determination of bisphenols, parabens, benzophenones, triclosan, and triclocarban in human urine by liquid chromatography-tandem mass spectrometry

Bruno Alves Rocha[a], Anderson Rodrigo Moraes de Oliveira[b], Fernando Barbosa Jr[a,*]

Comparison of the proposed procedure with previously reported methodologies in the literature for the determination of endocrine-disrupting chemicals (EDCs) in urine samples.

EDC					Sample volume (mL)	Method	Solvent volume (mL)	Extraction time	Running time (min)	Ref
Bisphenol	Paraben	Benzophenone	TCS	TCC						
X	X	X	X	X	5.0	AALLME	1,2-dichloroethane (0.75)	30 s	10	This study
X	X	X	–	–	5.0	DLLME	Trichloromethane/acetone, (0.75/0.50)	10 s	10	[31]
X	X	X	–	–	5.0	DLLME	Trichloromethane/acetone, (0.75/0.50)	10 s	26	[32]
X	–	–	X	–	5.0	DLLME	tetrachloroethane/tetrahydrofuran (0.022/1.0)	5 s	–	[49]
–	X	–	–	–	0.5	DLLME	1-decanol/metanol (0.058/0.65)	30 s	50	[50]
X	–	–	–	–	5.0	DLLME	tetrachloroethylene/acetonitrile (0.050/1.325)	60 s	10	[48]
X	–	–	–	–	5.0	DLLME	1,2-dichloroethane/acetone (0.5/0.75	10 s	7	[33]
X	X	X	X	X	0.5	LLE	Ethyl acetate (9.0)	180 min	4/5.5	[13]*
X	X	X	–	–	1.0	LLE	Methyl tert-butyl ether/ethyl acetate (7.5/1.5)	–	14	[58]
–	X	X	X	X	0.5	LLE	Ethyl acetate (9.0)	180 min	30/30	[59]*

* The determination of compounds (LC-MS/MS method) are not simultaneous.

Urinary concentrations and detection rates of endocrine-disrupting chemicals (in ng mL^{-1}, volume-based model) in Brazilian children (n = 50).

EDC	DR%[a]	GM[b]	Median	Min[c]	Max[d]
BPA	96	1.20	1.34	< LOQ	19.6
BPS	14	0.54	1.03	< LOQ	2.27
BPAP	0	–	–	–	–
BPP	12	0.14	0.13	< LOQ	0.21
BPF	24	1.27	1.00	< LOQ	4.68
BPAF	0	–	–	–	–
BPZ	0	–	–	–	–
MeP	100	40.1	41.9	2.29	1118
EtP	78	0.51	0.44	< LOQ	33.6
PrP	84	3.67	3.92	< LOQ	78.4
BuP	40	0.19	0.13	< LOQ	11.3
BzP	20	0.04	0.03	< LOQ	0.13
OH-MeP	100	2.53	2.56	0.17	28.5
OH-EtP	84	0.54	0.50	< LOQ	7.28
BP3	100	3.06	2.99	0.71	70.1
BP1	90	3.61	4.34	< LOQ	46.7
BP8	18	0.19	0.28	< LOQ	0.82
BP2	12	0.77	0.87	< LOQ	1.50
4OHBP	24	0.36	0.43	< LOQ	1.73
TCS	88	14.7	12.0	< LOQ	294
TCC	64	0.02	0.03	< LOQ	0.15

[a] DR%, detection in percentage.
[b] GM, geometric mean.
[c] min, minimum.
[d] max, maximum.

HB and Human Disease

Target Analytes

<5%

-Untarget substances
-Lifestyle and
-Other environment Factors
-Genetic

>95%

HB-Limitations

- Limited target analytes;
- Cross-sectional design (not take continuous measures);
- National estimates: no geographical and limited seasonal information;
- No data for specific population groups, sources, or uses of chemicals;
- Most of analysis are time-consuming and relatively expensive;
- Few Laboratories with routine capabilities.

Going Beyond the HB: The Age of the Exposome

In 2005, Dr. Christopher Wild, a cancer epidemiologist, in his article "Complementing the genome with an exposome: the outstanding challenge of environmental exposure measurement in molecular epidemiology", proposes for the first time the term "exposome", as the complementary environmental component to the genome, in determining the risk of a particular disease.

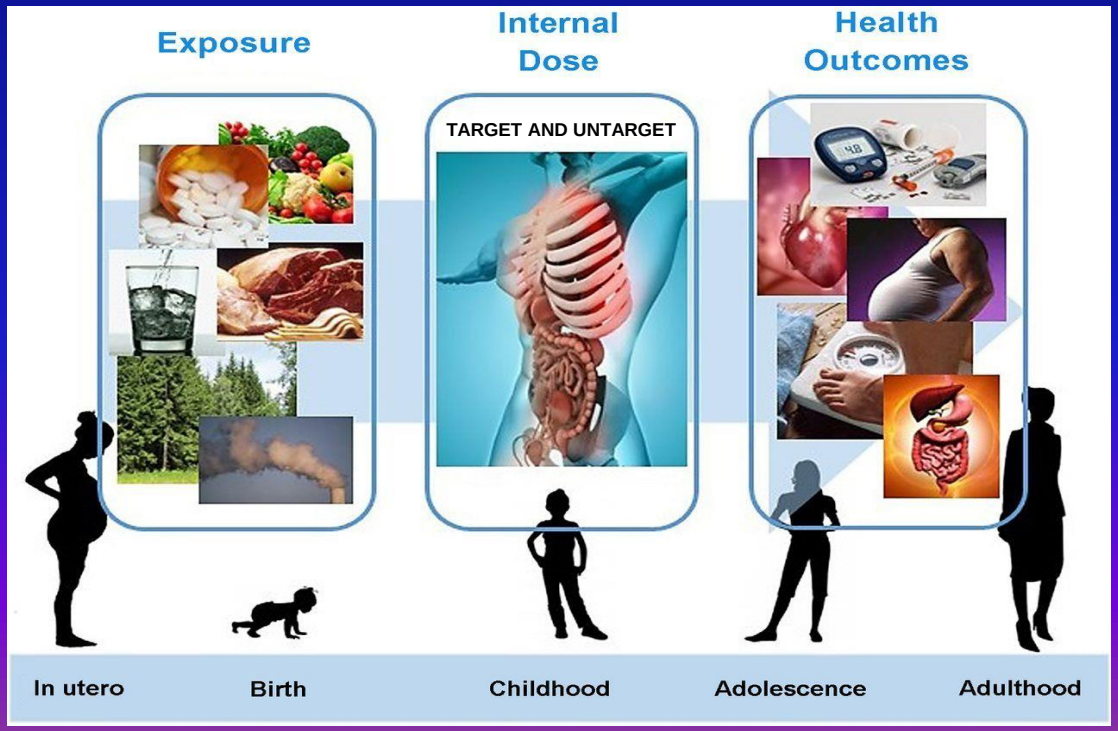
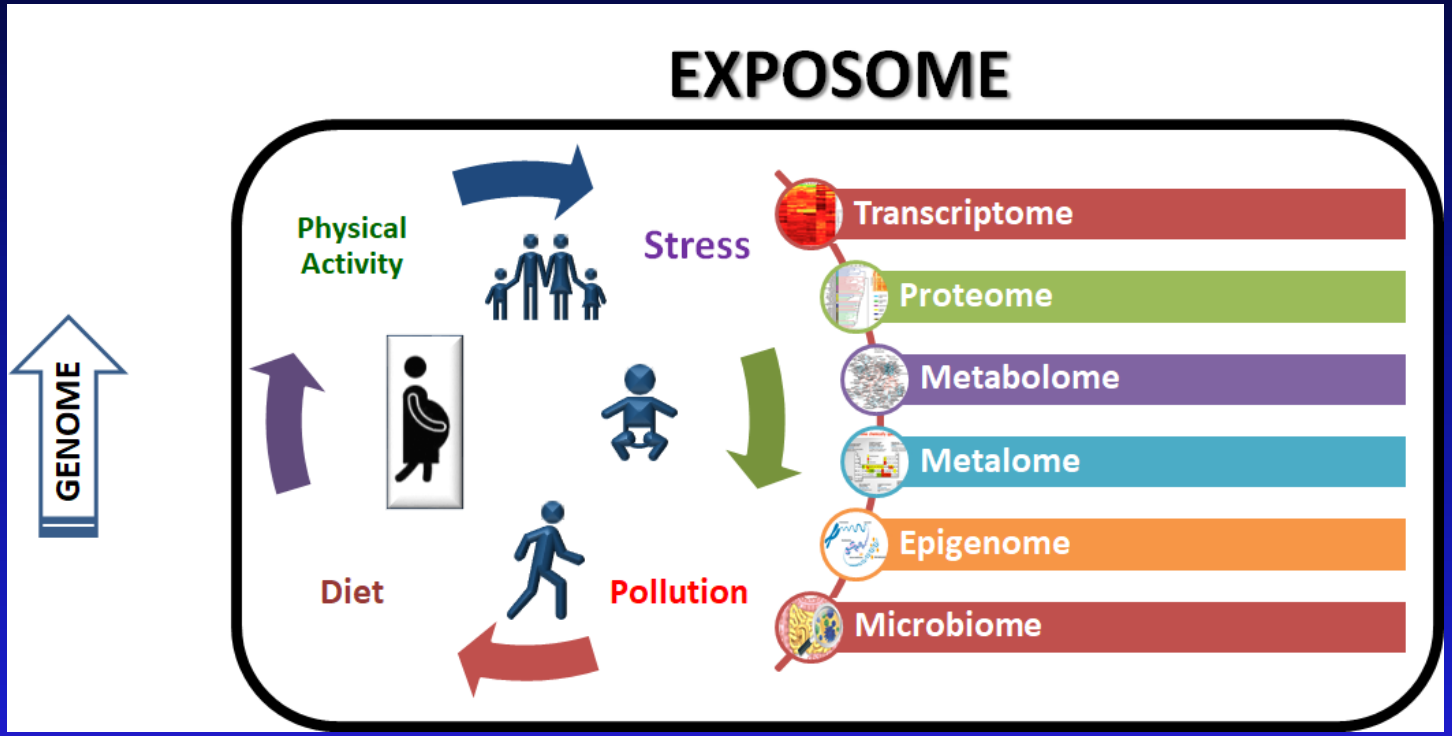
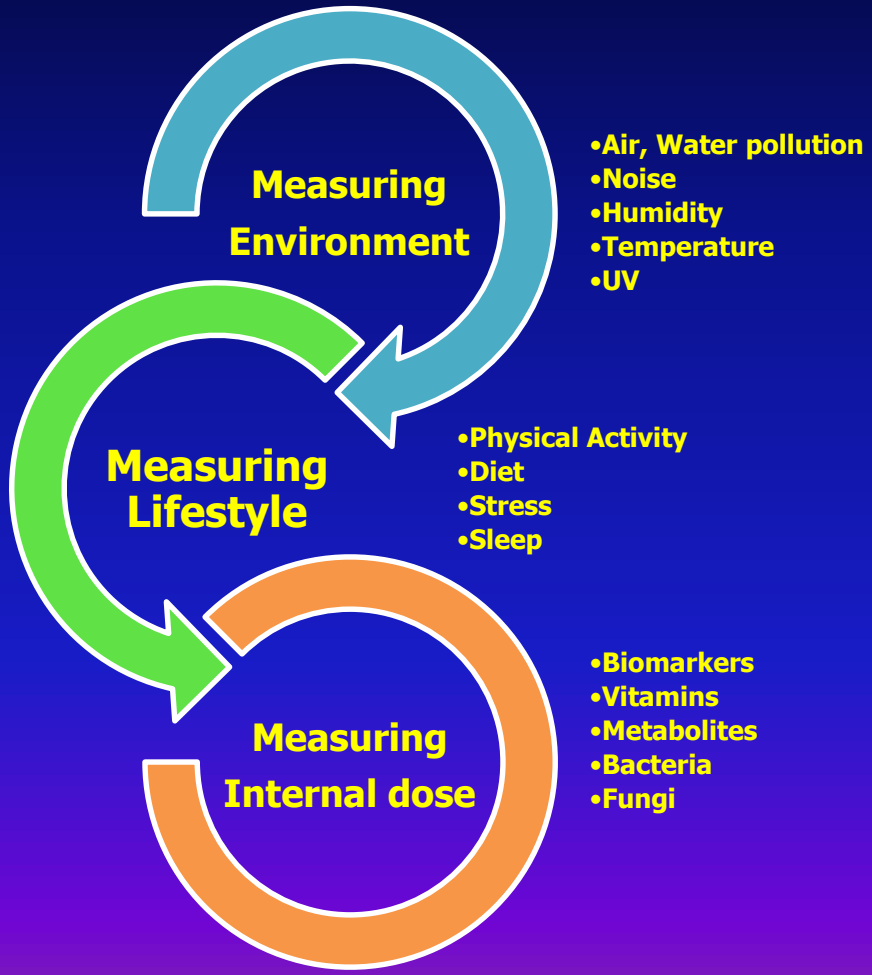


Diagram of the exposome



"Cumulative measures of environmental influences and associated biological responses throughout the life of an individual, including exposures of the environment, diet, lifestyle and endogenous processes"(SIROUX, AGIER,SLAMA, 2016)

MEASURING YOUR EXPOSOME (INTERNAL AND EXTERNAL)



External Exposome (EEXP)

Traditional Monitoring

- More accuracy
- Much More Analytes
- Active collection
- Spot sample
- Not Real Time-exposure
- Limitations of Seasonal Variatons
- Fixed Stations (Apps)
- Costly

Personalized Systems (trends)

- Personalized Systems (Colletion and further analysis)
- Personalized Systems (collection and Analysis)
- Near-Real Time Monitoring
- Usually Passive Collection
- Usually Less Analytes
- Cheap
- Less accuracy

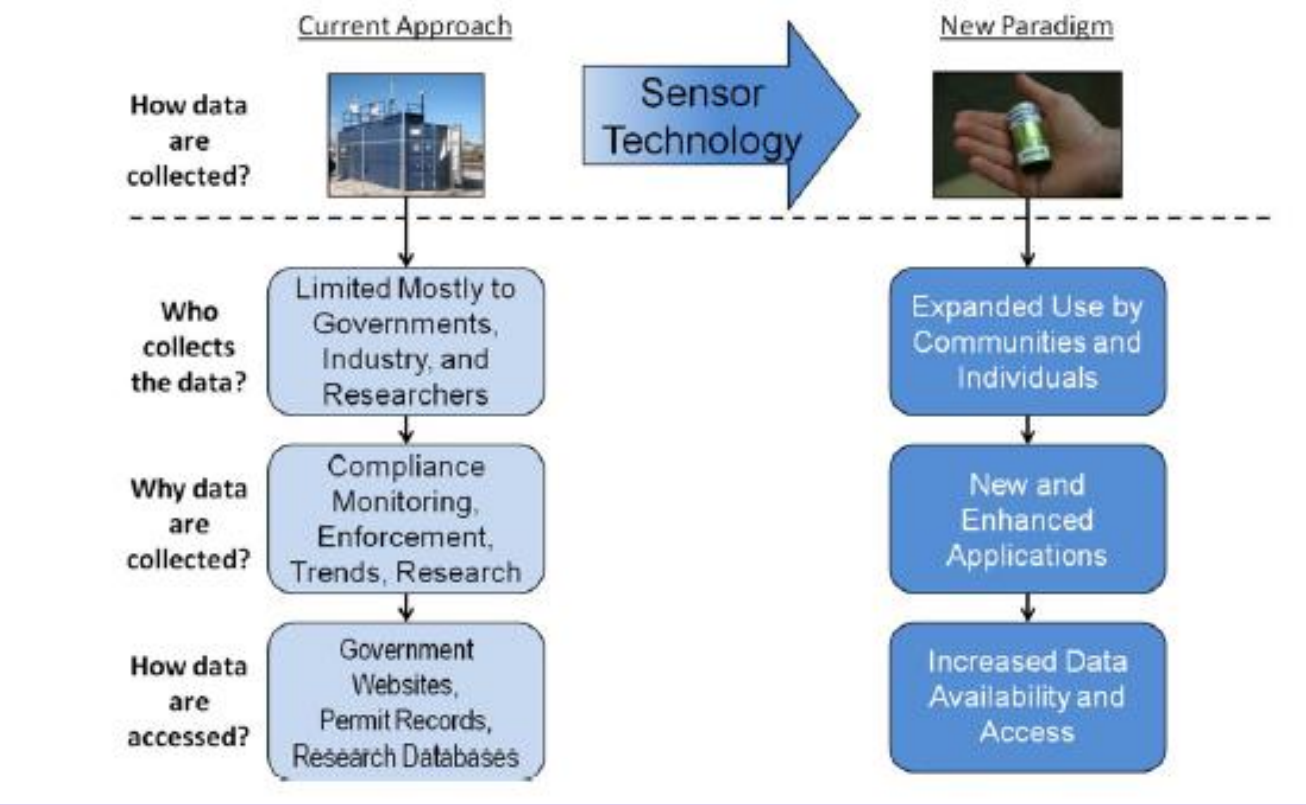
Environmental Science & Technology

Feature

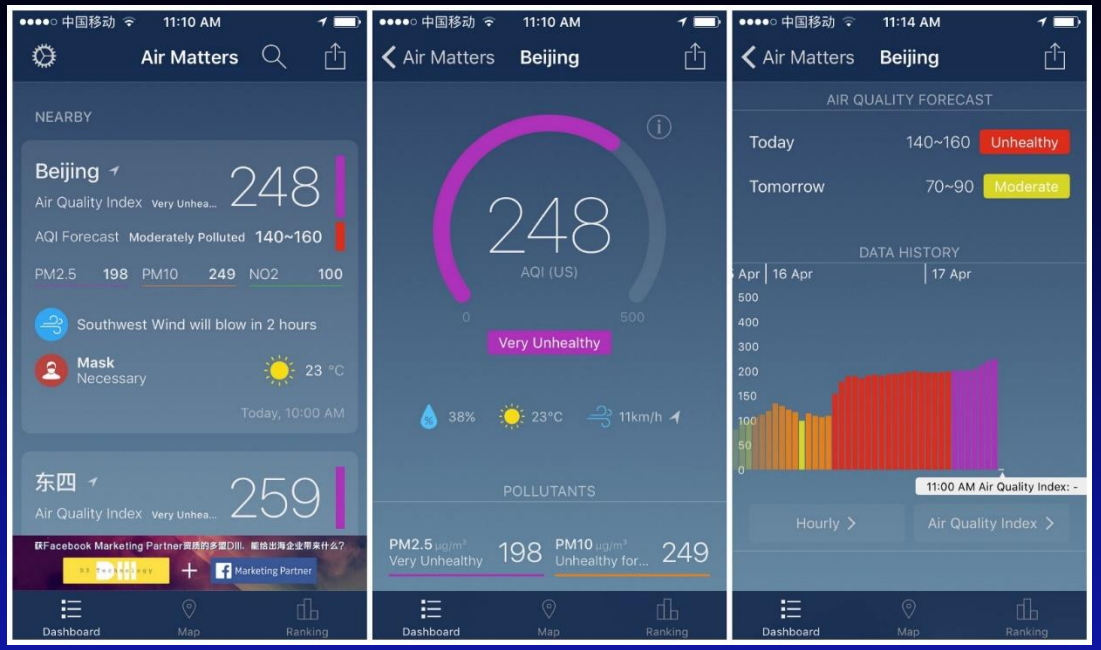
pubs.acs.org/est

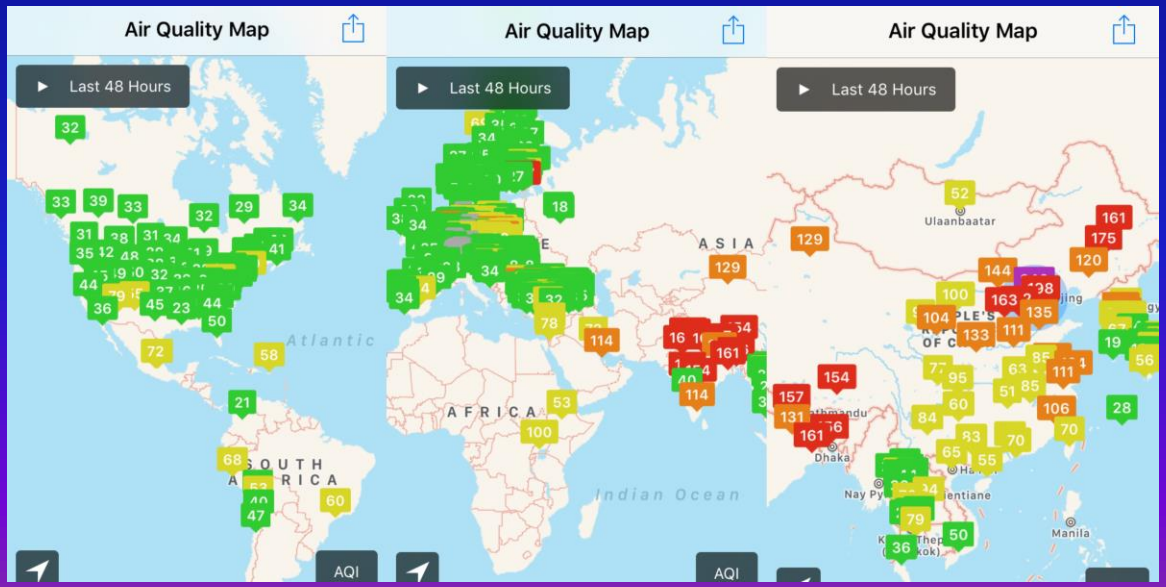
The Changing Paradigm of Air Pollution Monitoring

Emily G. Snyder,*[,†] Timothy H. Watkins,[†] Paul A. Solomon,[‡] Eben D. Thoma,[†] Ronald W. Williams,[†] Gayle S. W. Hagler,[†] David Shelow,[§] David A. Hindin,[∥] Vasu J. Kilaru,[†] and Peter W. Preuss[⊥]



Air Matters
Google Play





External Exposome (EEXP)
(Tracking personalized exposure)

Assessing the Exposome with External Measures: Commentary on the State of the Science and Research Recommendations

Michelle C. Turner,[1,2,3,4] Mark Nieuwenhuijsen,[1,2,3] Kim Anderson,[5] David Balshaw,[6] Yuxia Cui,[6] Genevieve Dunton,[7] Jane A. Hoppin,[8] Petros Koutrakis,[9] and Michael Jerrett[10,11]

Annu. Rev. Public Health 2017. 38:215–39

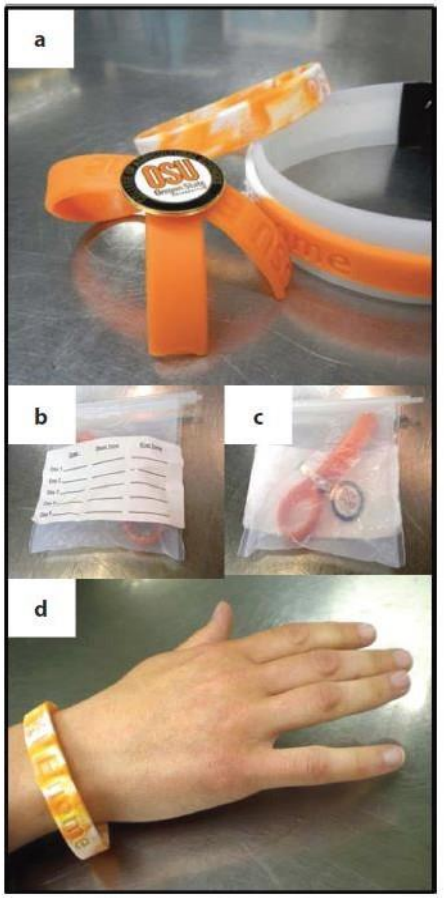


Figure 7

Examples of silicone personal sampling samplers. (*a*) Configurations of wristbands used in the study including a single wristband, one cut and worn as a lapel, and one worn as a stacked wristband in which only the outer band was analyzed; (*b–c*) bags used for transport that were attached to track participant identification and exposure time in the occupational deployments; (*d*) single wristband deployment (debossed writing as pictured: "OSU EINOME" for Oregon State University Environmental Integrated Organic Monitor of Exposure) (adapted from 71).

ENVIRONMENTAL Science & Technology

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Article

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Silicone Wristbands as Personal Passive Samplers

Steven G. O'Connell, Laurel D. Kincl, and Kim A. Anderson*

ABSTRACT: Active-sampling approaches are commonly used for personal monitoring, but are limited by energy usage and data that may not represent an individual's exposure or bioavailable concentrations. Current passive techniques often involve extensive preparation, or are developed for only a small number of targeted compounds. In this work, we present a novel application for measuring bioavailable exposure with silicone wristbands as personal passive samplers. Laboratory methodology affecting precleaning, infusion, and extraction were developed from commercially available silicone, and chromatographic background interference was reduced after solvent cleanup with good extraction efficiency (>96%). After finalizing laboratory methods, 49 compounds were sequestered during an ambient deployment which encompassed a diverse set of compounds including polycyclic aromatic hydrocarbons (PAHs), consumer products, personal care products, pesticides, phthalates, and other industrial compounds ranging in log K_{ow} from −0.07 (caffeine) to 9.49 (tris(2-ethylhexyl) phosphate). In two hot asphalt occupational settings, silicone personal samplers sequestered 25 PAHs during 8- and 40-h exposures, as well as 2 oxygenated-PAHs (benzofluorenone and fluorenone) suggesting temporal sensitivity over a single work day or week ($p < 0.05$, power =0.85). Additionally, the amount of PAH sequestered differed between worksites ($p < 0.05$, power = 0.99), suggesting spatial sensitivity using this novel application.

Table 1. Compounds Identified from AMDIS Spectra against Chemical Libraries during Ambient Exposures[a]

groups	compounds	CAS	log K_{ow}	no. of WBs	possible use or occurrence
PAHs	1-methylnaphthalene	90−12−0	3.87	16	compounds from petrogenic and pyrogenic sources
	anthracene	120−12−7	4.45	6	compounds from petrogenic and pyrogenic sources
	fluorene	86−73−7	4.18[a]	5	compounds from petrogenic and pyrogenic sources
	1,6-dimethylnaphthalene	575−43−9	4.26[a]	4	compounds from petrogenic and pyrogenic sources
	1-methylphenanthrene	832−69−9	5.08[a]	3	compounds from petrogenic and pyrogenic sources
	1,2-dimethylnaphthalene	573−98−8	4.31[a]	2	compounds from petrogenic and pyrogenic sources
	acenaphthylene	208−96−8	4.07	1	compounds from petrogenic and pyrogenic sources
	pyrene	129−00−0	4.88	1	compounds from petrogenic and pyrogenic sources
	retene	483−65−8	6.35[a]	1	compounds from petrogenic and pyrogenic sources
consumer products	tonalide	1506−02−1	5.70	20	fragrance in cosmetics, detergents, fabric softeners, household cleaning products
	carvone	99−49−0	3.07[a]	14	oil of caraway seeds, used in perfumes, soaps
	triclosan	3380−34−5	4.76	9	active agent in deodorants and antiseptic products
	caffeine	58−08−2	−0.07	6	common component of coffee, sodas, and other beverages
	nicotine	54−11−5	1.17	4	active ingredient in tobacco products
	eugenol	97−53−0	2.49	4	clove perfumes, essential oils, dental medicine (analgesic)
	celestolide	13171−00−1	5.93(est)[b]	2	musk fragrance in cosmetics or perfumes[a]
	musk ketone	81−14−1	4.30	1	fragrance in cosmetics, perfumes
	phantolide	15323−35−0	5.85(est)[b]	1	musk fragrance[a]
	phthalimide	85−41−6	1.15	1	used in dyes, fungicide
pesticides	benzyl benzoate	120−51−4	3.97	18	acaricide and Insecticide
	N,*N*-diethyl-m-toluamide	134−62−3	2.02	11	insect and acarid repellant used for households and domestic purposes (DEET)
	promecarb artifact	3228−03−3	3.52(est)[b]	6	possible metabolite of a nonsystemic contact insecticide
	methoprene	40596−69−8	5.50	5	broad spectrum insecticide
	fipronil	120068−37−3	4.00	3	insecticide designed for pet use targeting fleas and ticks
	fipronil-sulfone	120068−36−2	4.42(est)[b]	2	metabolite of fipronil[c]
	fipronil, desulfinyl-	111246−15−2	4.22(est)[b]	1	photodegredate of fipronil[c]
	trifluralin	1582−09−8	5.34	1	pre-emergent herbicide
phthalates	diethyl phthalate	84−66−2	2.47	23	vehicle for fragrances and cosmetics
	butyl benzyl phthalate	85−68−7	4.73	19	plasticizer for floor tile, foams, carpet backing
	di-n-octyl phthalate	117−84−0	8.10	11	plasticizer for cellulose and vinyl resins
	di-n-hexyl phthalate	84−75−3	6.82	9	used in making plastisols, which are used for dip-molded plastics and automobile parts
	dicyclohexyl phthalate	84−61−7	6.20 (est)	6	plasticizer for cellulose, chlorinated rubber, and other polymers
	dimethylphthalate	131−11−3	1.60	5	plasticizer for cellulose and vinyl resins

Analytical and Bioanalytical Chemistry (2018) 410:3059–3071
https://doi.org/10.1007/s00216-018-0992-z

PAPER IN FOREFRONT

Silicone wristbands compared with traditional polycyclic aromatic hydrocarbon exposure assessment methods

Holly M. Dixon[1] · Richard P. Scott[1] · Darrell Holmes[2] · Lehyla Calero[2] · Laurel D. Kincl[3] · Katrina M. Waters[4] · David E. Camann[5] · Antonia M. Calafat[6] · Julie B. Herbstman[2] · Kim A. Anderson[1]

Currently there is a lack of inexpensive, easy-to-use technology to evaluate human exposure to environmental chemicals, including polycyclic aromatic hydrocarbons (PAHs). This is the first study in which silicone wristbands were deployed alongside two traditional personal PAH exposure assessment methods: active air monitoring with samplers (i.e., polyurethane foam (PUF) and filter) housed in backpacks, and biological sampling with urine. We demonstrate that wristbands worn for 48 h in a non-occupational setting recover semivolatile PAHs, and we compare levels of PAHs in wristbands to PAHs in PUFs-filters and to hydroxy-PAH (OH-PAH) biomarkers in urine. We deployed all samplers simultaneously for 48 h on 22 pregnant women in an established urban birth cohort. Each woman provided one spot urine sample at the end of the 48-h period. Wristbands recovered PAHs with similar detection frequencies to PUFs-filters. Of the 62 PAHs tested for in the 22 wristbands, 51 PAHs were detected in at least one wristband. In this cohort of pregnant women, we found more significant correlations between OH-PAHs and PAHs in wristbands than between OH-PAHs and PAHs in PUFs-filters. Only two comparisons between PAHs in PUFs-filters and OH-PAHs correlated significantly ($r_s = 0.53$ and $p = 0.01$; $r_s = 0.44$ and $p = 0.04$), whereas six comparisons between PAHs in wristbands and OH-PAHs correlated significantly ($r_s = 0.44$ to 0.76 and $p = 0.04$ to <0.0001). These results support the utility of wristbands as a biologically relevant exposure assessment tool which can be easily integrated into environmental health studies.

Table 3 Correlation table for 20 PAHs analyzed in air-monitoring backpacks (PUFs and filters) and wristbands

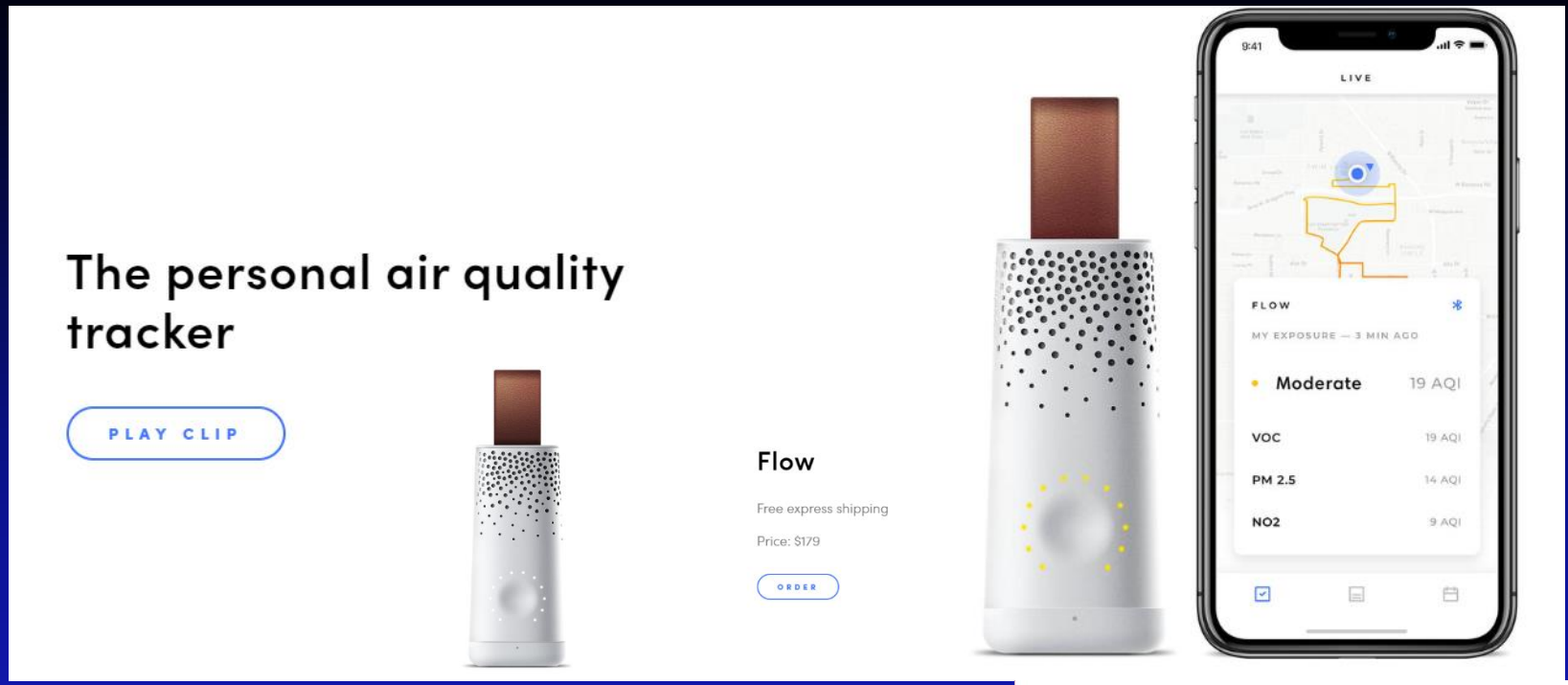
PAH	Wristband PAH and PUF PAH		Wristband PAH and PUF-filter PAH	
	r_s	p-value	r_s	p-value
Naphthalene	**0.71**	**0.0002***	**0.71**	**0.0002***
2-Methylnaphthalene	**0.47**	**0.03***	**0.47**	**0.03***
1-Methylnaphthalene	**0.49**	**0.02***	**0.49**	**0.02***
Acenaphthylene	a	a	a	a
Acenaphthene	**0.69**	**0.0004***	**0.69**	**0.0004***
Fluorene	**0.71**	**0.0002***	**0.71**	**0.0002***
Phenanthrene	**0.54**	**0.009***	**0.54**	**0.009***
Anthracene	b	b	b	b
2-Methylphenanthrene	0.15	0.50	0.14	0.53
1-Methylphenanthrene	0.41	0.06	**0.43**	**0.05***
Fluoranthene	**0.56**	**0.007***	**0.54**	**0.009***
Pyrene	0.26	0.24	0.28	0.20
Benz[*a*]anthracene	−0.03	0.90	0.03	0.89
Chrysene/isochrysene	a	a	0.09	0.69
Benzo[*b*]fluoranthene	a	a	0.23	0.29
Benzo[*k*]fluoranthene	a	a	0.18	0.43
Benzo[*a*]pyrene	a	a	0.15	0.52
Indeno[1,2,3-*cd*]pyrene	c	c	b	b
Dibenz[*a*,*h*]anthracene	c	c	c	c
Benzo[*ghi*]perylene	a	a	0.33	0.13

[a] >50% detections in wristbands and <50% detections in PUFs and filters

[b] >50% detections in PUFs and filters and <50% detections in wristbands

[c] <50% detections in wristbands and PUFs and filters

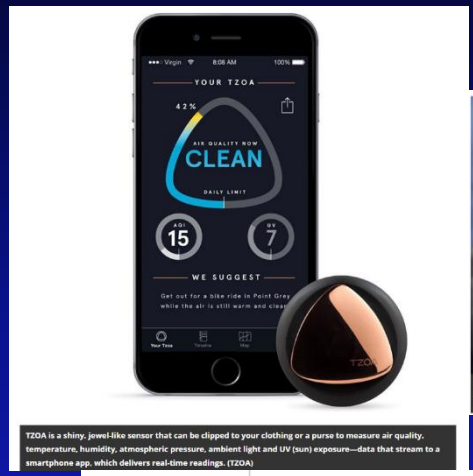
* and **bold type** indicate $\alpha < 0.05$



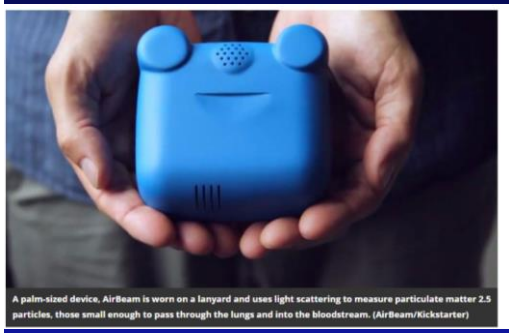
Track your personal exposure
Flow measures real-time concentrations of NO2, VOC, PM2.5 and PM10.

External Exposome (EEXP)

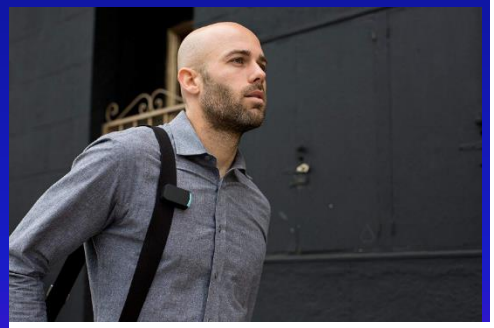
(Accuracy ????)

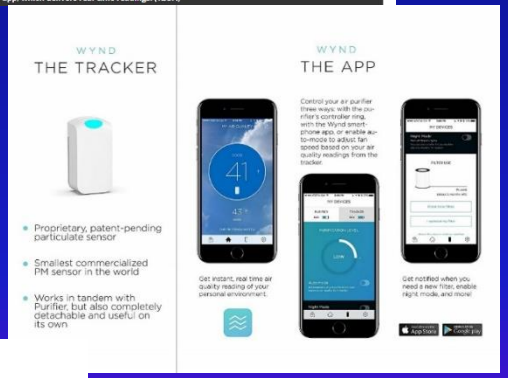


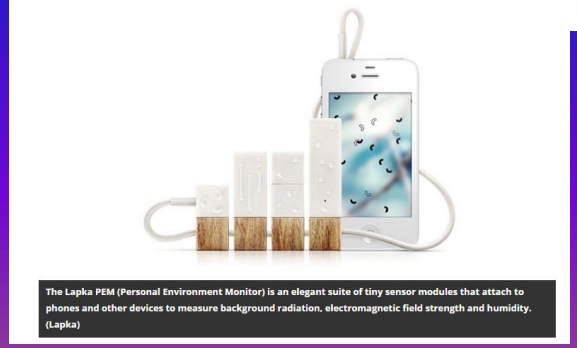
TZOA is a shiny, jewel-like sensor that can be clipped to your clothing or a purse to measure air quality, temperature, humidity, atmospheric pressure, ambient light and UV (sun) exposure—data that stream to a smartphone app, which delivers real-time readings. (TZOA)



A palm-sized device, AirBeam is worn on a lanyard and uses light scattering to measure particulate matter 2.5 particles, those small enough to pass through the lungs and into the bloodstream. (AirBeam/Kickstarter)







The Lapka PEM (Personal Environment Monitor) is an elegant suite of tiny sensor modules that attach to phones and other devices to measure background radiation, electromagnetic field strength and humidity. (Lapka)

External Exposome (EEXP)

Air pollution sensors can be separated into two main categories, those that measure the concentration of gas phase species and those that measure either particulate matter (PM) mass concentrations or various properties of particles (e.g., scattering or absorption). All sensors systems consist of a few basic elements that include (1) the sensor element that responds to the species of interest and varies with the pollutant mass in a given volume of sampled air; (2) the transducer that converts the responses to electrical signals; (3) data storage capability or a link to a communication device (e.g., microradio transmitter or cell phone); and (4) a source of power (e.g., battery or energy harvesting).

Most commercially available gas sensors are based on two main principles: (1) those that depend on interactions between the sensing material (electrochemical cell or metal oxide semiconductor) and gas phase component such as nitrogen dioxide (NO_2), ozone (O_3), carbon monoxide (CO), and volatile organic compounds (VOC) and (2) those that measure absorption of light at visible (e.g., for O_3 and CO_2) or infrared wavelengths (e.g., CO_2), or by chemiluminescence (NO_2) (see examples, Tables 2 and 3). Particulate matter mass can be measured directly by changes in frequency of an oscillating sensor element[12] or indirectly based by light scattering using a proportionality constant that relates the scattered light to a defined (e.g., <2.5 μm) aerodynamic diameter [AD]) PM mass concentration.[8] Light scattering and absorption by particles are important particle properties that have direct relationships to visibility and climate change. Table 1 provides a brief summary

Environmental Pollution 223 (2017) 102–110

Contents lists available at ScienceDirect

Environmental Pollution

journal homepage: www.elsevier.com/locate/envpol

Characteristics and applications of small, portable gaseous air pollution monitors☆

Grant R. McKercher [a], Jennifer A. Salmond [b], Jennifer K. Vanos [a, c, *]

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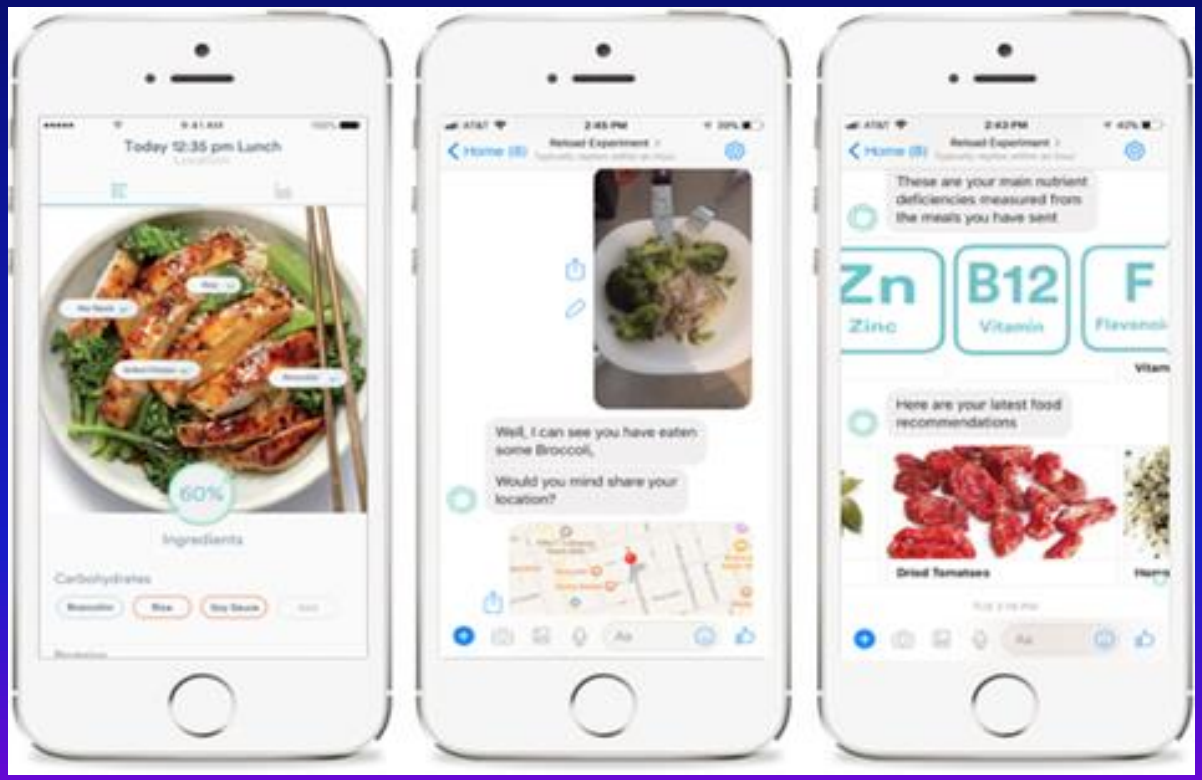
External Exposome (EEXP)
(Personalized Systems)

Challenge

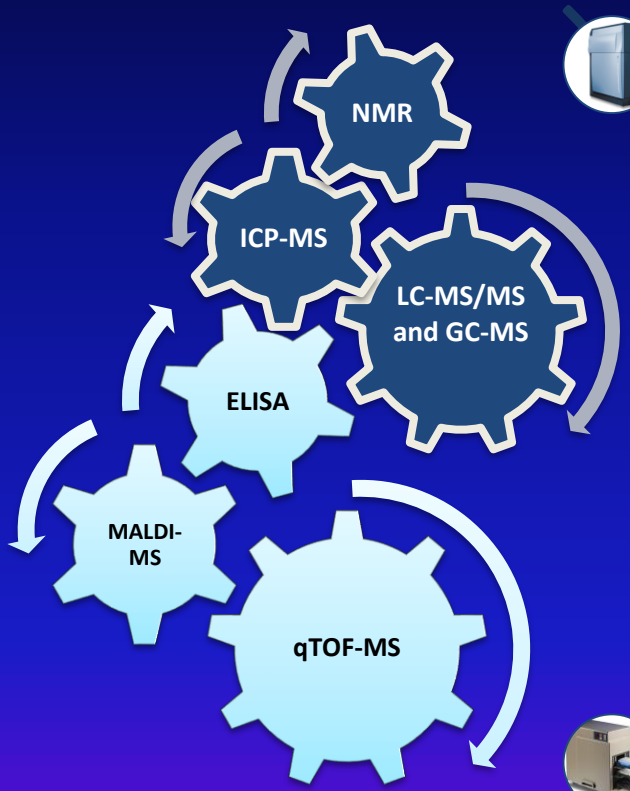
- **Studies regarding their accuracy or the comparison between miniaturized sensors and reference methods still seem to be sparse;**

Apps
Nutrition/Diet
Lifestyle / Physical Activity Tracking
(based on data mining)



Internal Exposome (IEXP)

TARGET AND UNTARGET ANALYTES



- Proteome
- Metabolome
- Metalome
- Organic Contaminants
- Drugs
- Vitamins
- Inflamatory markers

Target Analytes > 1500

Internal Exposome (IEXP)

TARGET AND UNTARGET ANALYTES

The Blood Exposome and Its Role in Discovering Causes of Disease

Stephen M. Rappaport,[1] Dinesh K. Barupal,[2] David Wishart,[3] Paolo Vineis,[4,5] and Augustin Scalbert[2]

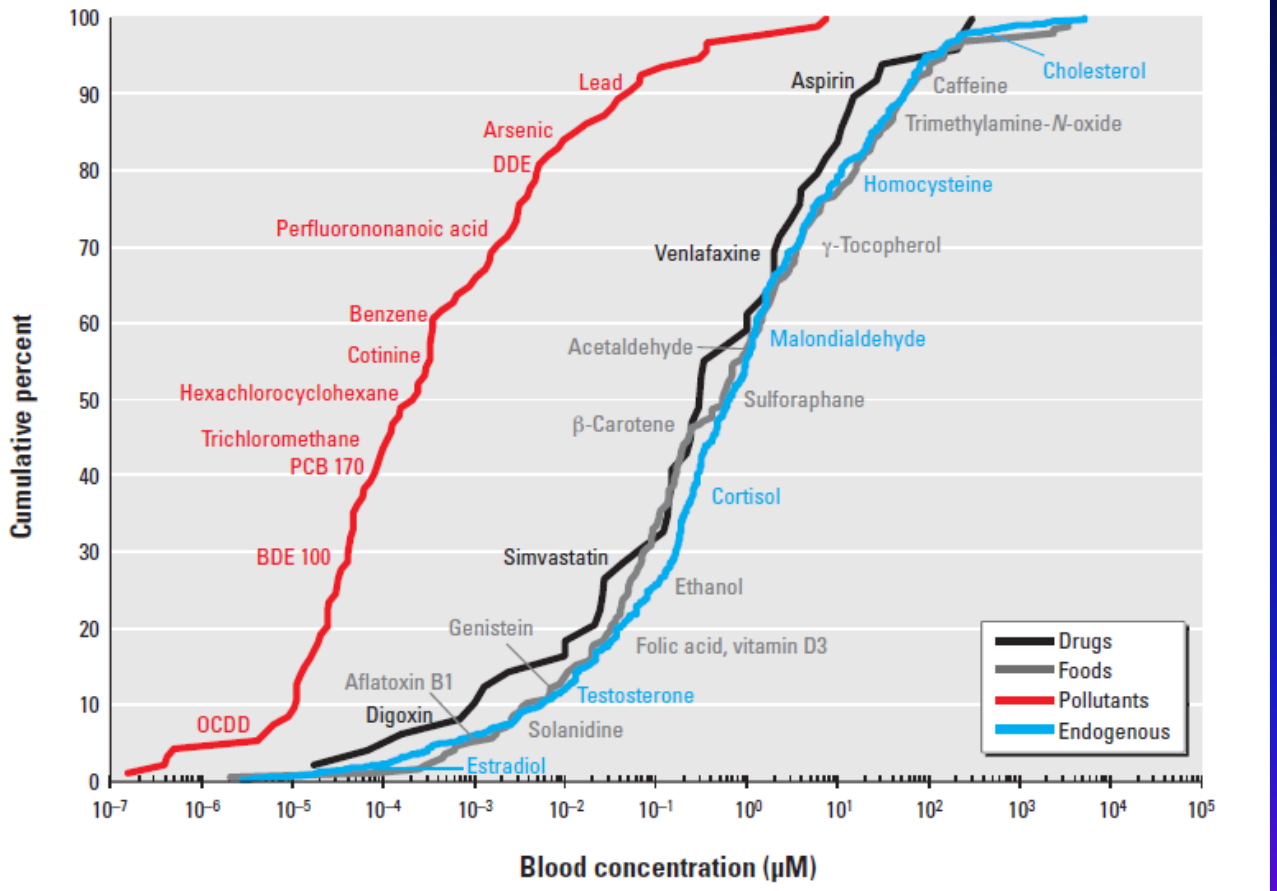
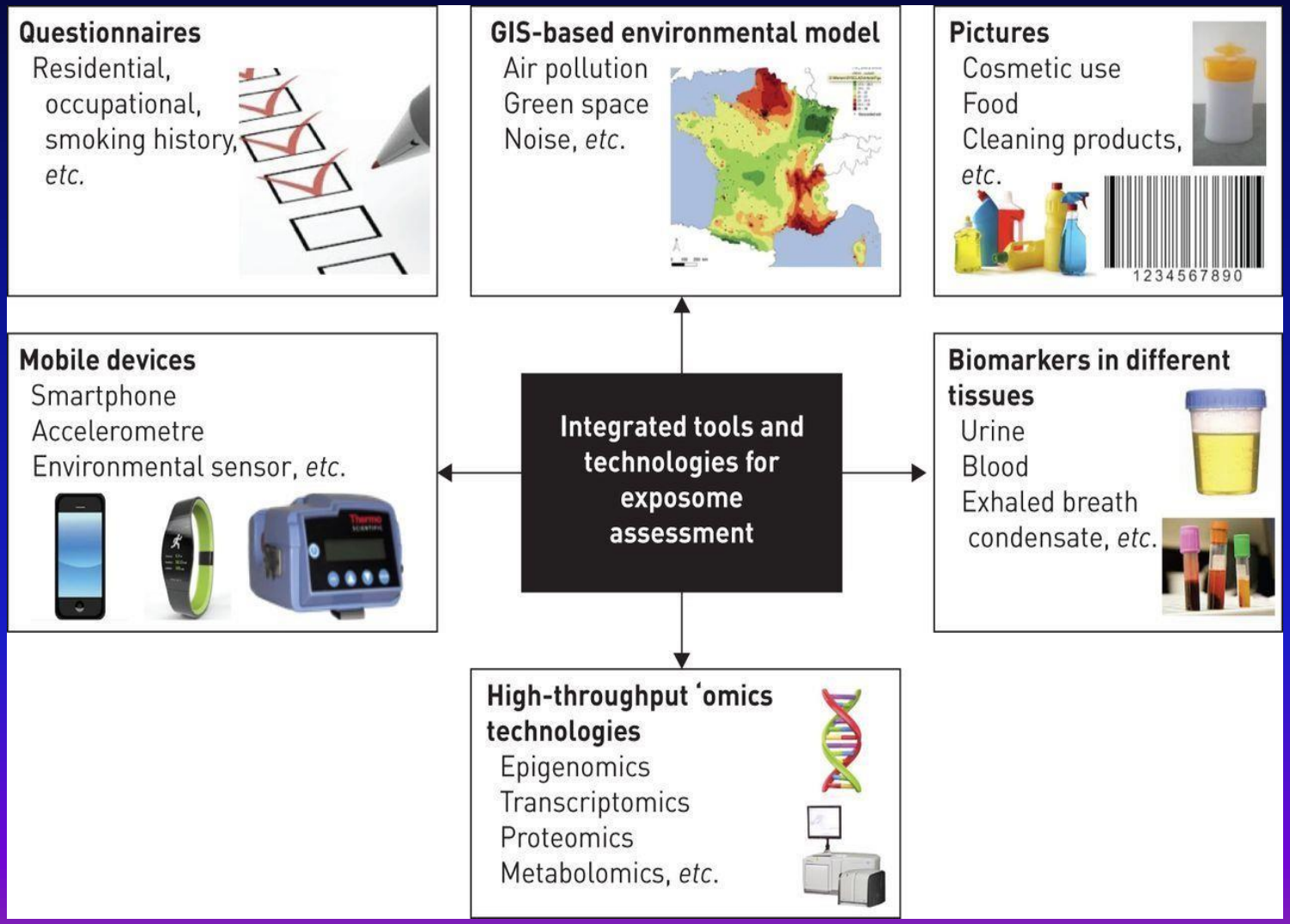


Figure 2. Small molecules and metals in human blood. Each curve represents the cumulative distribution of chemical concentrations from a particular source category (pollutants, $n = 94$; drugs, $n = 49$; food chemicals, $n = 195$; endogenous chemicals, $n = 1,223$). Abbreviations: BDE 100, 2,2′,4,4′,6-pentabromodiphenyl ether; DDE, 1,1-bis-(4-chlorophenyl)-2,2-dichloroethene; OCDD, 1,2,3,4,6,7,8,9-octachlorooxanthrene; PCB 170, 2,2′,3,3′,4,4′,5-heptachloro-1,1′-biphenyl.

Data Mining for data integration (Internal and external exposome)



Challenges and Trends (IEXP)

- ✓ High-throuput Analysis (HTAs);
- ✓ Methods Based on Multi-Analytes Determination;
- ✓ Fast, sensible and easy procedures

(sample preparation and determination);

- ✓ Very Costly (Requires Implementation of Facilities);
- ✓ Open possibilites for the development of point-of-care systems (specific biomarkers);
- ✓ Development and application of Algorithms

(Data Treatment-Data Mining-Big Data) (mandatory).

Environment International 116 (2018) 269–277

Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

Advanced data mining approaches in the assessment of urinary concentrations of bisphenols, chlorophenols, parabens and benzophenones in Brazilian children and their association to DNA damage

Bruno A. Rocha[a,b], Alexandros G. Asimakopoulos[b,c], Masato Honda[b], Nattane L. da Costa[d], Rommel M. Barbosa[d], Fernando Barbosa Jr[a], Kurunthachalam Kannan[b,e,*]

Human exposure to endocrine disrupting chemicals (EDCs) has received considerable attention over the last three decades. However, little is known about the influence of co-exposure to multiple EDCs on effect-biomarkers such as oxidative stress in Brazilian children. In this study, concentrations of 40 EDCs were determined in urine samples collected from 300 Brazilian children of ages 6–14 years and data were analyzed by advanced data mining techniques. Oxidative DNA damage was evaluated from the urinary concentrations of 8-hydroxy-2′-deoxyguanosine (8OHDG). Fourteen EDCs, including bisphenol A (BPA), methyl paraben (MeP), ethyl paraben (EtP), propyl paraben (PrP), 3,4-dihydroxy benzoic acid (3,4-DHB), methyl-protocatechuic acid (OH-MeP), ethyl-protocatechuic acid (OH-EtP), triclosan (TCS), triclocarban (TCC), 2-hydroxy-4-methoxybenzophenone (BP3), 2,4-dihydroxybenzophenone (BP1), bisphenol A bis(2,3-dihydroxypropyl) glycidyl ether (BADGE·2H_2O), 2,4-dichlorophenol (2,4-DCP), and 2,5-dichlorophenol (2,5-DCP) were found in > 50% of the urine samples analyzed. The highest geometric mean concentrations were found for MeP (43.1 ng/mL), PrP (3.12 ng/mL), 3,4-DHB (42.2 ng/mL), TCS (8.26 ng/mL), BP3 (3.71 ng/mL), and BP1 (4.85 ng/mL), and exposures to most of which were associated with personal care product (PCP) use. Statistically significant associations were found between urinary concentrations of 8OHDG and BPA, MeP, 3,4-DHB, OH-MeP, OH-EtP, TCS, BP3, 2,4-DCP, and 2,5-DCP. After clustering the data on the basis of i) 14 EDCs (exposure levels), ii) demography (age, gender and geographic location), and iii) 8OHDG (effect), two distinct clusters of samples were identified. 8OHDG concentration was the most critical parameter that differentiated the two clusters, followed by OH-EtP. When 8OHDG was removed from the dataset, predictability of exposure variables increased in the order of: OH-EtP > OH-MeP > 3,4-DHB > BPA > 2,4-DCP > MeP > TCS > EtP > BP1 > 2,5-DCP. Our results showed that co-exposure to OH-EtP, OH-MeP, 3,4-DHB, BPA, 2,4-DCP, MeP, TCS, EtP, BP1, and 2,5-DCP was associated with DNA damage in children. This is the first study to report exposure of Brazilian children to a wide range of EDCs and the data mining approach further strengthened our findings of chemical co-exposures and biomarkers of effect.

Table 1
Unadjusted urinary concentrations and detection rates of various endocrine disrupting chemicals (EDC) including bisphenols, chlorophenols, parabens and benzophenones (ng/mL) in Brazilian children.

Abbreviation	Name	Chemical name	DR%[a]	GM[b]	50th	Minimum[c]	Maximum[c]
BPA	Bisphenol A	2,2-Bis(4-hydroxyphenyl)propane	98	1.74	1.66	0.30	35.9
BPS	Bisphenol S	4,4′-Sulfonyldiphenol	23	nc	< LOD	0.06	22.6
BPAP	Bisphenol AP	4,4′-(1-Phenylethylidene)bisphenol	5	nc	< LOD	0.20	1.88
BPB	Bisphenol B	2,2-Bis(4-hydroxyphenyl)butane	3	nc	< LOD	0.09	3.42
BPP	Bisphenol P	4,4′-(1,4-Phenylenediisopropylidene)bisphenol	16	nc	< LOD	0.09	1.28
BPF	Bisphenol F	4,4′-Dihydroxydiphenylmethane	9	nc	< LOD	0.56	8.33
BPAF	Bisphenol AF	4,4′-(Hexafluoroisopropylidene)-diphenol	1	nc	< LOD	0.45	1.53
BPZ	Bisphenol Z	4,4′-Cyclohexylidenebisphenol	0.3	nc	< LOD	3.67	3.67
BPM	Bisphenol M	4,4′-(1,3-Phenylenediisopropylidene)bisphenol	0	nd	nd	nd	nd
BADGE	–	Bisphenol A diglycidyl ether	20	nc	< LOD	0.10	4.76
BADGE.2H_2O	–	Bisphenol A bis(2,3-dihydroxypropyl) glycidyl ether	57	0.30	0.24	0.10	33.8
BADGE.H_2O	–	Bisphenol A (2,3-dihydroxypropyl) glycidyl ether	14	nc	< LOD	0.10	2.03
BADGE.H_2O·HCl	–	Bisphenol A (3-chloro-2-hydroxypropyl) (2,3-dihydroxypropyl) glycidyl ether	8	nc	< LOD	0.05	1.26
BADGE.HCl	–	Bisphenol A (3-chloro-2-hydroxypropyl) glycidyl ether	1	nc	< LOD	0.10	0.49
BADGE.2HCl	–	Bisphenol A bis(3-chloro-2-hydroxypropyl) glycidyl ether	7	nc	< LOD	0.48	1.31
BFDGE	–	Bisphenol F diglycidyl ether	0	nd	nd	nd	nd
BFDGE.2HCl	–	Bisphenol F bis(3-chloro-2-hydroxypropyl)glycidyl ether	0	nd	nd	nd	nd
BFDGE.2H_2O	–	Bisphenol F bis (2,3-dihydroxypropyl)glycidyl ether	0	nd	nd	nd	nd
3RNOGE	–	3-Ring Novolac glycidyl ether	0	nd	nd	nd	nd
4RNOGE	–	4-Ring Novolac glycidyl ether	0	nd	nd	nd	nd
MeP	Methyl-paraben	Methyl-paraben	100	43.1	38.8	0.20	10,647
EtP	Ethyl-paraben	Ethyl-paraben	83	0.19	0.32	0.003	185
PrP	Propyl-paraben	Propyl-paraben	97	3.12	2.68	0.03	3366
BuP	Butyl-paraben	Butyl-paraben	43	nc	< LOD	0.02	18.9
BzP	Benzyl-paraben	Benzyl-paraben	27	nc	< LOD	0.01	1.01
HeP	Heptyl-paraben	Heptyl-paraben	14	nc	< LOD	0.004	1.01
3,4-DHB	–	3,4-Dihydroxy benzoic acid	76	8.24	28.8	10.0	515
OH-MeP	–	Methyl-protocatechuic acid	100	2.17	2.16	0.07	72.6
OH-EtP	–	Ethyl-protocatechuic acid	71	0.22	0.23	0.05	7.28
TCS	Triclosan	5-Chloro-2-(2,4-dichlorophenoxy)phenol	90	8.26	14.0	0.02	874
TCC	Triclocarban	1-(4-Chlorophenyl)-3-(3,4-dichlorophenyl)urea	70	0.02	0.02	0.004	0.94
BP3	Benzophenone-3	2-Hydroxy-4-methoxybenzophenone	100	3.71	2.99	0.70	983
BP1	Benzophenone-1	2,4-Dihydroxybenzophenone	95	4.85	5.86	0.01	1910
BP8	Benzophenone-8	2,2′-Dihydroxy-4-methoxybenzophenone	29	nc	< LOD	0.01	2.69
BP2	Benzophenone-2	2,2′,4,4′-Tetrahydroxybenzophenone	8	nc	< LOD	0.25	8.25
4-OHBP	–	4-Hydroxybenzophenone	38	nc	< LOD	0.02	2.92
2,4-DCP	Dichlorophenol	2,4-Dichlorophenol	99	2.60	2.47	0.35	56.7
2,5-DCP	Dichlorophenol	2,5-Dichlorophenol	99	4.59	3.19	0.080	810
2,4,5-TCP	Trichlorophenol	2,4,5-Trichlorophenol	16	nc	< LOD	0.084	10.1
2,4,6-TCP	Trichlorophenol	2,4,6-Trichlorophenol	42	nc	< LOD	0.021	4.58

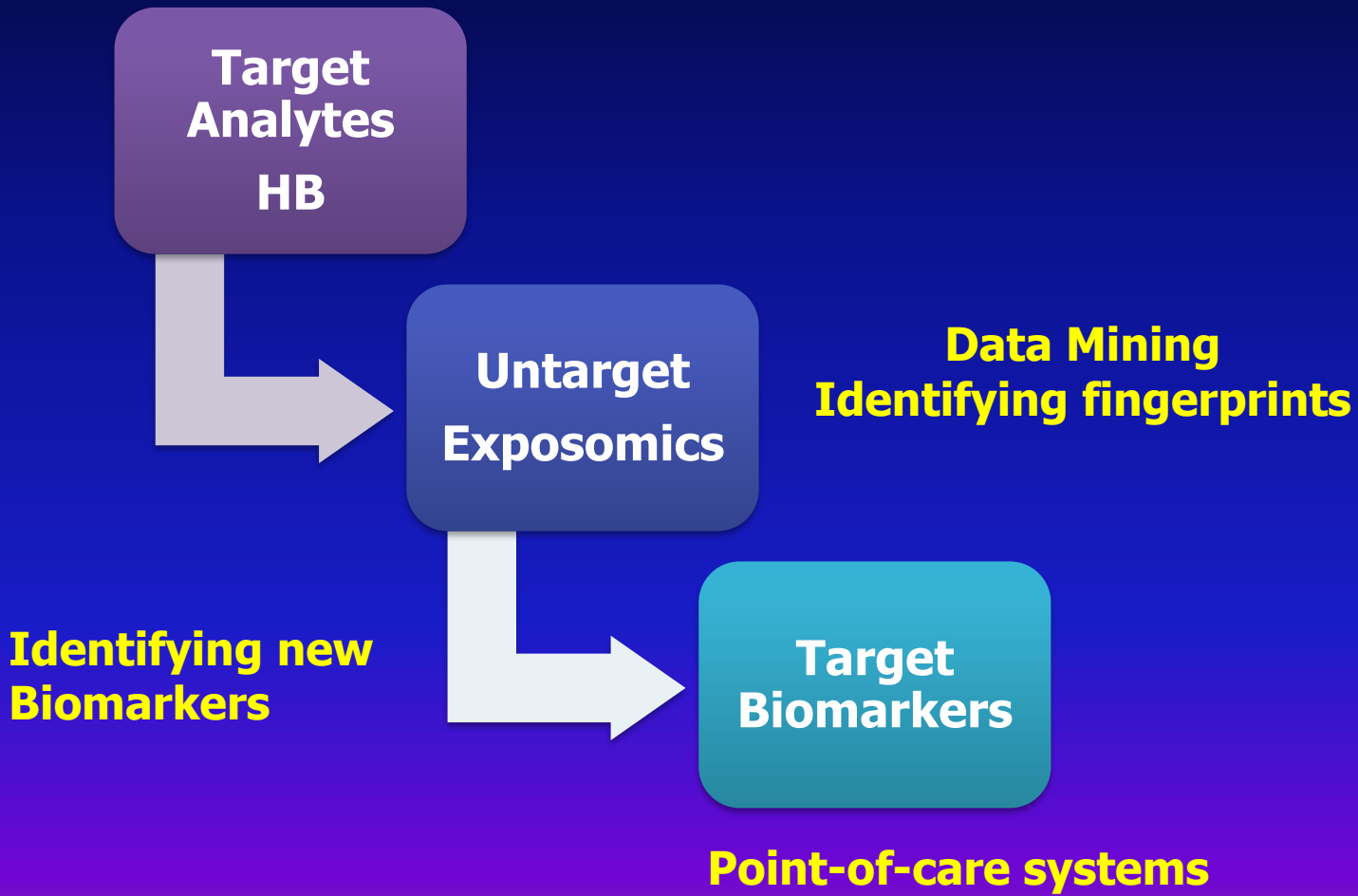
Abbreviations:

[a] DR%, detection rate in percentage.

[b] GM, geometric mean (nc: not calculated; GMs were calculated only for analytes with detection rate higher than 50%); nd = not detected

[c] Minimum/maximum detected among positive samples.

TRENDS


Target Analytes
HB
Untarget
Exposomics
Target Biomarkers
Data Mining
Identifying fingerprints
Identifying new Biomarkers
Point-of-care systems

Biosensors and point-of-care (POC) systems
(For personalized and constant monitoring)

ChemPubSoc Europe
DOI: 10.1002/celc.201600758
CHEMELECTROCHEM Reviews

Special Issue

Electrochemical Biosensors in Point-of-Care Devices: Recent Advances and Future Trends

Everson T. S. G. da Silva,[a] Dênio E. P. Souto,[a] José T. C. Barragan,[a] Juliana de F. Giarola,[a] Ana C. M. de Moraes,[a] and Lauro T. Kubota*[a]

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CHEMELECTROCHEM Reviews

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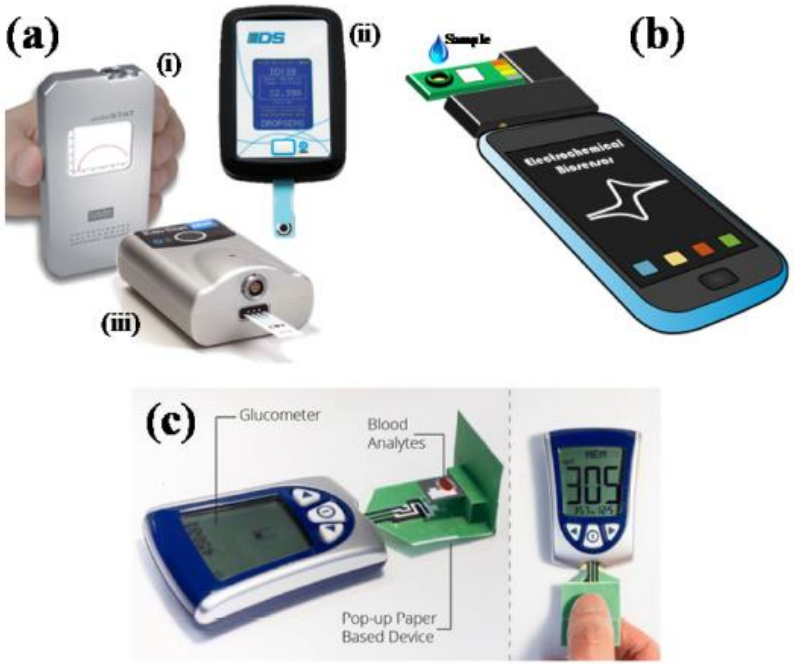


Figure 1. Portable electrochemical readers that can be employed in electrochemical biosensing. A) Commercially available pocket-sized potentiostats: i) PocketStat (from IVIUM Technologies®); ii) DropStat (from DropSens®), and iii) EmStat (from PalmSens®). B) Smartphone-based potentiostats (designed based on ref. [16]). C) Conventional glucometer adapted for other electrochemical biosensing applications (reprinted from ref. [17] with permission; copyright (2016) American Chemical Society).

Commercial POC-Systems Markers of Heart Attack Roche- COBAS h232

Benefits

The ideal fit for "on-the-spot care and share" in pre-hospital settings and emergency rooms settings

Fast

On-the-spot results are available in 3 steps and 12 minutes or less[1,2,3,4,5]

Portable

Handheld point of care system is lightweight and easy to use, even in mobile situation[6]

Connected

Wireless technology ensures immediate availability of results at all Points of Care (requires **cobas**® POC IT solution)[6]

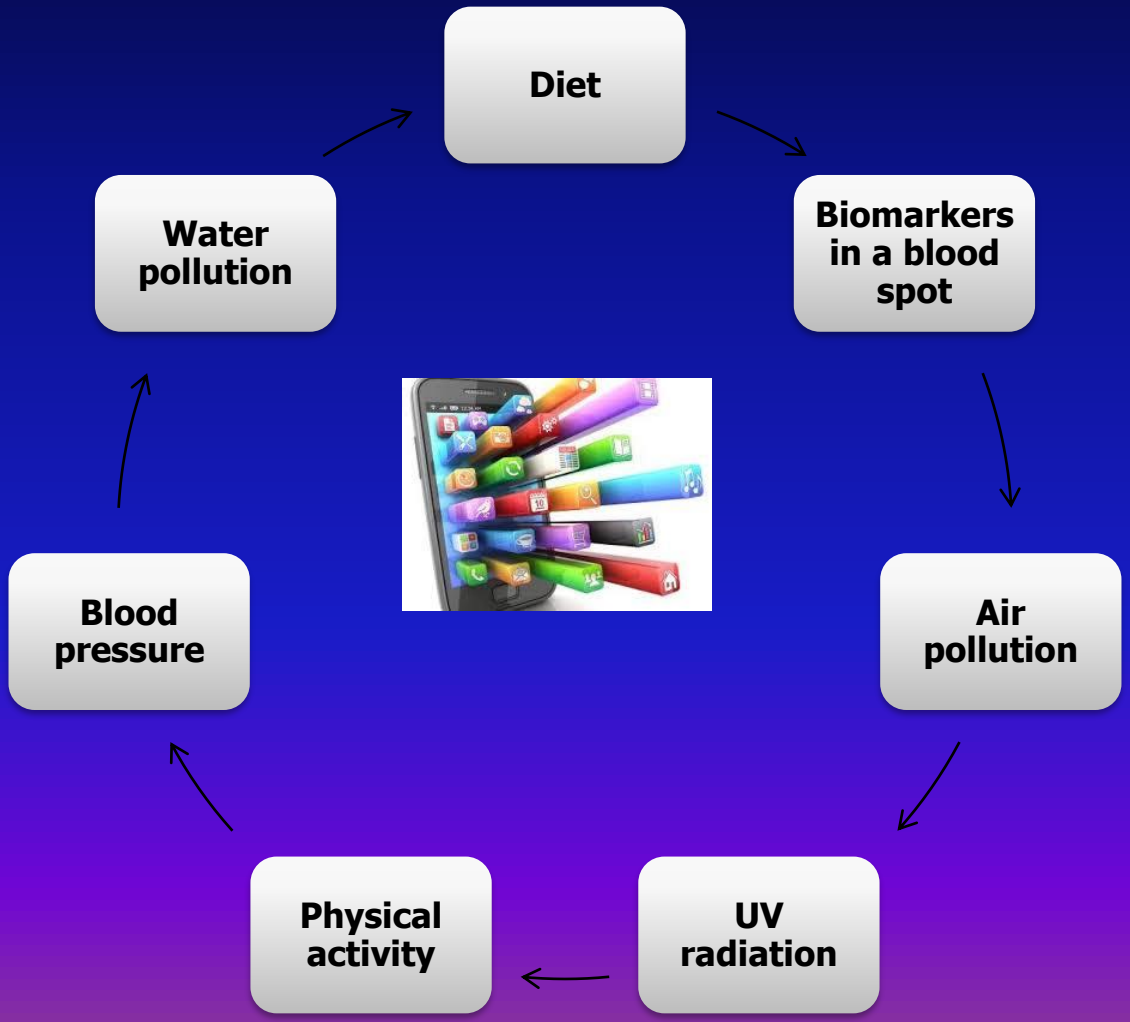
Confident

Accurate results, standardized with Roche central laboratory tests[7]

Roche COBAS h232

TEST	MEASURING RANGE	TIME TO RESULT	CLINICAL UTILITY
Troponin	40 – 2,000 ng/L	12 min	Identification of patients with suspected acute myocardial infarction at high risk of mortality[4]
NT-proBNP	60 – 9,000 pg/mL	12 min	Aid in diagnosis of patients with suspected heart failure, in monitoring of patients with compensated left ventricular dysfunction and in risk of stratification of patients with acute coronary syndromes[5]
CK-MB	1.0 – 40 ng/mL	12 min	Support the diagnosis of acute coronary syndrome and myocardial infarction, assessment of re-infarction[1]
D-Dimer	0.1 - 4.0 µg/mL	8 min	Exclusion of deep vein thrombosis and pulmonary embolism[2]
Myoglobin	30 – 700 ng/mL	8 min	Early marker of myocardial damage to assist diagnosis of acute coronary syndrome and myocardial infarction[3]

Exposomic Perspective: ERA of the Smart-Health (Telehealth) and IT: Everything in a smart-phone



Acknowledgments

Acknowledgments

Thank you for your attention!!!

Despite the powerful nature of biomonitoring (Wilhelm et al. 2004), the utility and interpretation of the data are controversial. The controversy stems in part from the fact that the pace at which biomonitoring data are being generated has eclipsed the development of basic epidemiology, toxicology, and exposure-assessment techniques that are needed to evaluate

HB-Limitations

Traditional biomonitoring for determination of exposure	
Advantages	Disadvantages
• Well-established and reliable methods for both long-lived (biologically persistent) chemicals and short-lived chemicals with continuous exposures • Highly selective methods • Provides accurate and precise measurements of biologically persistent chemicals • Often targets known chemicals of toxicologic importance • Reference data exist for most chemicals • Targeted approach allows specific hypotheses of well-documented chemicals to be studied	• Limited to a select group of known chemicals (~ 250) • Studies such as NHANES do not take continuous measures, thereby limiting detection of short-lived chemicals • Suspected chemicals of concern are less likely to be captured • Time-intensive methods development and validation • Chemicals added for monitoring not always the most important from a toxicologic perspective • Analyses are expensive and time-consuming • Few laboratories with expanded capabilities • Multiple methods required for a large suite of chemicals • Typically requires 500–2,000 µL of blood or other biospecimens for each chemical analyzed

Exposomic approaches

Exposomic approaches for determination of exposure	
Advantages	Disadvantages
• Agnostic approaches are encouraged for detection of emerging exposures of concern • Techniques (and development of techniques) promote identification of unknown/emerging exposures of concern • Links exogenous exposures to internal biochemical perturbations • A large number of features can be detected (> 10,000) for the cost of a single traditional biomonitoring analysis • Includes biomolecular reaction products (e.g., protein adducts, DNA adducts) for which traditional biomonitoring measurements are often lacking or cumbersome • Requires a small amount of biologic specimen (~ 100 µL or less) for full-suite analysis • Enables detection of "features" that are linked to exposure or disease for further confirmation • Encourages techniques to capture short-lived chemicals • Aims to measure biologically meaningful lifetime exposures, both exogenous and endogenous, of health relevance	• Agnostic approach can be problematic for grant funding • May not detect chemicals present at low levels • Cannot detect all analytes present in chemical space • A reference or baseline value may not be possible to define • Extensive bioinformatics required for data reduction/analysis • Requires carefully collected and well-maintained biospecimens • Can only measure chemicals that are isolated in extraction process (e.g., acetonitrile extraction would not necessarily capture lipophilic chemicals) • Relies heavily upon library searching of spectra for annotation with standard confirmation coming later, which can be quite time-consuming and labor-intensive • May be difficult to link measures to exposure source • Includes lifetime exposures but does not place enough emphasis on defining and measuring windows of susceptibility (e.g., *in utero*) to accurately capture the most biologically important exposures

Human biomonitoring

HBM Expert Panel-Germany

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New human biomonitoring methods for chemicals of concern—the German approach to enhance relevance

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The selection of substances is based on recommendations by a high-ranking panel of experts from science and research, industry and relevant public authorities.

Human biomonitoring

HBM Expert Panel-List of priorities

In that list the substances are classified in 13 groups: 1) Phthalates and substitutes; 2) Flame retardants; 3) Per-and polyfluorinated alkyl substances (PFAS); 4) Chemicals used in cosmetics; 5) (Musk) fragrances; 6) Allergenic substances; 7) (Phenol-)Benzothiazoles; 8) SVHC candidates (REACH Art. 57); 9) Aromatic amines; 10) Metals; 11) Nano particles; 12) Contaminants in food; 13) Others. Substance attribution to a group follows either its chemical constitution or use (e.g. Phthalates, including other plasticizers) or its potential health effect (Allergenic substances) depending on the main characteristics. The basic criteria for selection of substances besides their toxicology are their good or very good bioavailability (health relevance), a high likelihood of consumer exposure (consumer relevance) and non-existence or unsuitability of an existing HBM-method (for mother compound or metabolites).

Human biomonitoring and Analytical Methods

HB Expert Panel-List of priorities

The burden of major industrial chemicals on the population can be appraised precisely only when analytical methods are in place for the largest possible number of chemical substances.

Every year new substances are selected for which HB detection methods are to be developed for the first time.

It is planned to have analytical methods available by 2020 for more than 40 of new selected substances