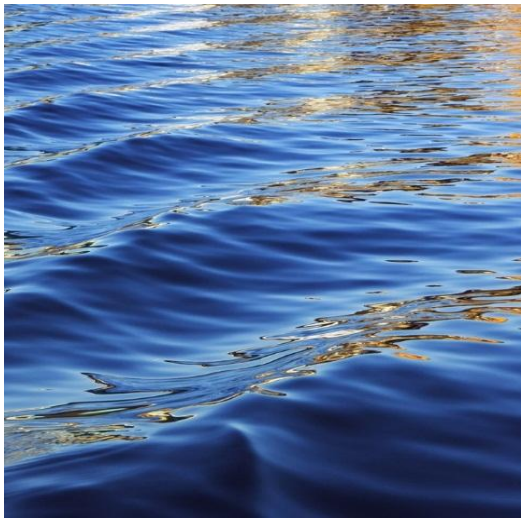
Innovative and Integrative Approaches for Advancing Public Health Protection through Water Infrastructure Sustainability

U.S. EPA Grant R834867

Michael J Plewa
Benito J Mariñas

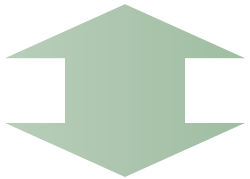
April 10, 2013



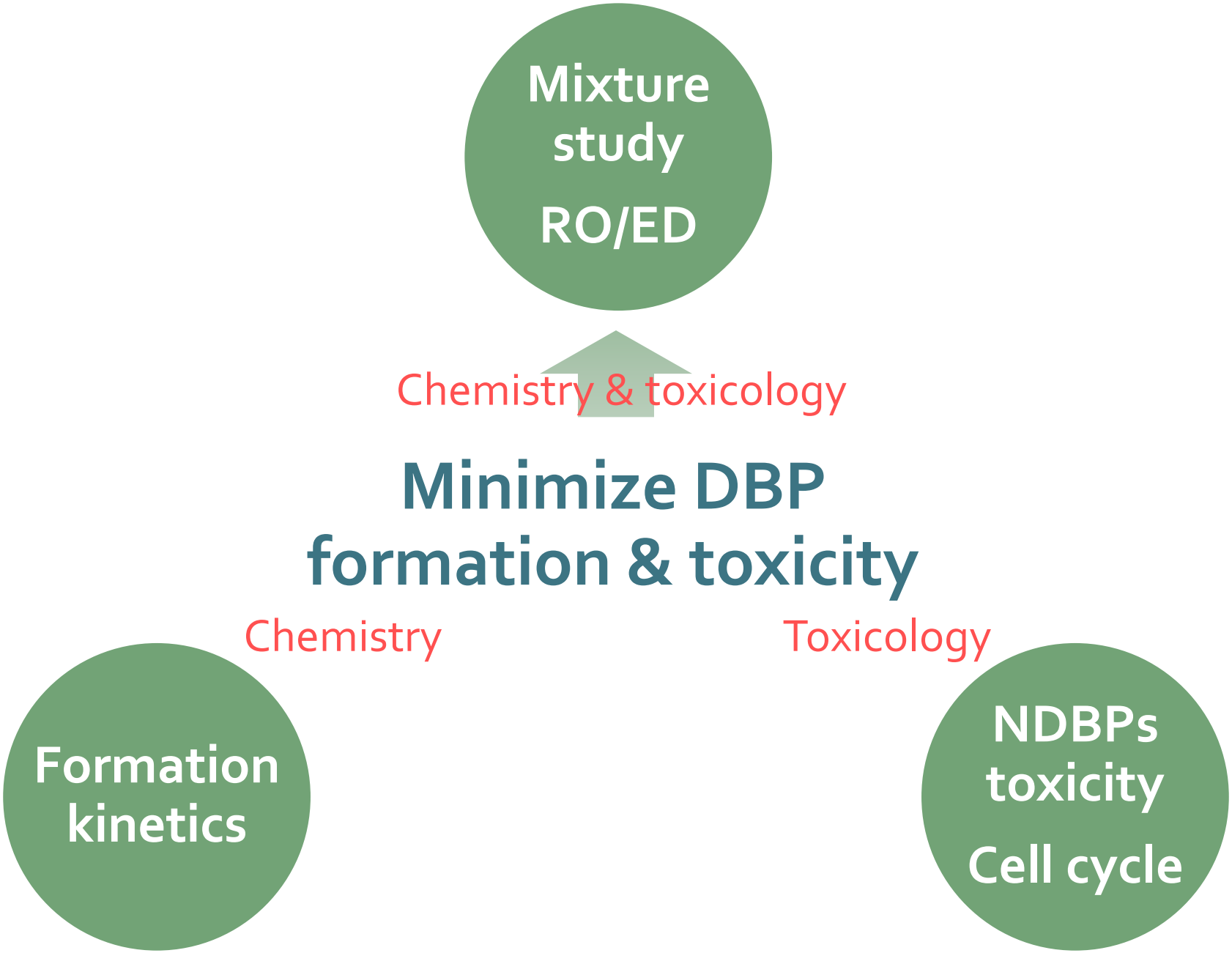
ILLINOIS
UNIVERSITY OF ILLINOIS AT URBANA-CHAMPAIGN

Rehabilitation for Distribution System

Advanced concepts for linking public health protection with water infrastructure sustainability



Minimize DBP formation and toxicity


Mixture study
RO/ED
Chemistry & toxicology
Minimize DBP formation & toxicity
Chemistry
Toxicology
Formation kinetics
NDBPs toxicity
Cell cycle

Understand DBP Chemistry and Toxicology

Mixture study using reverse osmosis/electrodialysis RO/ED:

Developed methods for concentrating representative DBPs from water samples.

Formation kinetics:

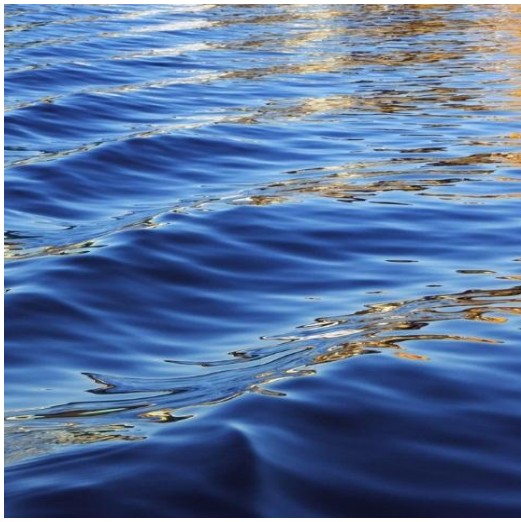
Understand the formation of haloacetonitriles and haloacetamides.

Toxicology:

Conduct quantitative comparative mammalian cell cytotoxicity and genotoxicity of NDBPs (haloacetonitriles, haloacet-amides). Toxicity of precursor haloacetaldehydes. Develop and use inhibition of cell cycle progression by DBPs as a genomic toxicity metric.

Water Processing for Mixture Study

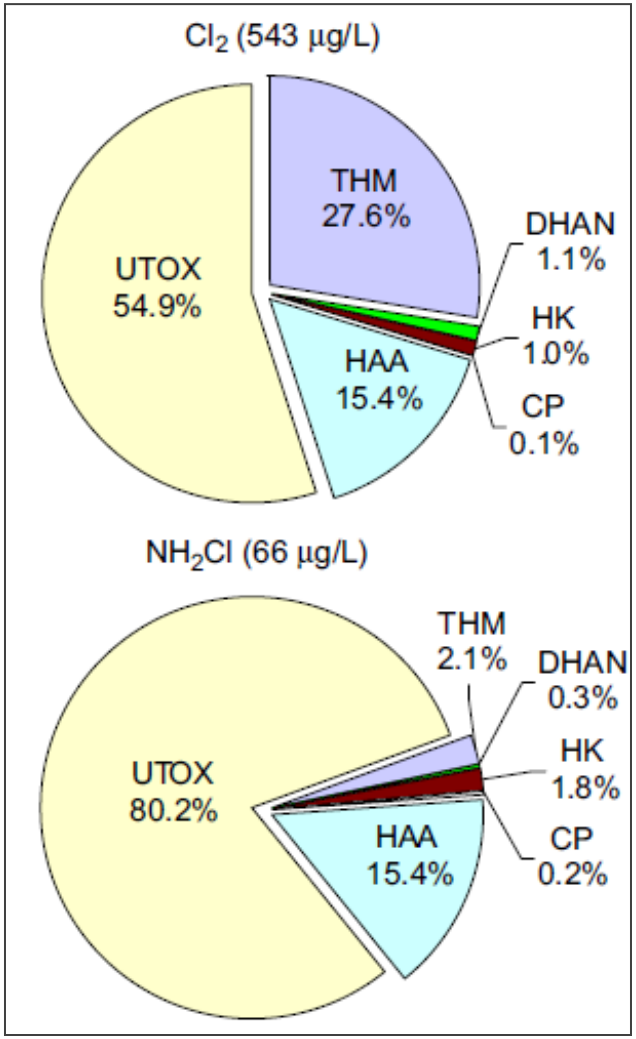
Reverse osmosis (RO)/Electrodialysis(ED)



Unknown TOX

- Over 600 DBPs have been identified.
- Most of the total organic halide (TOX) in drinking water is unknown.
- The analyses of single chemicals cannot capture the nature of complex DBP mixtures.
- Whole-mixture studies can detect:
  - Toxic effect of the unidentified fraction of TOX.
  - Possible interaction between DBPs.

Simmons, J. E. et al. *Environ. Health Perspect.* **2002,** *110*, (supplement 6), 1013-1024.

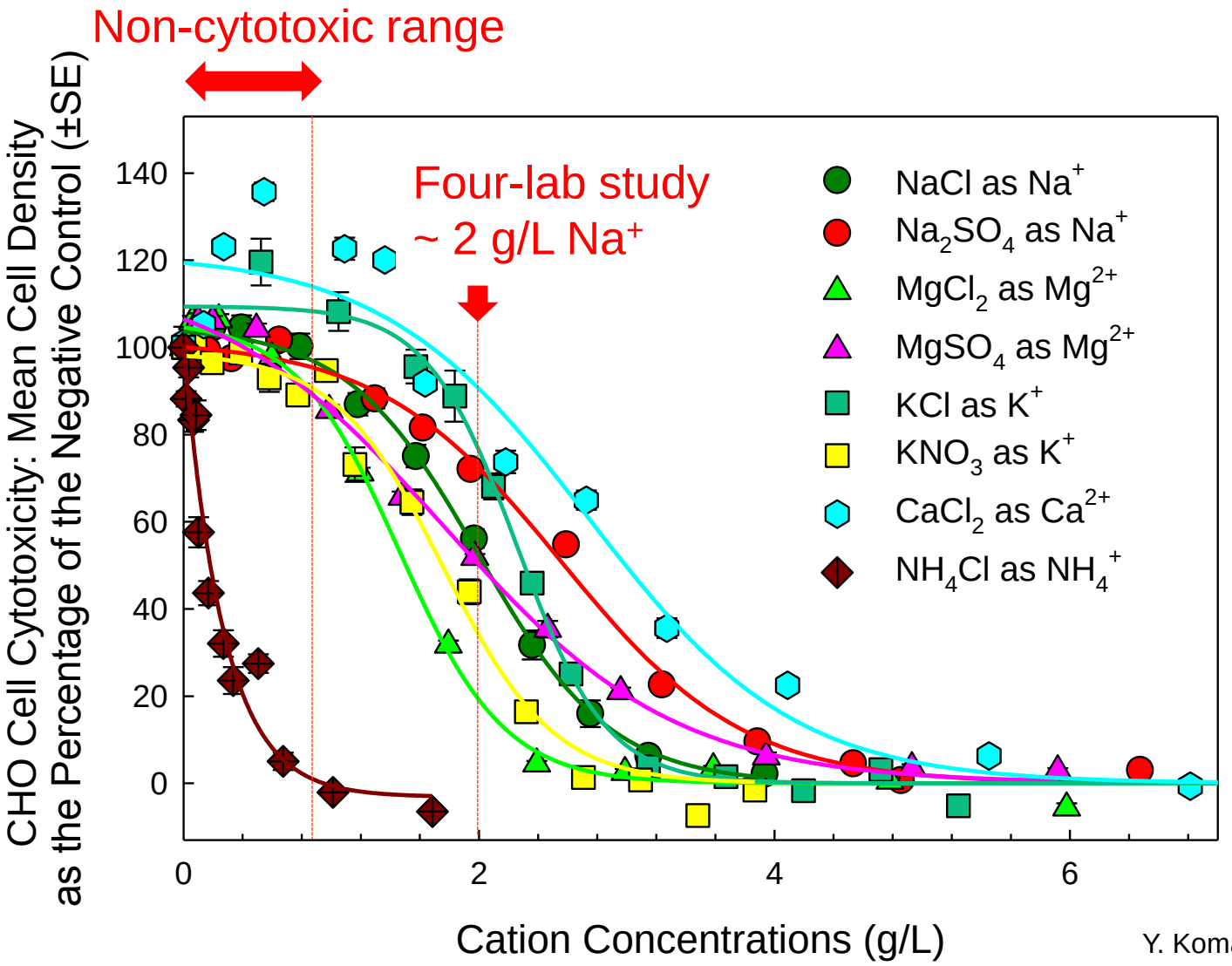


Hua & Reckhow, *Water Research*, **2007**, *41*, 1667-1678

Challenges for Mixture Studies

- Reverse osmosis (RO) membrane was used to concentrate DBP mixtures.
- Buildup of inorganics may impact toxicity analyses due to osmotic stress and other confounding factors.

Cytotoxic Level of Inorganic Salts



Y. Komaki, Ph.D. Research

Challenges to Generate Samples for Mixture Studies

- Inorganic buildup may lead to cytotoxic artifacts.
  - Salts need to be removed.

Reverse Osmosis and Electrodialysis

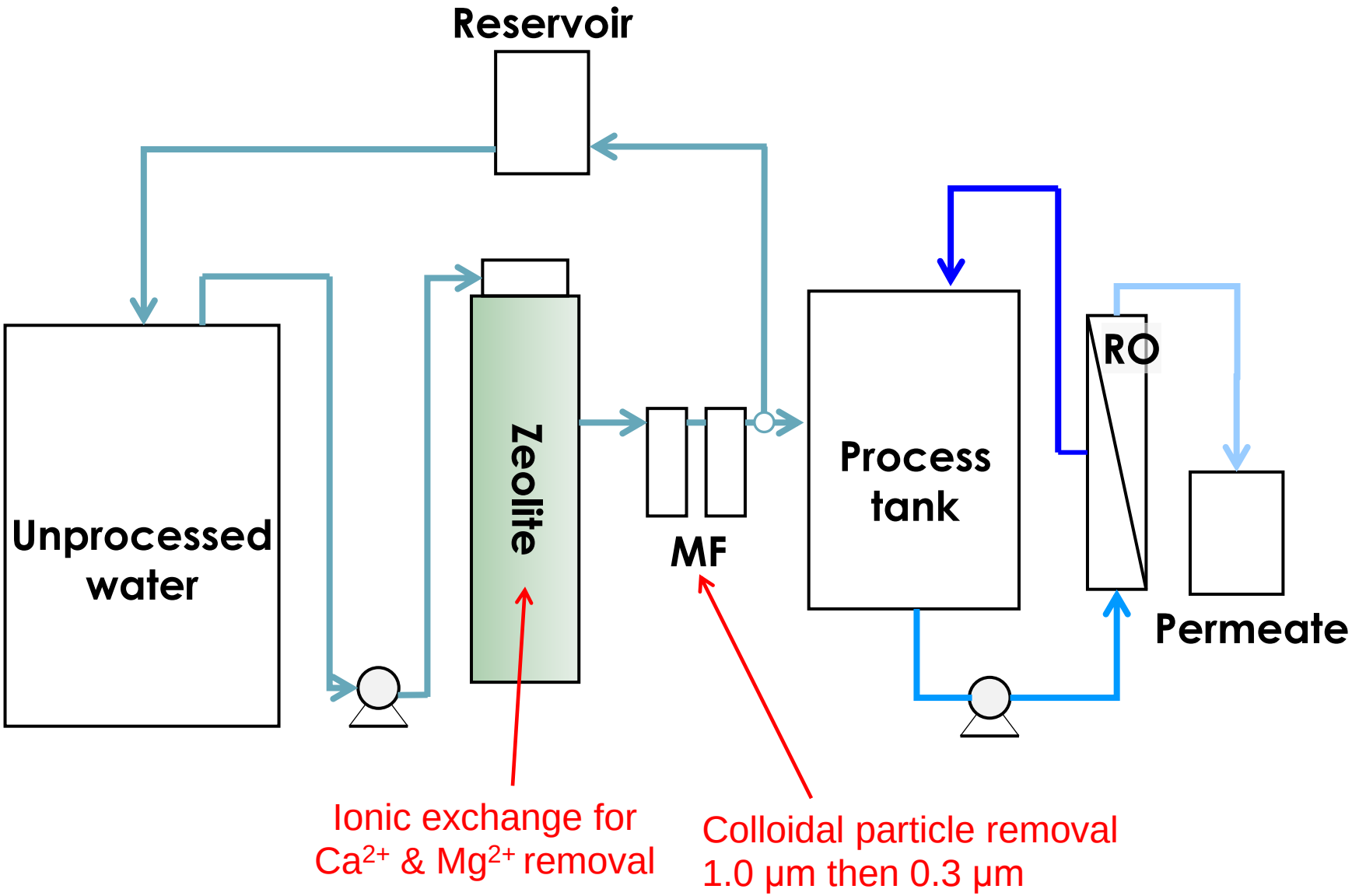
- RO/ED is a promising method to concentrate organic matter with minimum losses.
- We are developing a process that will concentrate DBPs without corresponding high salt levels for toxicity analyses.

RO/ED Process

1. RO phase: concentrate water sample
2. Simultaneous RO/ED phase: remove water from sample without generating excessive osmotic pressure
3. Final ED phase: remove salts from water sample

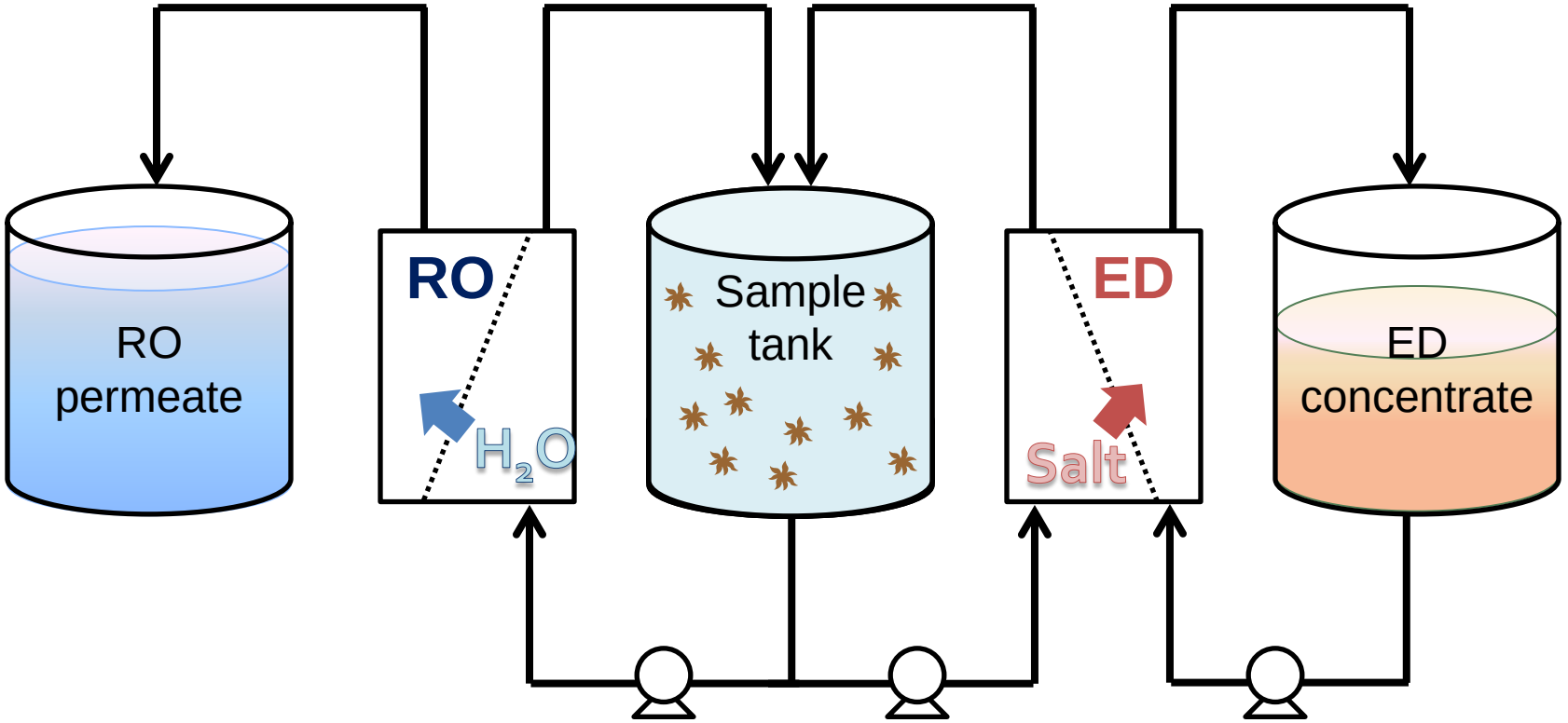
Large scale RO system is under development

RO Setup for NOM Concentration

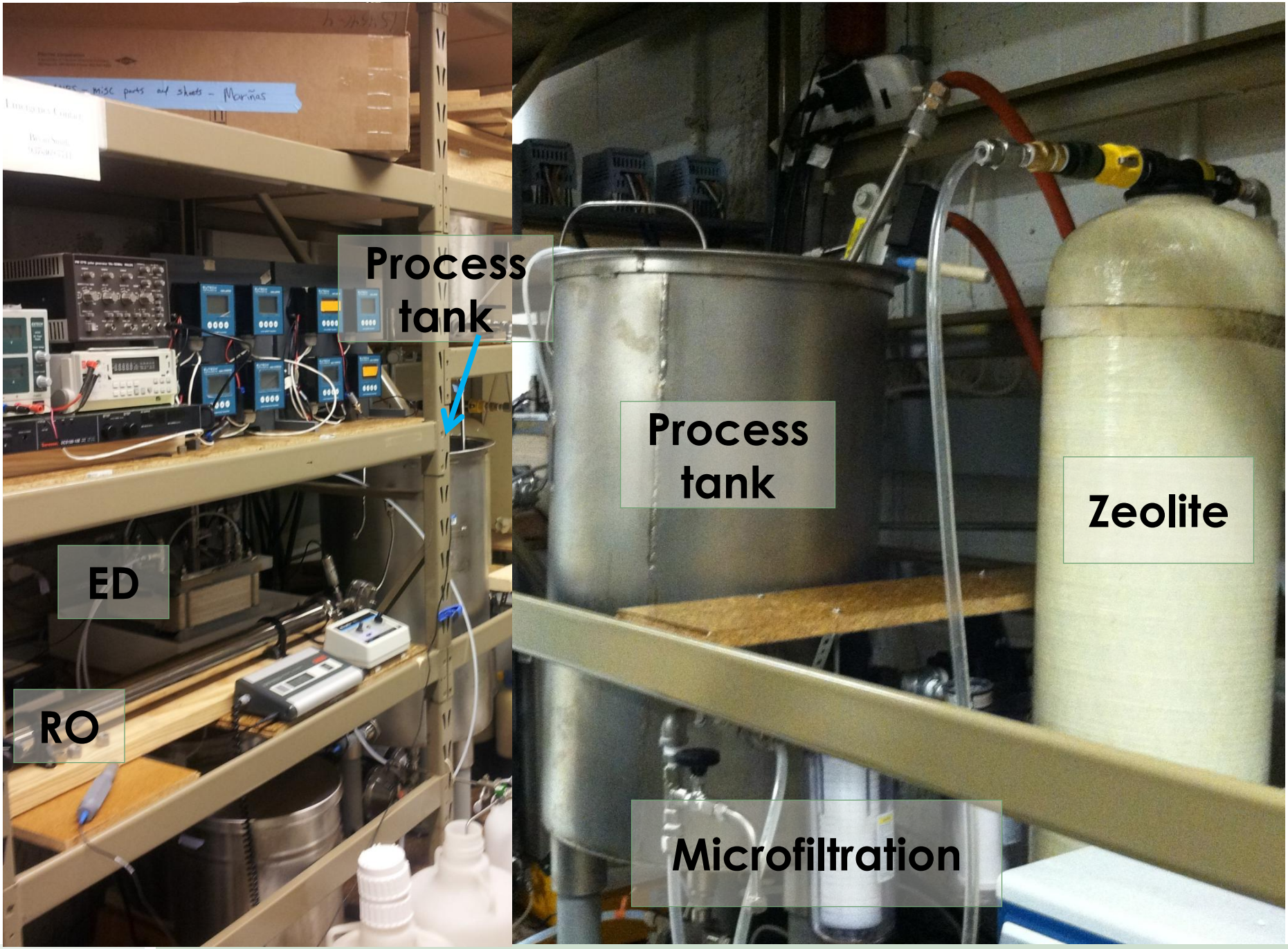


Combined RO/ED System

RO concentrate/retentate = ED diluate



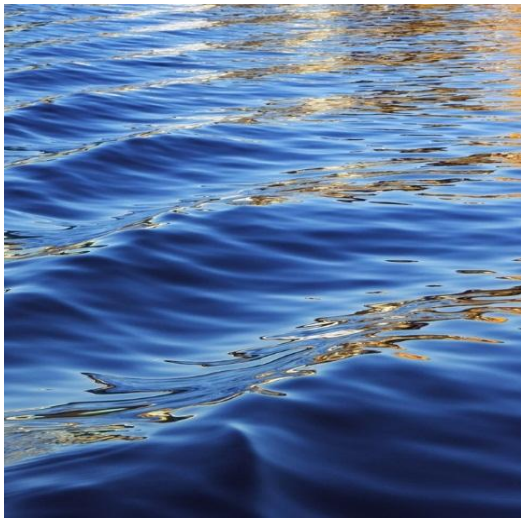
Adapted from Gurtler et al., *Journal of Membrane Science,* **2008**, *323*, 328-336


Process tank
ED
RO
Process tank
Zeolite
Microfiltration

Progress Status of Mixture Study

- This new RO/ED system will concentrate effluent from a surface water treatment plant.
- The RO/ED system will be compared to XAD extraction.
- High bromide and iodide water (0.5 mg/L Br^-+0.1 mg/L I^-) will be compared with low bromide and iodide water.
- TOCl, TOBr and TOI levels will be correlated with toxicity analyses.
- Analytical chemistry of DBP profiles will be correlated with mammalian cell cytotoxicity and genotoxicity data.

Haloacetonitrile and Haloacetamide Formation Kinetics



Origin of the Nitrogen in Haloacetamides and Haloacetonitriles: Organic Matter or NH_2Cl?

Suwanee River NOM
Leonardite HA
Elliot Soil HA
Pahokee Peat HA

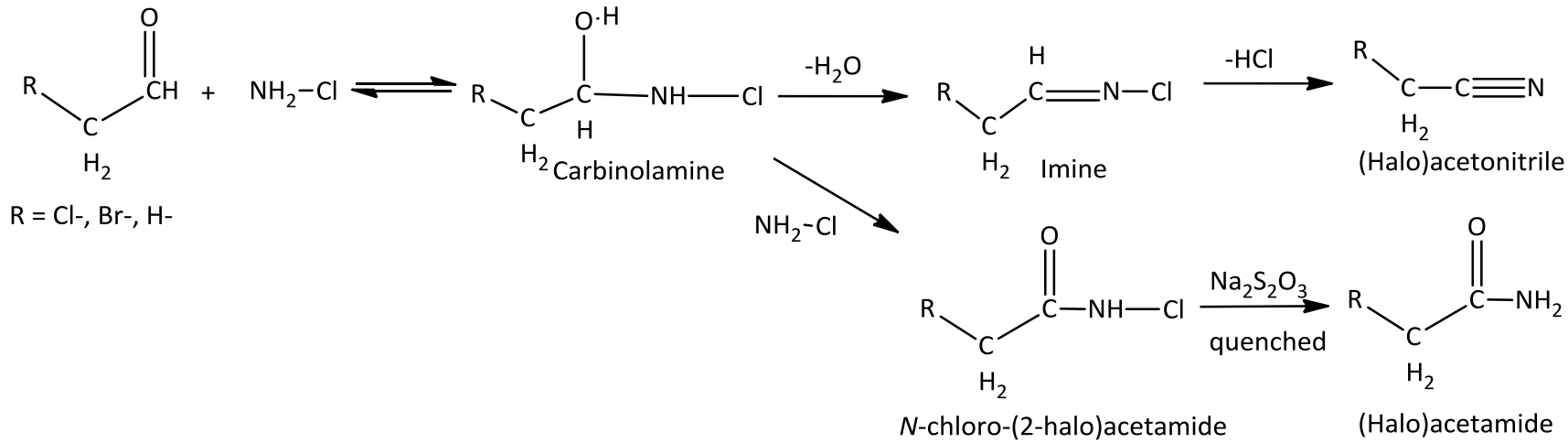
+ $^{15}NH_2Cl$

>70% of Haloacetamides and Haloacetonitriles Incorporated ^{15}N

Huang, et al. *ES&T*, 2012, 46, (19), 10624-10631
Yang, et al. *Water Research,* 2010, 44, (9), 2691-2702

New Results on the Chemistry of NDBP Formation

- Formation pathway of chloroacetonitrile and *N*,2-dichloroacetamide from chloramination of chloroacetaldehyde

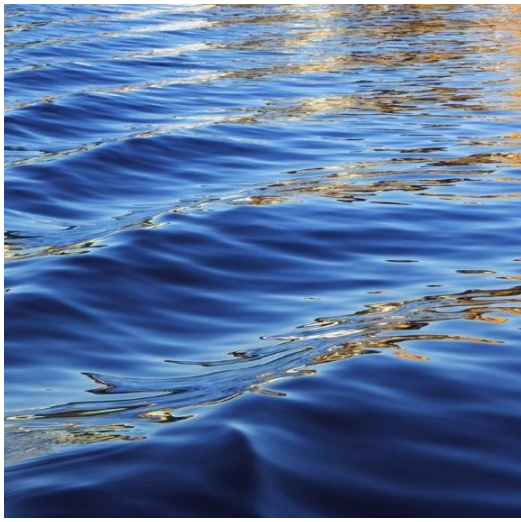


Formation of newly identified NDBP

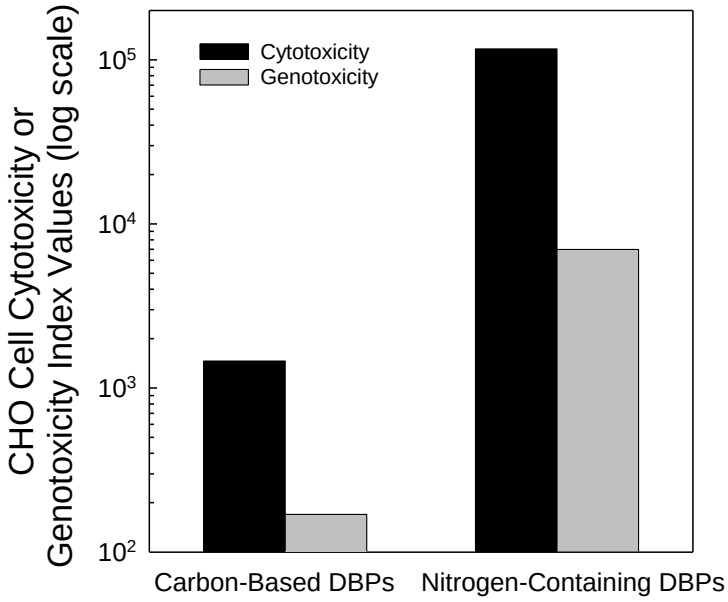
S. Kimura, Ph.D. Research

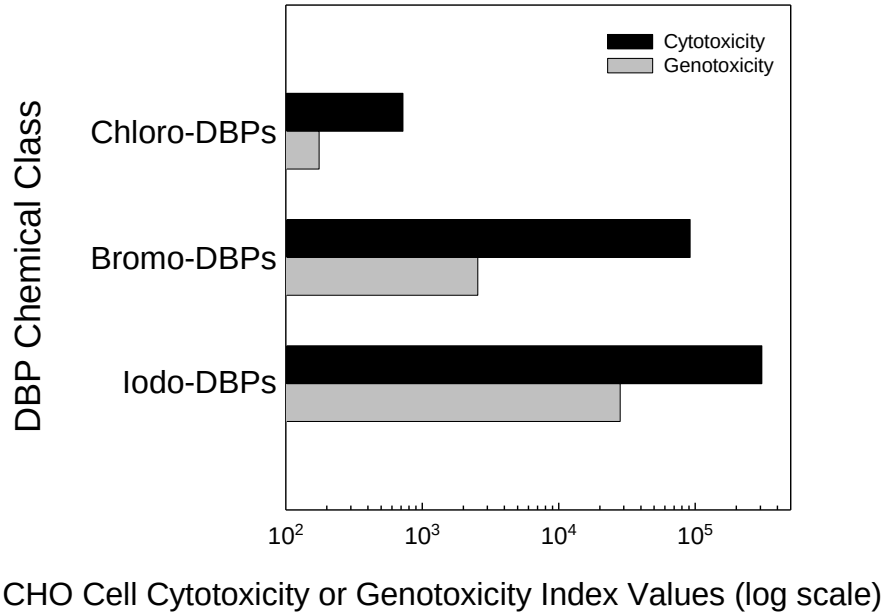
Mammalian Cell Cytotoxicity and Genotoxicity

Integration with HAN and HAcAm Toxicity



Comparative Cytotoxicity and Genotoxicity of NDBPs and IDBPs

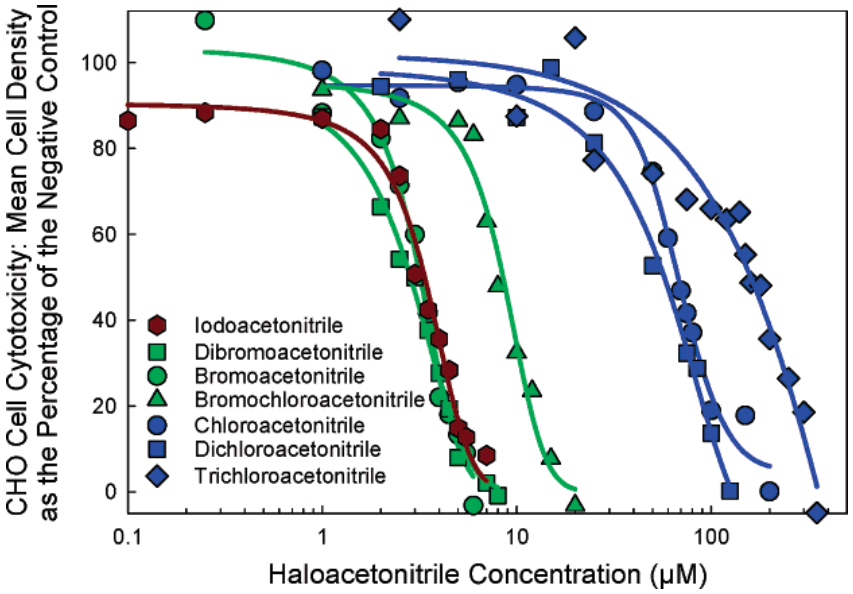


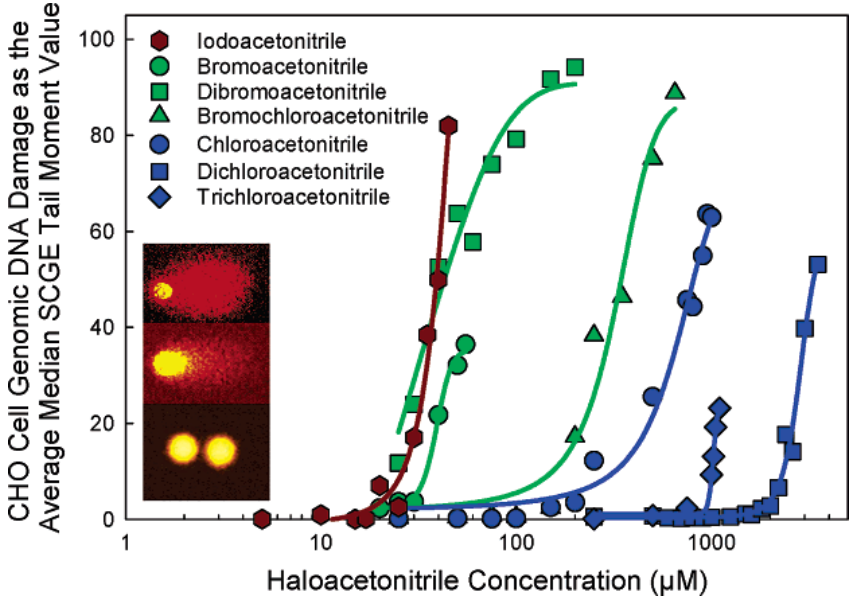


NDBPs are more toxic than CDBPs; Iodo-DBPs are more toxic than their Br^- and Cl^- analogues

Plewa, M. J.; Wagner, E. D., *Mammalian Cell Cytotoxicity and Genotoxicity of Disinfection By-Products*. Water Research Foundation: Denver, CO, 2009; p 134.

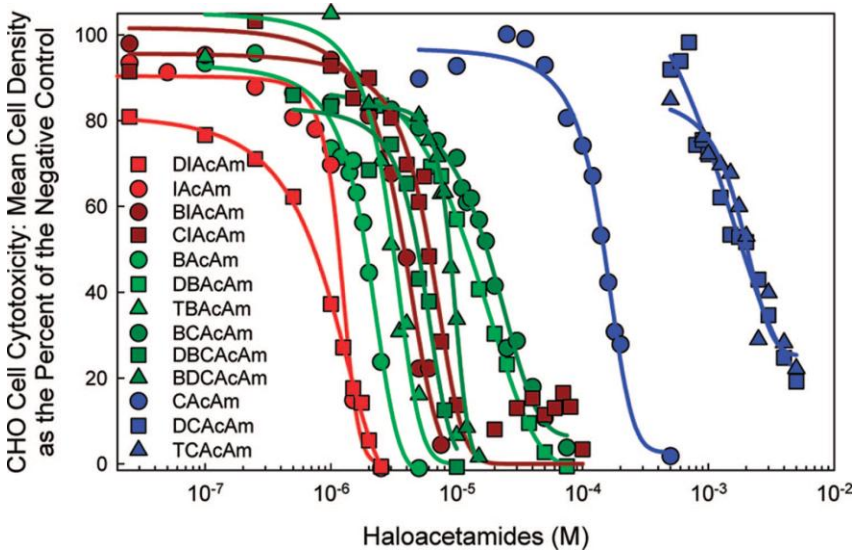
Mammalian Cell Cytotoxicity and Genotoxicity of Haloacetonitrile DBPs

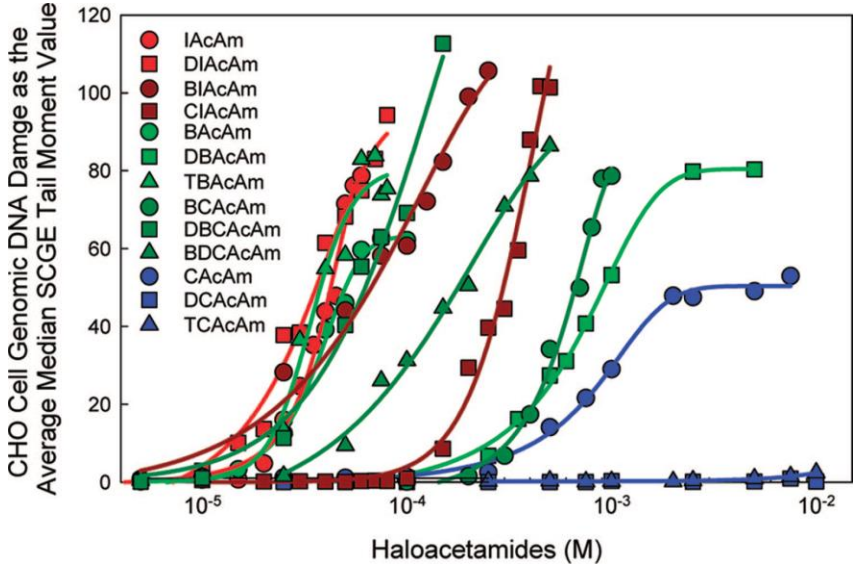




Muellner, M. G.; Wagner, E. D.; McCalla, K.; Richardson, S. D.; Woo, Y. T.; Plewa, M. J., Haloacetonitriles vs. regulated haloacetic acids: Are nitrogen containing DBPs more toxic? *Environ. Sci. Technol.* **2007,** *41*, (2), 645-651.

Mammalian Cell Cytotoxicity and Genotoxicity of Haloacetamide DBPs

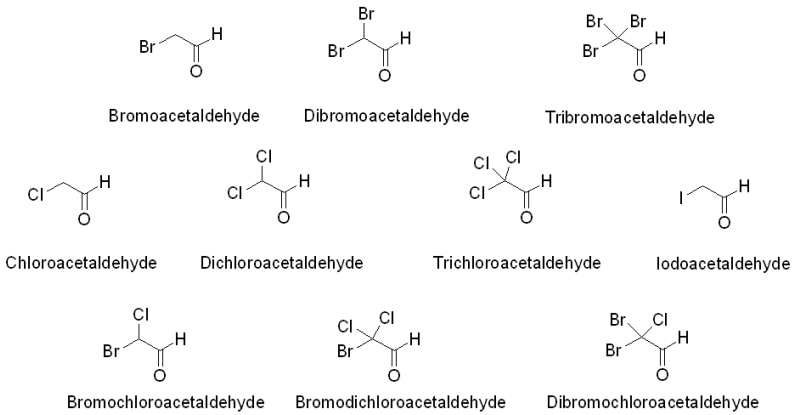


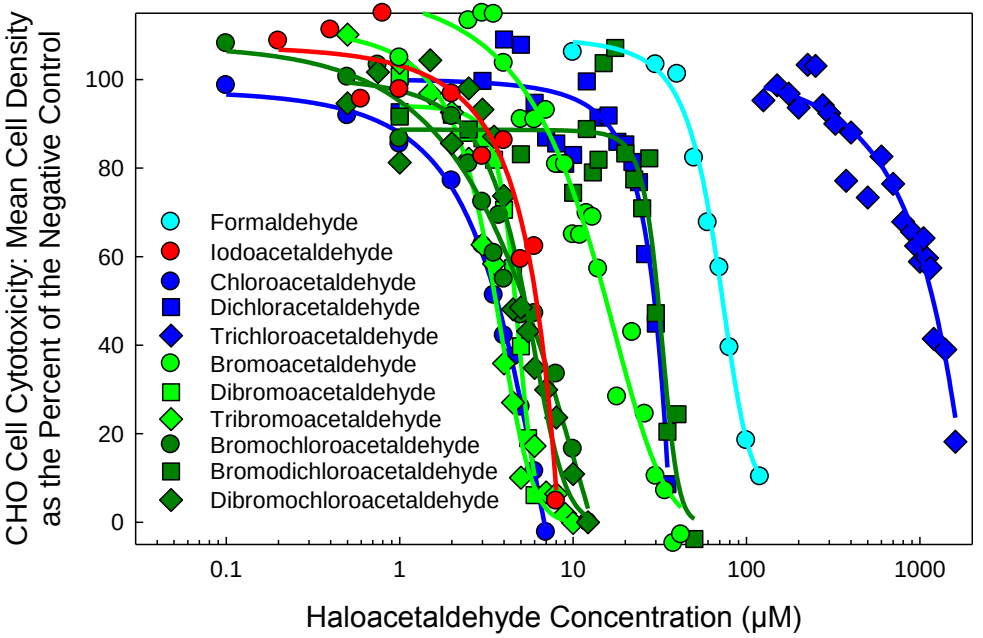


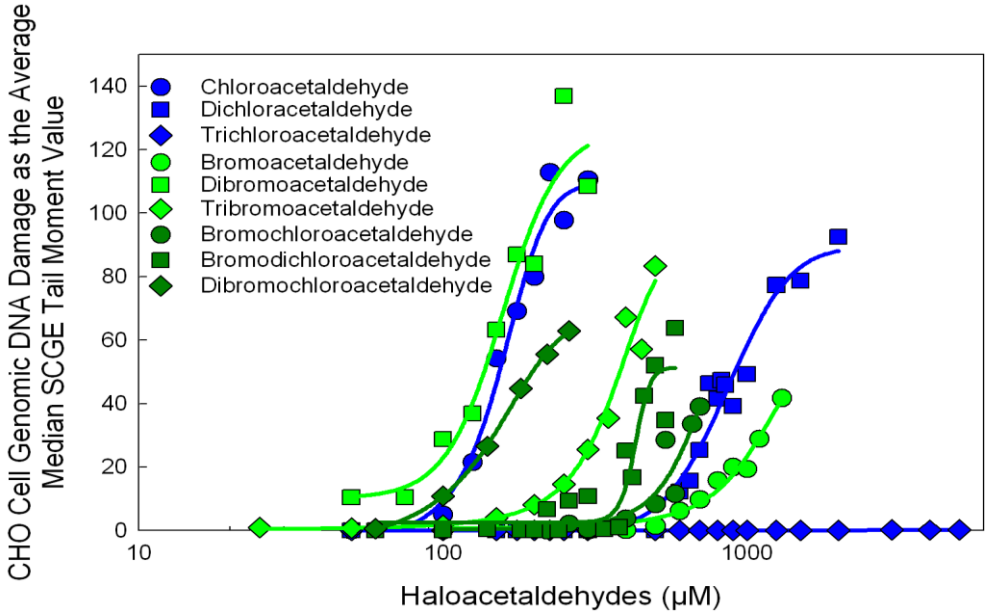
Plewa, M. J.; Muellner, M. G.; Richardson, S. D.; Fasano, F.; Buettner, K. M.; Woo, Y. T.; McKague, A. B.; Wagner, E. D., Occurrence, synthesis and mammalian cell cytotoxicity and genotoxicity of haloacetamides: An emerging class of nitrogenous drinking water disinfection by-products. *Environ. Sci. Technol.* **2008,** *42*, (3), 955-961.

Haloacetaldehydes (HALs)

- HALs are cytotoxic in mammalian cells and induce genotoxic damage including DNA-DNA crosslinks, or DNA-protein crosslinks.

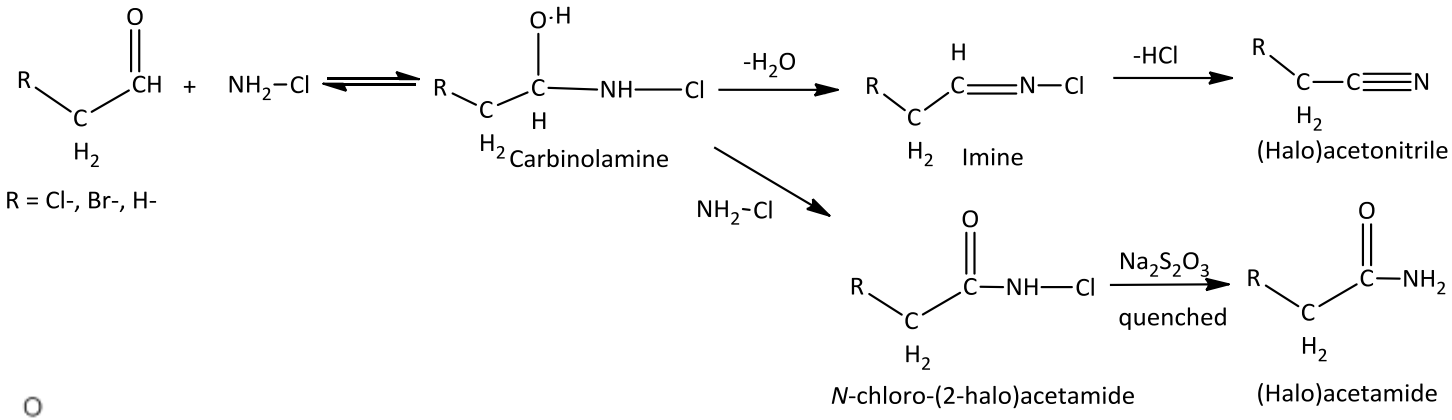


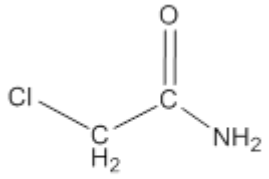




C. Jeong, Ph.D. Research

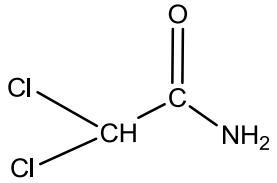
N-2-Dichloroacetamide is a New Toxic NDBP





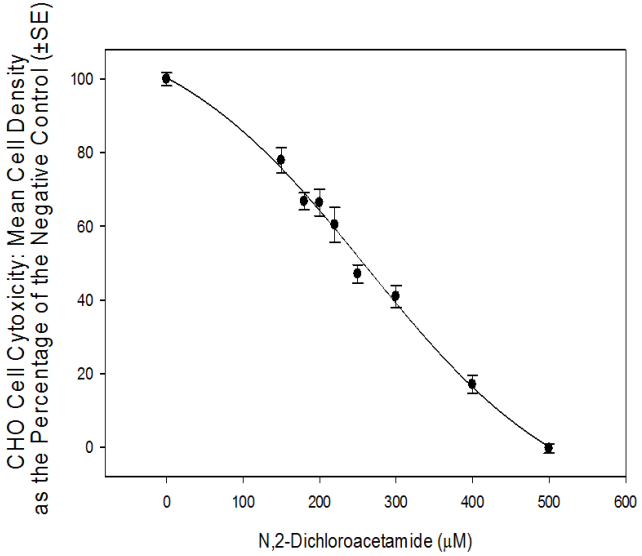
Chloroacetamide

LC_{50} = 148 µM



Dichloroacetamide

LC_{50} = 1.9 mM

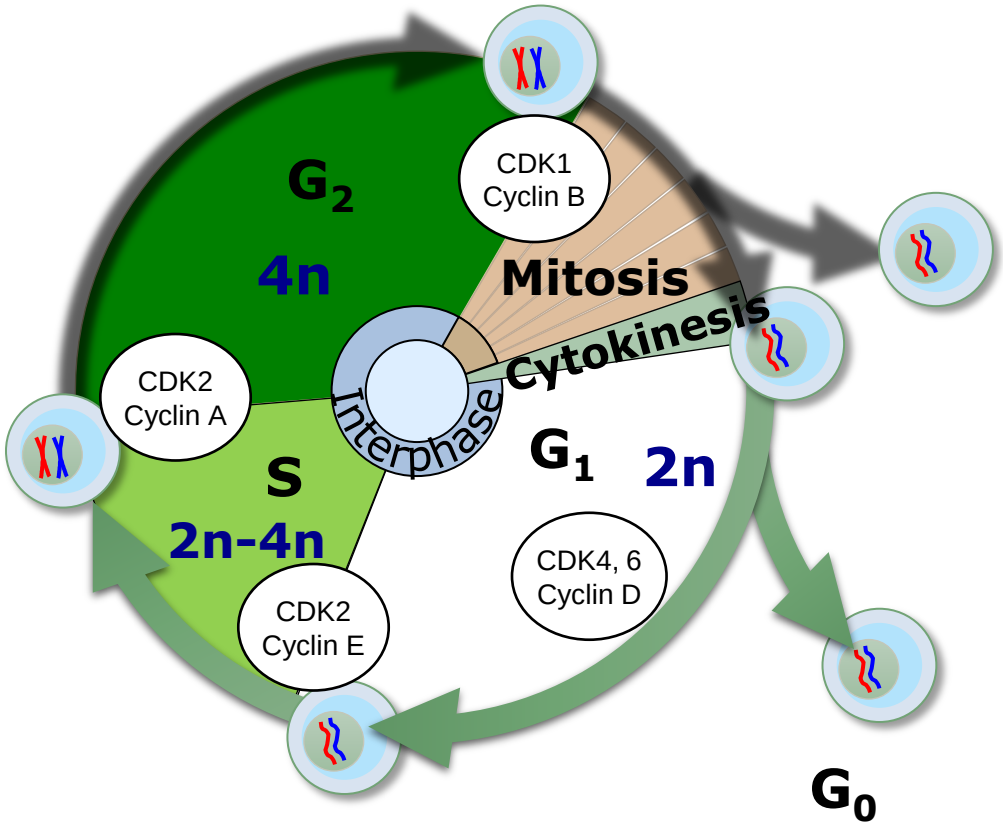


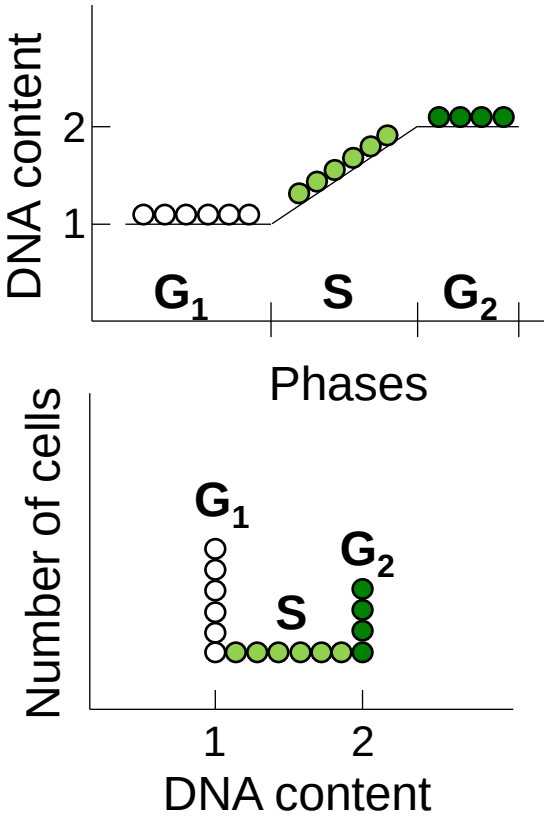
LC_{50} = 256 µM

S. Kimura, Ph.D. Research

Throughout the Cell Cycle the Genome is Monitored for Damage

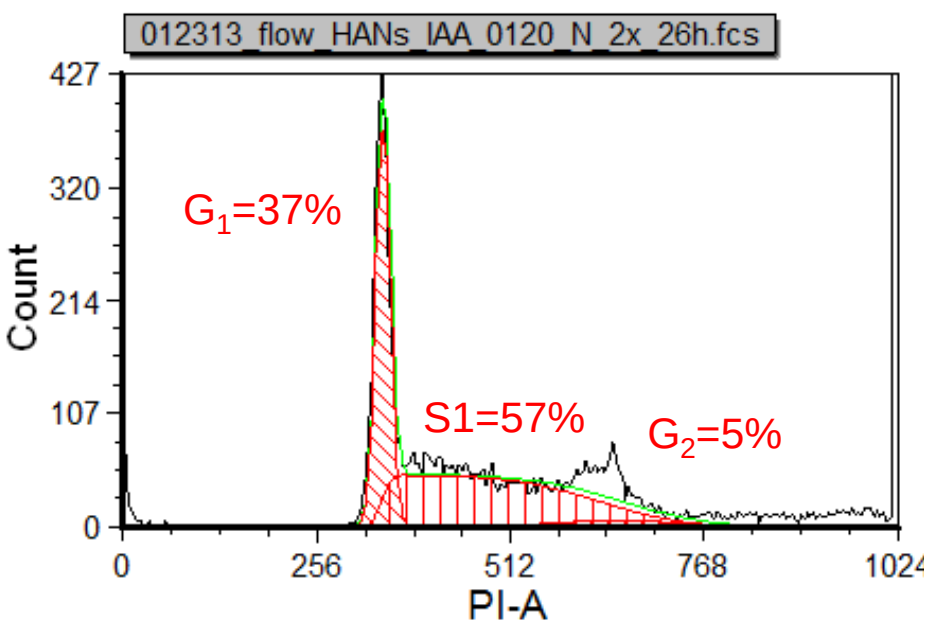
- Since each chromosome is duplicated during the S phase, cells in G_2 phase have double the amount of DNA than cells in G_1.
- Cyclin-dependent kinases (CDKs) and the cyclin proteins regulate progression through the stages of the cell cycle.



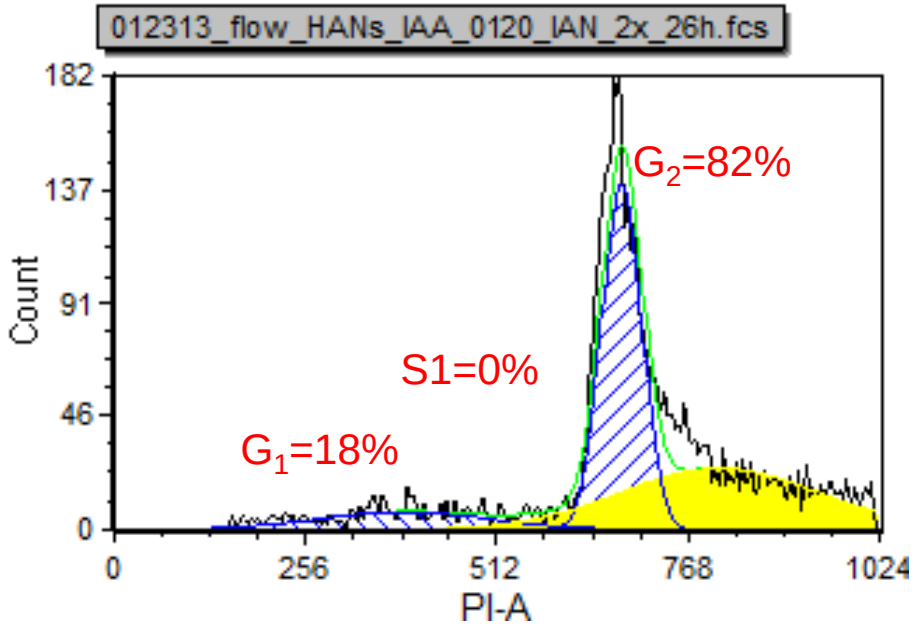


Haloacetonitriles Block the Cell Cycle

Negative control



Iodoacetonitrile 6 μM



Mode of action of NDBPs

Y. Komaki, Ph.D. Research

Summary of Toxicology

- Mammalian cell cytotoxicity and genotoxicity analyses of 10 haloacetaldehydes were completed and added to the comparative quantitative toxicity database.
- Molecular mechanisms of HAA toxicity were resolved.

  (Pals, J.; Ang, J.; Wagner, E. D.; Plewa, M. J., Biological mechanism for the toxicity of haloacetic acid drinking water disinfection byproducts. *Environ. Sci. Technol.* **2011,** *45*, 5791–5797.)

- Chloroacetonitrile, bromoacetonitrile, and iodoacetonitrile block the cell cycle at G_2. HAAs do not block the cell cycle.
- These results contribute to the understanding of the toxic mode of action of HAN DBPs.
- *N*-2-Dichloroacetamide is a new toxic NDBP.

Project Summary

Mixture study using RO/ED:

Large scale RO/ED system is under development.

Formation kinetics:

Formation pathway of chloroacetonitrile and chloroacetamide was identified.

Toxicology:

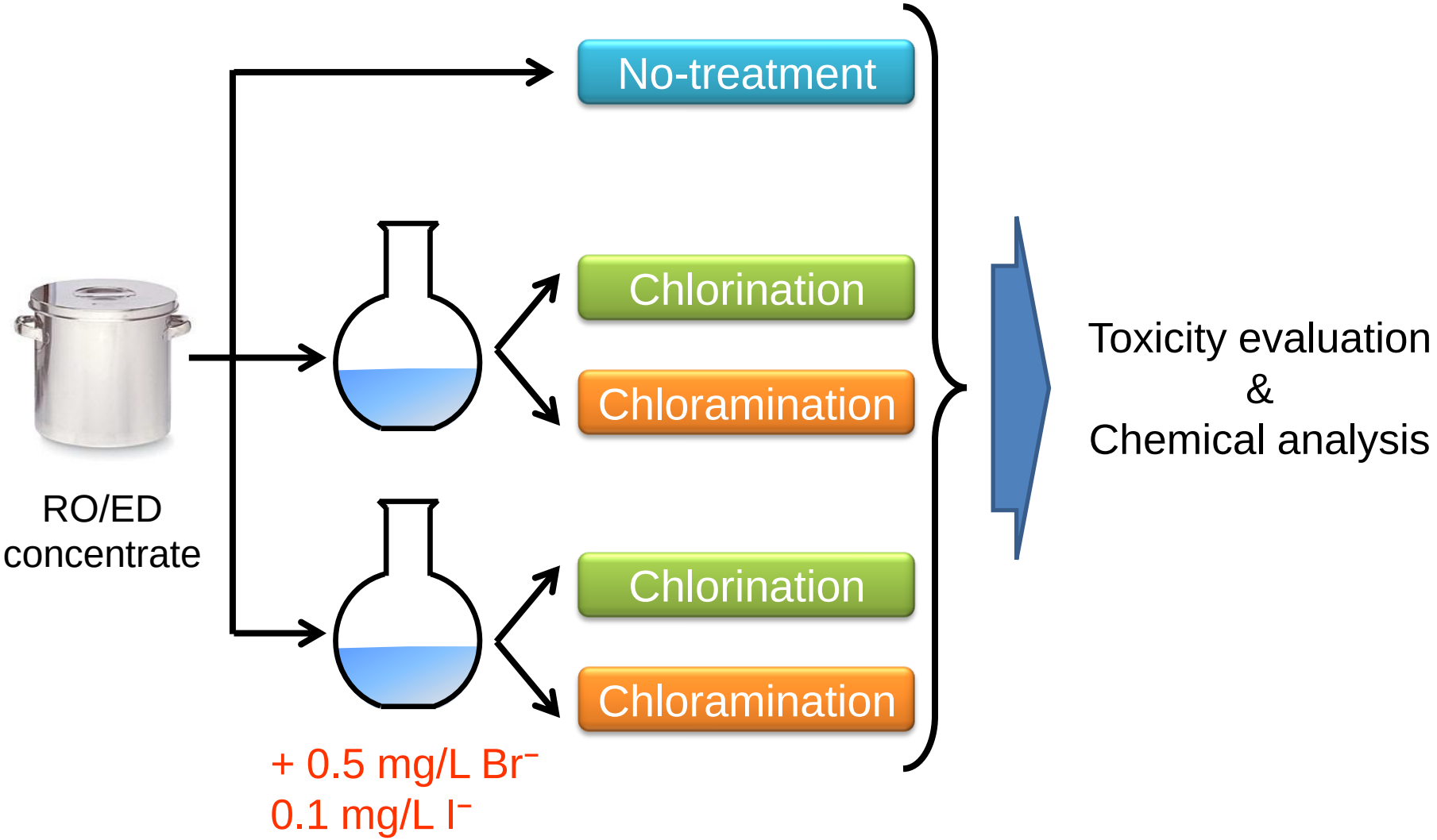
Completed haloacetaldehyde analyses. Analysis of intermediate and new DBPs. Inclusion of mammalian cell cycle blockage with cytotoxicity and genotoxicity studies.

Current and Future Work

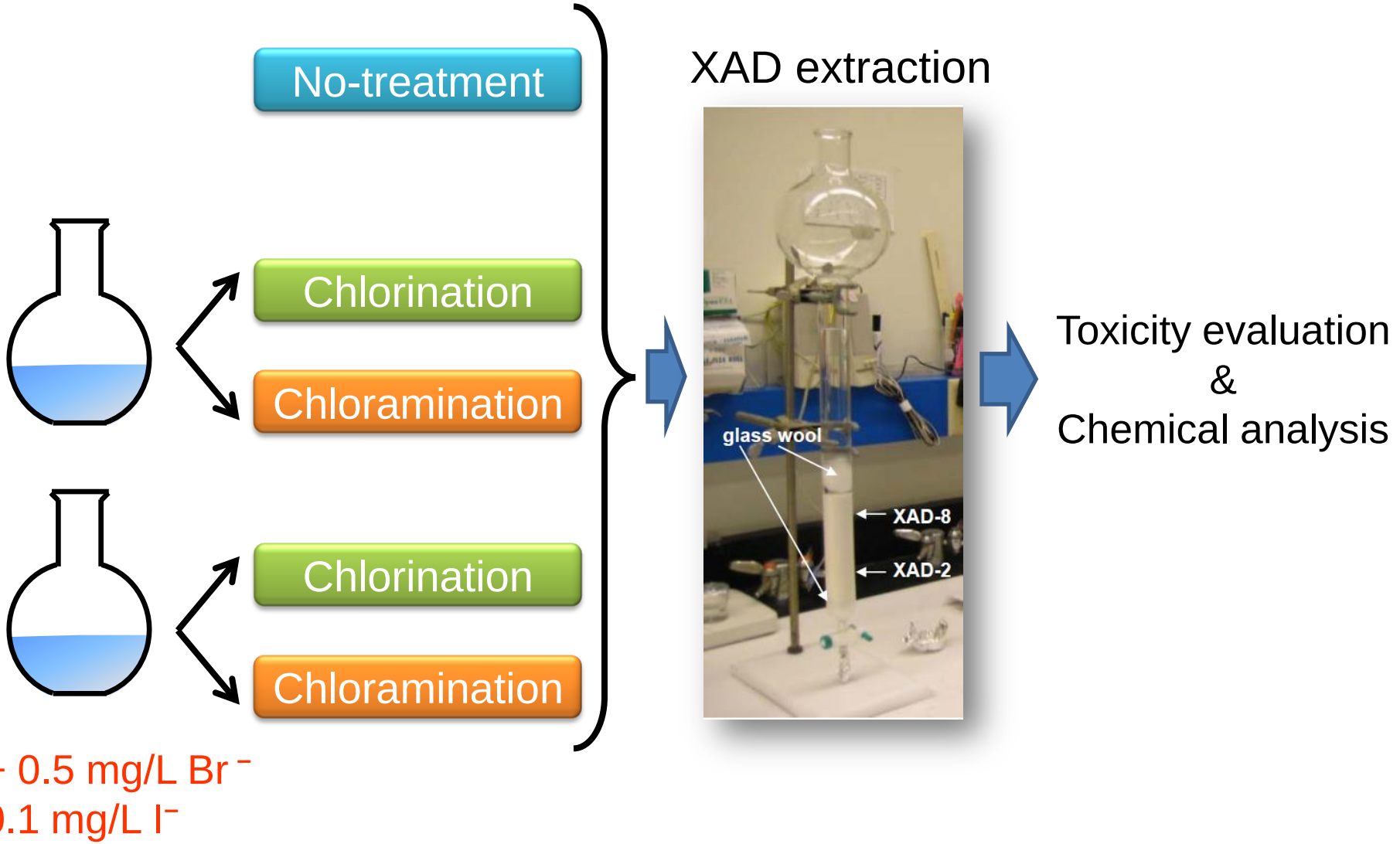
- Comparison of RO/ED with XAD will demonstrate the utility of this new extraction technology against an EPA standard (RO or XAD).
- Comparison of chloramination and chlorination will determine which disinfection procedure generates the least toxic water under specific conditions (low versus high halide).
- Integrating quantitative *in vitro* mammalian cell toxicity metrics with analytical chemistry measurements will provide a physical basis for differences in the induction of adverse biological outcomes.
- DNA repair analyses will provide an insight into the distribution of DNA lesions throughout the genome induced by the different disinfection and/or concentration methods.

Komaki, Y.; Pals, J.; Wagner, E. D.; Marinas, B. J.; Plewa, M. J., Mammalian cell DNA damage and repair kinetics of monohaloacetic acid drinking water disinfection by-products. *Environ. Sci. Technol.* **2009,** *43*, (21), 8437–8442.

Experimental Plan with RO/ED Concentrate



Experimental Plan with XAD Extraction



Expected Outcomes

- Different disinfection methods may generate different toxicological responses.

Jeong, C. H.; Wagner, E. D.; Siebert, V. R.; Anduri, S.; Richardson, S. D.; Daiber, E. J.; McKague, A. B.; Kogevinas, M.; Villanueva, C. M.; Goslan, E. H.; Luo, W.; Isabelle, L. M.; Pankow, J. F.; Grazuleviciene, R.; Cordier, S.; Edwards, S. C.; Righi, E.; Nieuwenhuijsen, M. J.; Plewa, M. J., The occurrence and toxicity of disinfection byproducts in European drinking waters in relation with the HIWATE epidemiology study. *Envion. Sci. Technol.* **2012,** *46*, (21), 12120-12128.

- High levels of Br^- and I^- may generate disinfected water with higher levels of toxicity. This will provide additional information for utilities considering changing from chlorine to alternative disinfection practices.
- The toxicity from RO/ED concentrated water samples versus XAD-extracted water samples will be determined.
- Analytical chemistry of DBPs will be conducted with the RO/ED and XAD samples from each treatment group (U.S. EPA collaborators).
- The toxicology of the complex mixtures from the water samples will be compared with their DBP profiles.

Acknowledgements

- Dr. Elizabeth Wagner, University of Illinois
- Dr. Susan Richardson, U.S. EPA
- Dr. Jane-Ellen Simmons, U.S. EPA
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- Susana Kimura, graduate student
- Bryan Smith, graduate student
- Clara Jeong, graduate student
- Justin Pals, graduate student

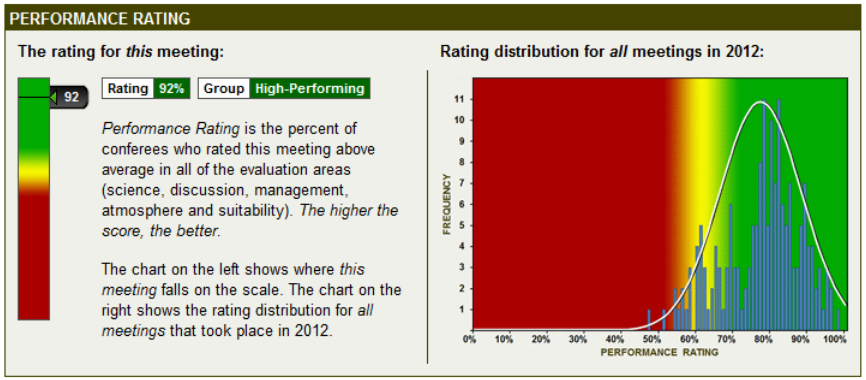
EPA Star Grant R834867and Center of Advanced Materials for the Purification of Water with Systems, National Science Foundation Science and Technology Center, under Award CTS-0120978.

Gordon Research Conference on Water Disinfection Byproducts August 2015

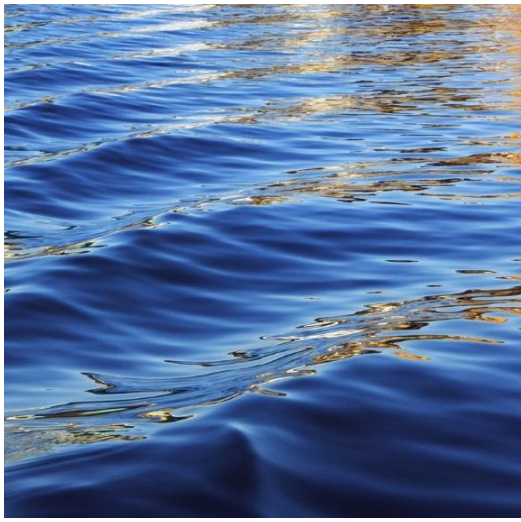
Mount Holyoke College, South Hadley, MA

Dr. Michael Plewa, University of Illinois, Chair
Dr. William Mitch, Yale University, Vice-Chair

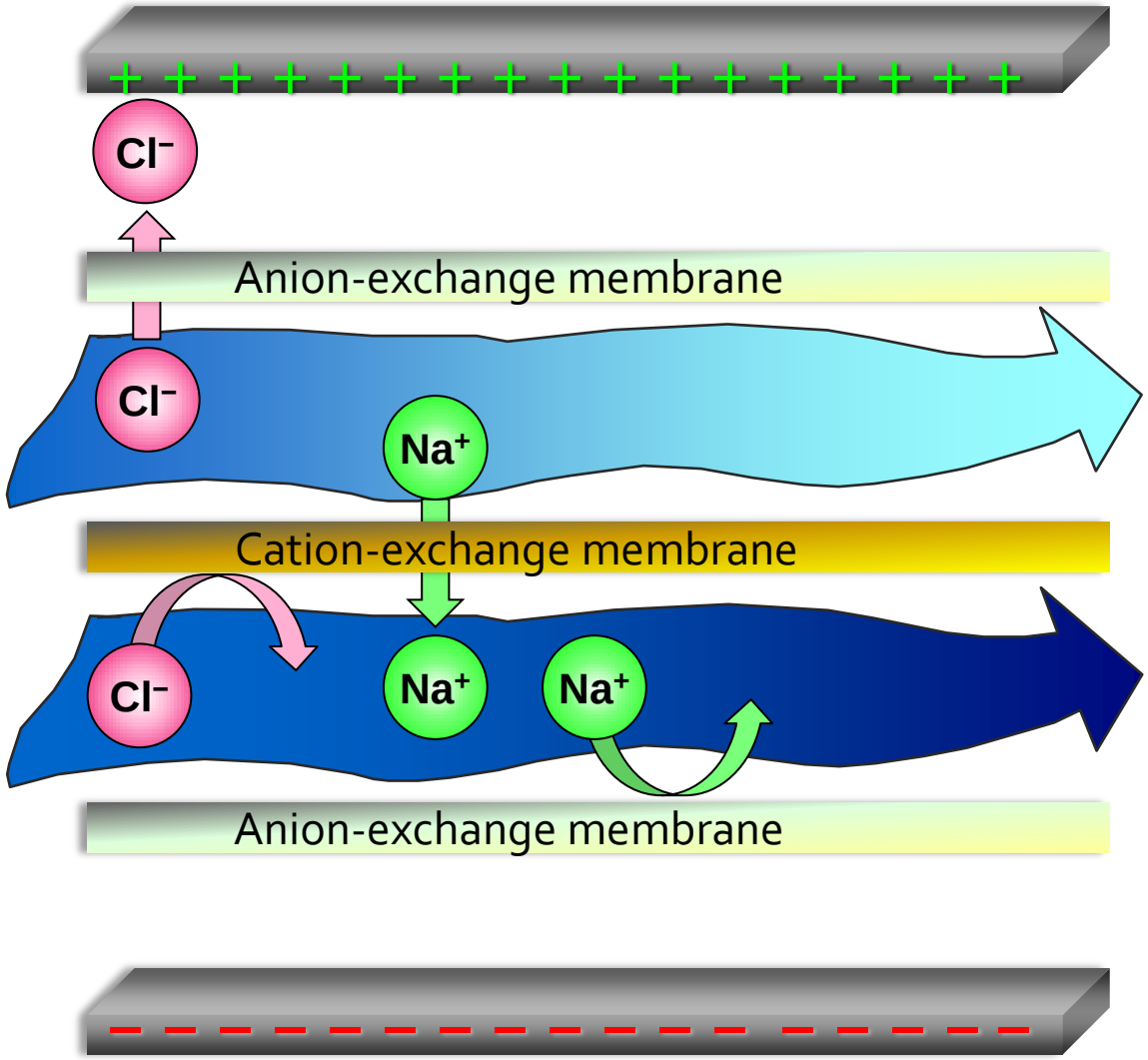
Performance rating of 92% for the 2012 DBP GRC



Appendix



Electrodialysis (ED) process



- Widely used for desalination
- Well–established method for removal of electrolytes

Dilute

Concentrate

Experimental Matrix

	Halide addition	Disinfection	Work flow
RO/ED control	–	–	RO/ED → toxicity test (RO/ED → XAD → toxicity test)
RO/ED no halide, chlorination	–	Chlorination	RO/ED → disinfection → toxicity test (RO/ED → disinfection → XAD → toxicity test)
RO/ED no halide, chloramination	–	Chloramination	RO/ED → disinfection → toxicity test (RO/ED → disinfection → XAD → toxicity test)
RO/ED + halide, chlorination	+ Br^-, I^-	Chlorination	RO/ED → disinfection → toxicity test (RO/ED → disinfection → XAD → toxicity test)
RO/ED + halide, chloramination	+ Br^-, I^-	Chloramination	RO/ED → disinfection → toxicity test (RO/ED → disinfection → XAD → toxicity test)
XAD control	–	–	XAD → toxicity test
XAD no halide, chlorination	–	Chlorination	Disinfection → XAD → toxicity test
XAD no halide, chloramination	–	Chloramination	Disinfection → XAD → toxicity test
XAD + halide, chlorination	+ Br^-, I^-	Chlorination	Disinfection → XAD → toxicity test
XAD + halide, chloramination	+ Br^-, I^-	Chloramination	Disinfection → XAD → toxicity test