Ecotoxicology Stakeholder and Engagement Session

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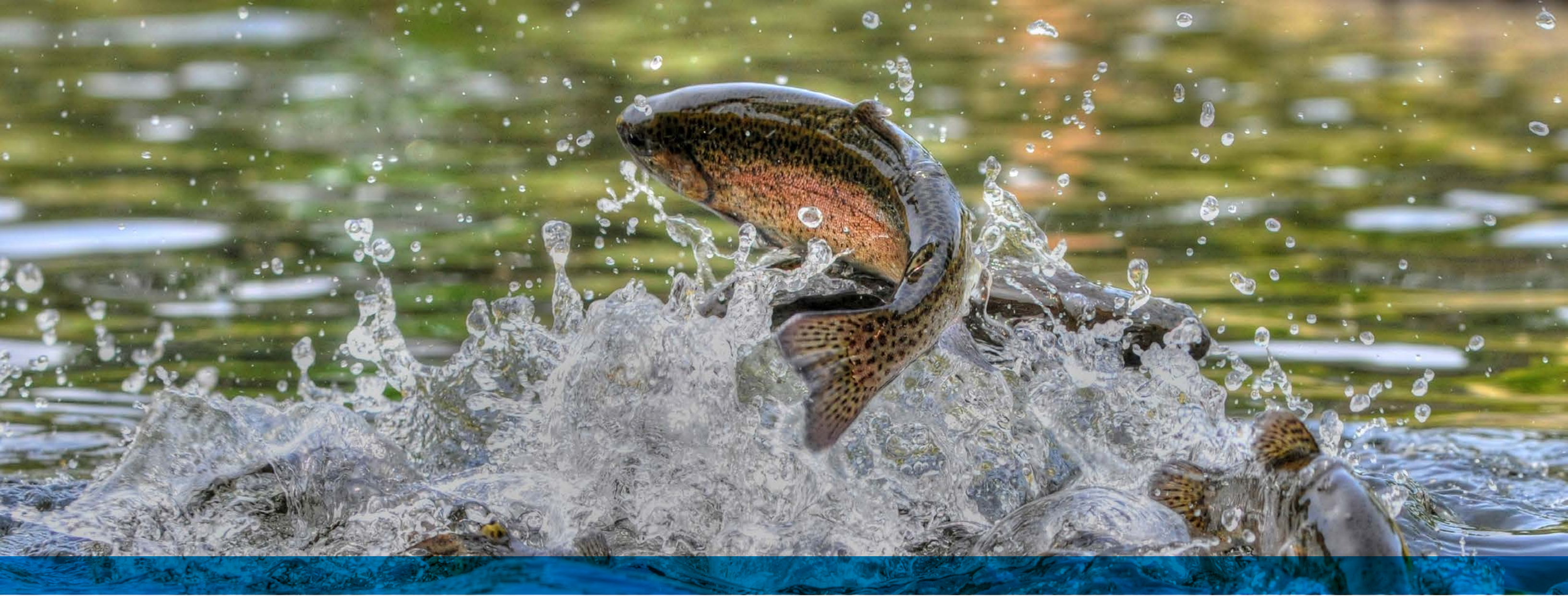

Summary

In order to provide input into the opportunities for genomics*-focused approaches in ecotoxicology, two workshops were recently held with relevant stakeholders to solicit their opinions. The information will be used to inform Genome Canada as they launch a new Request for Applications (RFA) in early 2020 in Natural Resources and the Environment. Ecotoxicology is the study of toxicology within the ecological context; that is, how contaminants within the environment, mainly dispersed through human activity, natural resource development, and urbanization, affect ecological systems. Current tools in ecotoxicology are limited by sensitivity, speed, and the ability to relate the effects on a single sentinel species to a whole ecosystem. The integration of genomic tools into ecotoxicology methodology could provide much more sensitive tools for industry, regulators, and scientists to use in monitoring, risk mitigation, and regulatory guidance. Several cross-cutting themes emerged from the workshop: 1) integration of stakeholders, for example end users, and members from industry and government, to ensure that their needs and concerns are addressed; 2) development of holistic tools that address the gene to organism impact of toxins; 3) development of validated monitoring tools that will help evaluate and predict the ecosystem response to contaminants ; and 4) international collaboration to leverage data already available all the while considering the Canadian context and its unique challenges. Genomics was seen to hold great promise by all the stakeholders for the development of new tools that would allow for accurate assessment of environmental impact and risk mitigation.

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* Genomics is the science that aims to decipher and understand the entire genetic information of an organism (i.e. microorganisms, plants, animals and humans) encoded in DNA and corresponding complements such as RNA, proteins and metabolites. In this case, the definition of genomics includes related disciplines such as bioinformatics, epigenomics, metabolomics, metagenomics, nutrigenomics, pharmacogenomics, proteomics and transcriptomics.

Introduction

Ecosystems and the development of natural resources are of great importance to Canada both on an economic and societal level. The value of Canada's natural resource assets totalled $715 billion in 2017[1], even when excluding the significant revenue from recreational and tourism activities. However, while Canadians benefit from the rich resources that exist in the country as well as ongoing urbanization, they increasingly expect that the development and reclamation of natural resource assets, is done using sustainable processes that limit the introduction of toxins and harm to the environment. Preserving the environment and the biodiversity of ecosystems also allows for great ecological resilience to face challenges such as climate change[2]. Ecotoxicology is the discipline that has developed in order to be able to monitor, predict and assess the effect of human activities such as natural resource development, climate change and urbanization on the ecosystem.

Ecotoxicology is the study of toxicology within the ecological context; that is, how contaminants, mainly dispersed through human activity within the environment, affect ecological systems. It is an example of a discipline that cuts across many natural resource sectors (such as mining, energy and forestry) with both industrial and regulatory implications and has been used to assess risk and make statutes and recommendations for industry to follow. To further understand the toxic effects of chemical, physical, and biological processes, ecotoxicology has started to turn to new technologies such as genomics to inform risk mitigation and develop new approaches to prevent or remediate harm. Ecotoxicogenomics as a discipline is providing much more sensitive tools for industry, regulators and scientists to better inform decision makers and to use in the development of these new approaches.

In order to provide input into the opportunities for genomics-focused approaches in ecotoxicology, two workshops were recently held with relevant stakeholders to solicit their opinions. The first, a small focused workshop, was held by Genome Quebec and Genome Canada on Oct 17th, 2019 at the Canadian Ecotoxicity Workshop (Appendix 1). This meeting provided the foundation for a national consultation on November 22nd, 2019, comprised of over 90 stakeholders from industry, academia, government and the not-for-profit sector. The consultation was comprised of stakeholder presentations and an open discussion. Copies of the presentations can be found in Appendix 2. This document summarizes those discussions and provides some context for the potential of genomics in the ecotoxicology sector. This information will be used to inform Genome Canada as they launch a new Request for Applications (RFA) in early 2020 in Natural Resources and the Environment, and also more generally inform the vision of the Genomic Enterprise (Genome Canada and the Regional Genome Centres) to put genomics in the hands of those who will use it to create health, environmental, and socio-economic benefits for Canadians.

"Ecotoxicology studies how contaminants—mainly dispersed through human activity within the environment—affect ecological systems."

Current State of the Sector – Challenges and Opportunities

Toxic effects from contaminant exposure are evident throughout all levels of biological organization from the molecular to population levels. Traditional ecotoxicological techniques have been used by academics, regulators and industry to monitor the impact of natural and industrial resource development, construction of infrastructure and more recently, climate change. However, many of the techniques are limited to one species (a sentinel species) which may not fully exemplify the complex biological ecosystem it represents. The tests are often on a single contaminant or undefined mixtures and are lengthy, all of which does not facilitate quick reactive measures to potential issues. Many of the tests are conducted in a laboratory, which while reproducible, are often not fully indicative of the environment being studied.

Therefore, while these data meet current internationally recognized methods and provide some useful information, they remain limited in assessing true impact[3]. The current technology has allowed for the generation of large amounts of data to understand how individuals are responding to contaminant exposure but neither provides an explanation on the mechanistic effects of contaminants at the individual/cellular level, nor on how complex ecosystems respond. Ecotoxicogenomics will allow for the study of the effects of contaminants from the molecular level moving up to communities, the establishment of baseline levels to determine degree of impact and monitor the evolution of ecosystems, and the identification of healthy indicators that can subsequently be used as early warning signs of disruptions to the ecosystem.

One of the greatest challenges with ecotoxicology in recent years is how to evaluate and predict the ecosystem response to environmental contaminants in a proactive way, in the context of climate change. How these multiple stresses will impact ecotoxicological parameters and indeed, which parameters are the most predictive of actual effects remains a pressing issue. In addition to environmental stressors, human impact to the ecosystem continues (e.g., urbanization, industrial expansion, water quality, agriculture) and how organisms respond to these human impacted events in the face of climate change remains an unresolved challenge.

"One of the greatest challenges with ecotoxicology is proactively evaluating and predicting the ecosystem's response to environmental contaminants."

Uptake of a new technology in this field is usually dictated by the approval of methods by regulatory bodies[3]. Validation against current technologies needs to be done prior to a new technology replacing the current standard. Validation in the environmental context is particularly challenging as ecosystems are complex and therefore different to analyze. This increases the resistance of industrial stakeholders to adopt these new technologies. For some of the sectors, such as mining, where there is low tolerance for unproven technology, adoption is slow[4]. In addition, in order for industry to use new technologies, there needs to be general and easy access to any given technology with standardized protocols and approaches. This remains a challenge as many newly developed genomic technologies are located within academic laboratories and not accessible generally.

The Role Genomics Can Play

It was clear during the workshop that stakeholders recognize the potential for genomics to provide tools that would allow for sensitive, efficient, and cost-effective methods for monitoring environmental toxins and their impact. Several cross-cutting themes described below emerged from the workshop: 1) integration of stakeholders to ensure that their needs and concerns are addressed; 2) development of holistic tools that address the gene to organism impact of toxins; 3) development of monitoring tools and 4) collaboration with ongoing work being done internationally.

There was a clear emphasis on the importance of integration of all stakeholders with the development of any new technology that could be used in order to facilitate its adoption. Stakeholders would include industry players, regulators, consultancy firms, service providers, the public, and specifically, in many cases of natural development, indigenous peoples, as regulations have increased the obligation to consult First Nations. It was noted that engaging and integrating indigenous communities within the projects would result in capacity building for this communities and that projects will benefit from pairing the genomic approaches with traditional knowledge. Attention must be given to the needs of these groups through the development of on-going and long-term relationships where communication and trust need to be firmly established. While all Genome Canada large scale applied projects (LSARP) need to link directly to user needs, there is also a requirement for GE^3LS (G = Genomics and its E^3 = Ethical, Environmental, Economic, L = Legal, and S =

Social Aspects) research. This social science research facilitates uptake of the genomic technologies by working with the stakeholders and genomic scientists to provide the insights needed to anticipate impacts of scientific advances in genomics, avoid pitfalls, and cultivate success[5]. This type of research was seen as essential by the workshop participants if genomics is to become an important tool in ecotoxicology. It is clear, however, that there is an openness to innovation driven by genomics. One stakeholder recounted a situation where they showed their clients that by using genomic tools for monitoring a specific environment, they were able to increase the detection limit while decreasing cost. This led to the development of new standards that are now being considered nationally.

"Legislation must rely on evidence provided by the scientific community in order to be able to act responsibly."

The integration of government representatives has also been deemed of importance as modifications to existing legislations as well as creation of new legislation require the expertise from both scientific and social scientists. With the thousands of chemicals in everyday use and more being produced, governments and regulatory bodies are continually trying to manage the presence of these chemicals in the environment related to the effects they may have on the ecosystem. Legislation must therefore rely on evidence provided by the scientific community in order to be able to act responsibly and eco-toxicogenomics can provide insight into the effects on and the degree of response of the ecosystem. Refining, reducing, and replacing the use of animals such as fish, birds, and amphibians for this purpose addresses ethical concerns and the increasing legislative requirements to consider alternative test methods. As high-throughput genomic tools become available, studies have been able to assess exposure and effect at the molecular, cellular, and individual levels. Recent research in ecotoxicology has begun to identify the mechanism of action for many chemicals across many species with the goal of understanding toxicity and predicting sensitivity.

Concern was expressed by stakeholders in the workshop about validation of the tools and the ability to assess such things as false positives and false negatives and how they would be integrated into regulatory policy. This was of primary concern to regulators who need to make accurate risk assessment decisions on the information that is generated. Emphasis was placed on transparency and auditable methods. One example of a product-driven project in Canada using genomic tools and addressing the concerns of validation is EcoToxChip[6] by Dr. Nil Basu (McGill) and colleagues. Funded by Genome Canada, the goal of the project is to develop, test, validate, and commercialize genomic tools for the characterization, prioritization, and management of environmental chemicals and complex mixtures of regulatory concern.

Technologies that can be used widely in the field on an expansive, yet inexpensive way are not currently widely available. Environmental DNA (e-DNA) is an example of such a technology.

"Developing tools that can detect and measure e-DNA in the field holds promise as an efficient, non-invasive, large scale monitoring method."

e-DNA is DNA that is collected from environmental samples such as soil, water, or air, rather than directly sampled from an organism. As various organisms interact with the environment, DNA is expelled (for example through skin, hair, blood, feces) and accumulates in their surroundings[3]. This DNA can be further analyzed by high-throughput sequencing methods to determine presence or absence of different species (biodiversity monitoring). Developing tools that can detect and measure e-DNA in the field holds promise as an efficient, non-invasive, large scale monitoring method, however challenges remain. While using eDNA allows for a survey of what is in an ecosystem, there remains challenges in accurately determining the true abundance of organisms, and therefore relating it to specific perturbations in the environment. This challenge was clearly articulated by those at the workshop looking at these technologies for ongoing risk assessment. Several investments by Genome Canada and others in projects such as “Biomonitoring 2.0: A High-Throughput Genomics Approach for Comprehensive Biological Assessment of Environmental Change”[7] and “Assessing Freshwater Health Through Community Based Environmental DNA Metabarcoding”[8] both led by M Hajibabaei and team (University of Guelph) and more recently “Environmental DNA (“eDNA”), meta-barcoding and transcriptional profiling to improve sustainability of freshwater fisheries and fish culture”[9] led by D. Heath (University of Windsor) and team are further developing the use of eDNA and its ability to overcome these challenges.

The specificity that genomic technologies contributes could provide environmental health indicators that could act as an early warning system, identifying sub-lethal effects at sub-organism/molecular level. The following studies are described in more detail in the report from the Canadian Ecotoxicity Workshop (Appendix 1). For example, one approach is to study the transcriptome anchored in a toxin-induced phenotype. Recent studies have shown the power of whole embryo transcriptomics in identifying the mechanisms of action underlying an abnormal phenotype, leading to death[10,11,12]. However, there remains a lack of definitive identification of factors responsible for these health effects related to ecological aspects. Recent studies are starting to link these types of molecular initiating events with adverse outcomes at the population or ecosystem levels[13,14]. Adverse outcome pathway research provides mechanistic understanding of effects to help assess risk to environmental health[3,15]. It was clear from the stakeholders that data needs to be integrated to provide a holistic view of how these molecular changes are translated into the higher organism before any integration of the information derived from this research could be incorporated into a regulatory policy or a tool.

While it is important that tools are specific to the Canadian context, species and ecosystems specific to Canada, internationally, there are regulatory bodies and academic institutions that are looking to genomic technologies to provide more sensitive and accurate information than is currently available. Many of these groups are using metabolomics as it can provide not just a sensitive tool but a link between the gene and organism effects. It was recognized during the workshop that collaboration with these groups is essential. While Canadian research is already engaged in this area, further investment into ecotoxicogenomics will further cement Canada’s leadership position.

“While Canadian research is already engaged in ecotoxicogenomics, further investment will help cement Canada’s position of leadership.“

Conclusion

Canada has a unique opportunity to lead the global effort in ecotoxicology by actively pursuing new omics applications. It was clear that stakeholders from all sectors (industry, regulators, academics) are excited about the possibilities that genomics offers to them. Ongoing consultation was an important theme arising from the workshops. Engaging early and often with the relevant end users of the technology will allow the development of technologies that respond to the specific challenges and opportunities that are present in the environment by natural resource development and urbanization.

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Appendix 1

Report from the Canadian Ecotoxicity Workshop
October 17th, 2019

Genomics in Ecotoxicology:
Defying Canada's strategic opportunities and priorities in the dawn of a future Genome Canada funding competition

Genomics in Ecotoxicology:

Defying Canada's strategic opportunities and priorities in the dawn of a future Genome Canada funding competition

Quebec City, QC, October 17th, 2019

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i. Preamble

This is a summary of a strategic panel led by Genome Canada entitled *'Genomics in Ecotoxicology – Defying Canada's strategic opportunities and priorities in the dawn of a future Genome Canada funding competition'* during the 46th Annual Canadian Ecotoxicity Workshop (CEW) held in Quebec City on October 9th, 2019. The panel consisted of Diana Iglesias (Genome Québec), Karen Dewar (Genome Canada) and Vance L. Trudeau (University of Ottawa). Each gave a short presentation to set the stage for group discussions. The audience and participants (15) were attendees of the CEW. The content of this report therefore reflects the discussion of several scientists coming from academia, industry, and provincial and federal government on the importance of genomics for the ecotoxicology sector.

1. Importance of the ecotoxicology sector to the Quebec's economy

The "One Heath" effort integrates human, animal, and environmental health research into one holistic approach to find solutions to the challenges of today's world (American Veterinary Medical Association One Health Initiative Task Force 2008). Ecotoxicology, the study of toxicology with an ecological context, or how environmental contaminants affect wildlife, is a relevant field of study to contribute to this interdisciplinary initiative.

Ecosystems provide services of economic value and preserving their biodiversity allows for ecological resilience to disturbances such as climate change (Government of Canada 2011). For example, ecosystem services of Canada's boreal forest were estimated at CAN$ 93 billion in 2006 (Government of Canada 2011), with wildlife- and nature-related activities having a large contribution (e.g., CAN$ 11.4 billion to Canada's GDP in 1996, Gray et al., 2003). Similarly, the 54,800 km^2 Manicouagan-Uapishka World Biosphere Reserve boarded by the Saint Lawrence River and the Manicouagan reservoir in Quebec was estimated to have an economic value of CAN$ 1.3 billion per year providing freshwater for energy production and global climate regulation as ecosystem services (Kermagoret and Dupras 2018).
With the thousands of chemicals in everyday use and more bring produced, governments and regulatory bodies are continually trying to manage the presence of these chemicals in the environment related to the effects they may have on the ecosystem. Toxicity testing of these chemicals can provide scientific evidence to policy-making decisions and provide greater confidence for risk assessments (Krewski et al., 2010). As both a retrospective study (e.g., identify what are the chemical stressors in the environment) and a prospective study (e.g., predict what the ecological and health effects could be) (Zhang et al., 2018), ecotoxicological research is essential to understanding human impacts on the environment in Canada and elsewhere.

2. Current state of the sector

Ecotoxicogenomics is the study of the effects of ecology together with toxins on the genetic material of organisms. With traditional ecotoxicological techniques, toxic effects from contaminant exposure are evident throughout all levels of biological organization from molecular to population levels. Recent research in ecotoxicology has begun to identify the mechanism of action for many chemicals across many species with the goal of understanding toxicity and predicting sensitivity. One example of a product-driven project in Canada using genomic tools is EcoToxChip by Dr. Nil Basu (McGill) and colleagues (2019). As a well-funded project by Genome Canada, it has been able to advance the commercialization of genomic tools for scanning and prioritizing chemicals of interest. However, research gaps remain to advance genomic science itself.

As high-throughput genomic tools become available, studies have been able to assess exposure and effect at the molecular, cellular, and individual levels with a focus on aquatic species. One approach is to study the transcriptome anchored in a toxin-induced phenotype. For example, recent studies (e.g., Gutierrez-Villagomez et al. 2019a,b; Mathieu-Denoncourt et al., 2014) have shown the power of whole embryo transcriptomics to develop hypotheses on mechanism of action underlying an abnormal phenotype, leading to death. However, there is still a lack of definite identification of factors responsible for these health effects to relate to ecological aspects. Recent initiatives are starting to link these molecular initiating events with adverse outcomes at the population or ecosystem levels (Ankley et al., 2010, Villeneuve and Garcia-Reyero 2011). Similar to the exposome approach in epidemiology, adverse outcome pathway research provides mechanistic understanding of effects to help assess risk to environmental health (Escher et al., 2017).

3. Sector challenges and opportunities

One of the greatest challenges with ecotoxicology in recent years is how to evaluate the ecosystem response to environmental contaminants (Zhang et al., 2018). However, we are currently experiencing massive biodiversity declines describing the sixth mass extinction (McCallum 2015) with a large driver being climate change (Thomas et al., 2004). This includes wildlife (e.g., birds, amphibians, fish) as well as plants (e.g., traditional medicinal plants in unceded First Nations territories) (McCallum 2015; Alves and Rosa 2007). Even with a conservative mid-range climate-warming scenario, 15-37% of species will likely go extinct by 2050 (Thomas et al., 2004).

In addition to the stress of the temperature rising with climate change, organisms will have other challenges such as the alteration to oxygen levels that can interrupt normal cellular function. In addition to these environmental stressors, human impact to the ecosystem continues (e.g., urbanization, industrial expansion, water quality, agriculture). Therefore, there is a need to evaluate how these multiple stressors will impact ecotoxicological parameters. For example, how will organisms respond to a human impacted event (e.g., pesticide use, oil transport, water quality) in the face of climate change?
The technology currently available for ecotoxicological research has allowed for the generation of large amounts of data to understand how individuals are responding to contaminant exposure. However, with the ever-changing environment and increase in complexity of interactions between chemicals, there is a need to expand on this research and modify these tools for monitoring purposes. In addition, communication of this research with First Nations communities, government

officials, and the general public can be challenging when a clear link between molecular changes and alterations at the ecosystem level has not been clearly established.

4. The role of genomics in addressing the sector's challenges

Genomics is defined by Genome Quebec "as the comprehensive study, using high throughput technologies, of the genetic information of a cell or organism and its functions. The definition also includes related disciplines such as epigenomics, metabolomics, metagenomics, proteomics, transcriptomics, bioinformatics and synthetic biology as long as the link to genetic information is clear". Ecotoxicogenomics is when these 'omic tools are used in an ecological and environmental context to assess the ecosystem's response to contaminant exposure.

With the changing environmental landscape, especially in Northern regions, the promise of using ecotoxicogenomics in a regulatory decision framework is well acknowledged in the field. This includes for monitoring purposes (recovery and remediation) and in ecological impact and risk assessments. While the consideration of ecotoxicogenomic data in regulatory decisions is not a new idea, the challenge remains of linking the changes we see at the genomics level with adverse outcomes (Van Aggelen et al., 2010; Villeneuve and Garcia-Reyero 2011) and relaying this information to end-users, including government, regulatory officials, industrial partners, and First Nations communities.
For example, the large amount of molecular data helps to understand the mechanism of action for environmental contaminants. This information is necessary in a multilevel systems biology approach as it can identify potential biomarkers to predict adverse outcomes (Van Aggelen et al., 2010). In addition, using genomic tools allows for a high throughput assessment of response in key toxicity pathways and can be a proactive approach to help inform "greener" design in industry (e.g., for pesticides, pharmaceuticals).

5. Approach

To continue ecotoxicogenomic research with consideration of biodiversity declines and climate change, there is a need for advancing genomic science to include more ecologically and economically relevant species (e.g., genome sequencing for non-model species). This includes studies in the terrestrial environment in addition to the aquatic environment to broaden the scope of ecosystem coverage.
Moreover, efforts should be made to develop and evaluate alternative toxicity methods and non-invasive sampling techniques. For example, this could include the use of *in vitro* toxicity testing (Roggen 2011) and DNA barcoding or environmental DNA (eDNA, Zhang 2019). Such approaches must be developed with the idea (and validation), that they will be predictive of real-world situations. Note also, that invertebrates (e.g., *C. elegans*), or larval vertebrates (e.g., larval fish or amphibians) hold promise as complex, whole animal testing systems, that may be at the same time predictive of adult responses, and be more acceptable to the public and to regulatory agencies whose concern is animal welfare. Complex, developing embryos are considered better than *in vitro* cell lines for some applications. While eDNA is a promising monitoring tool, major improvement to the quantitative analysis is necessary for increased confidence in its predictions.

With the expansion in ecotoxicogenomic research, a step back with validation of the new fast-developing genomic tools with old toxicological techniques would be beneficial in order to move forward in the right direction. The vast amount of data generated could be curated into biological databases and the development of novel, artificial intelligence-based bioinformatic pipelines are needed to analyze, integrate, and interpret the data. This will help coordinate new genomics research with existing data and relate to adverse outcomes for applications such as impact and risk assessments (Krewski et al., 2010; Villeneuve and Garcia-Reyero 2011). Computational systems biology can also help in predicting sensitivity and response to contaminants in the environment for improvements to regulatory toxicity testing (Krewski et al., 2010).

In order to improve the translation and relevance of ecotoxicogenomic data to end-users, community-driven integration and partnerships will be essential. By including First Nations communities, National Parks and Conservation Areas Managers, NGOs, government and industrial partners, and social scientists in the early stage of research development, it allows for a more holistic approach to ecotoxicological problems in this changing world. Moreover, it will be essential to assess barriers to the uptake and understanding of genomic approaches by the end-users.

6. Conclusion

While our understanding of linking genomic research with animal health has been improving, there is a need to assess the interactions between genes and the environment. Many of the projects funded in the past have been focused on bacteria and microbes. While these are an important part of the ecosystem it is necessary to expand the scope to include the whole ecosystem, and in particular ecologically- and economically-important plants and animals. Impact and risk management decisions are continually being made thus advancing genomic research in the context of ecology and the environment can provide evidence to increase confidence and reduce the risk for all of Canada.

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Appendix 2

Presentations from the Ecotoxicology Stakeholder Engagement Workshop

Workshop Presentations:

Future Programs, Karen Dewar, Director Genomic Programs, Genome Canada

Challenges in Using Genomics in Ecotoxicology, Gaëlle Triffault-Bouchet, Ecotoxicologist, Centre d'expertise en analyse environnementale du Québec, Ministère de l'Environnement et de la Lutte contre les changements climatiques;

Applied Ecotoxicology and Genomics: practitioner's perspective, Shannon Bard, PhD, Director of Innovation, Hemmera

Challenges and Opportunities for Ecotoxicology in Science and Politics, The Honourable Rosa Galvez, PhD, P.Eng, FIC, FCSCE, Université Laval

NOVEMBER 22, 2020

Génome Québec

Genomics in Ecotoxicology- Consultation session

GenomeQuébec

STAKEHOLDER ENGAGEMENT & STRATEGY SESSION- PROGRAM

- Introduction
- Scope and purpose of the session
- LSARP2020 & GE3LS – **Karen Dewar**
- Ecotoxicity – Regional and National perspectives
  - Qc Regional perspective – **Gaëlle Triffault-Bouchet** (CEAEQ)
  - BC Regional and Industry perspective – **Shannon Bard** (Hemmera)
  - National perspective – Sen. **Rosa Galvez**
  - CEW consultation reporting – **Valerie Langlois** (INRS)
- Brainstorming session – moderated by **Alison Symington**
- Next steps
- Session close

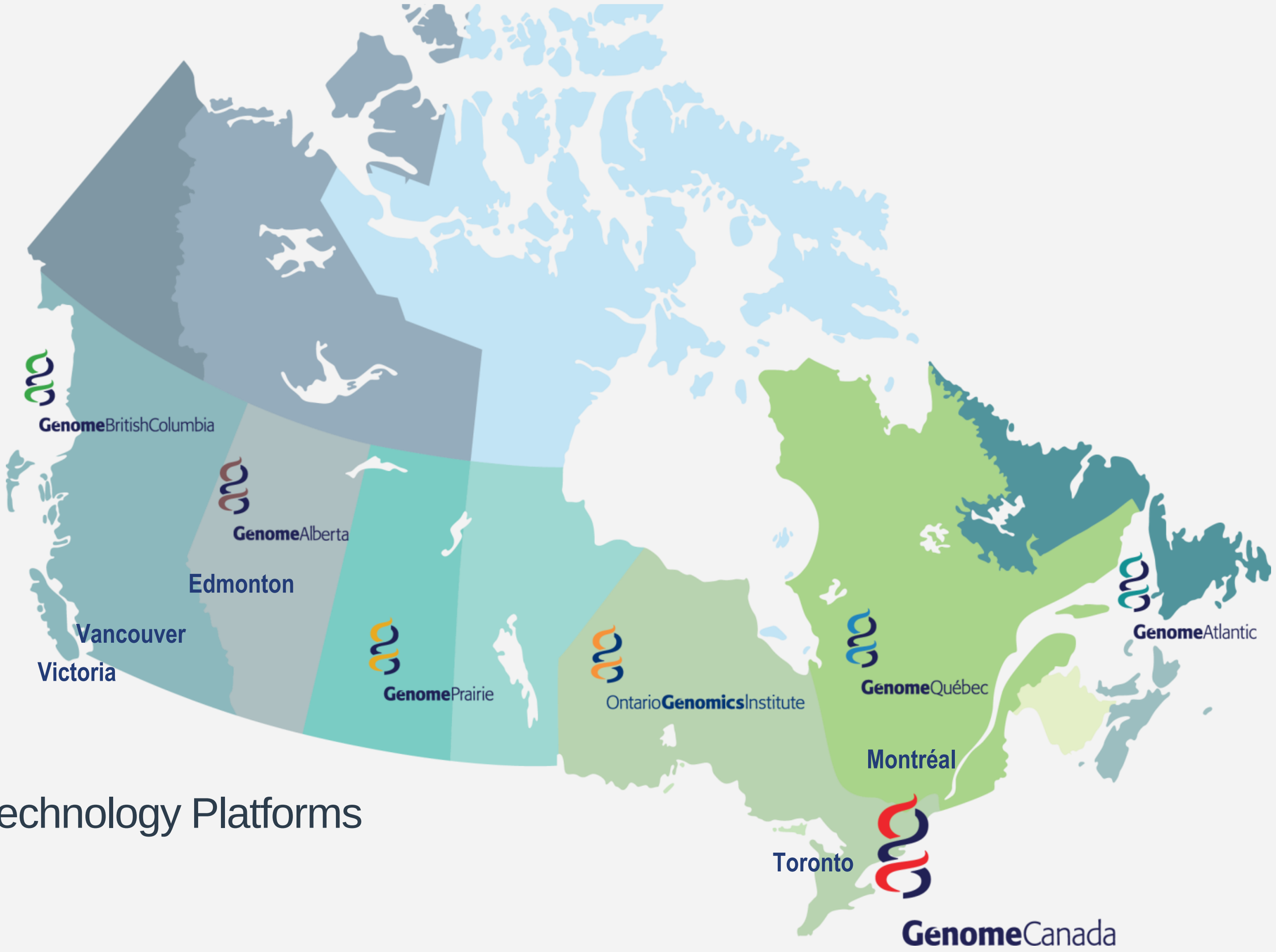
Genomics in Ecotoxicology – Solutions for Environmental Monitoring and Risk Assessment in Canada

Purpose of the session

- Bring together stakeholders (industry, academia, regulators, and government) from the Ecotoxicology sector to compile an up-to-date portrait of the sector and its societal and economic impact
- Stimulate discussion on challenges and opportunities in Ecotoxicology that can be addressed by genomics
- Inform the community about the discussion at CEW2019 on Genomics in Ecotoxicology
- Inform the design and investment strategy for Genome Canada's upcoming 2020 LSARP competition

GENOME ENTREPRISE- Genome Canada and the regional Genome Centres

- Created in 2000
- **6** regional centers
- **7** key economic sectors
    - Health
    - Environment
    - Forestry
    - Agriculture
    - Fisheries and aquaculture
    - Energy
    - Mines
- 10 Accessible Genomics Technology Platforms



GLOBAL CHALLENGES GENOMIC SOLUTIONS

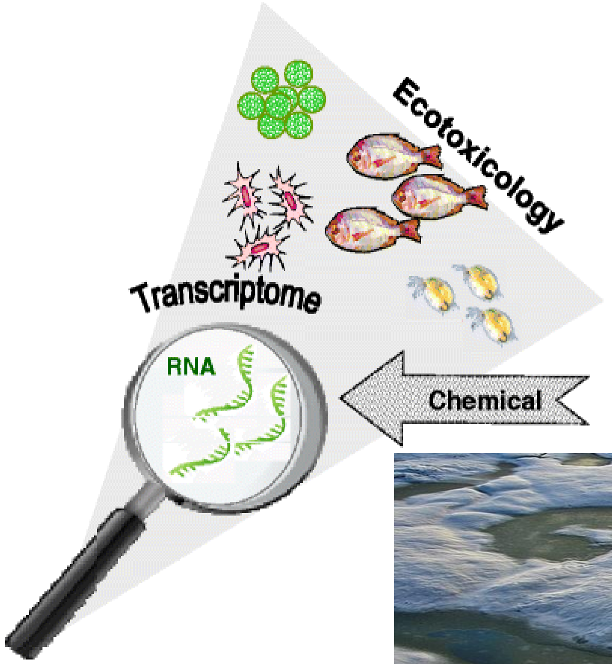
Environmental monitoring strategic session

GenomeCanada

Future Programs:

2020 Large-Scale Applied Research Project Competition in areas of Natural Resources and the Environment to be launched in 2020 (likely in January 2020).

Note that the regional Genome Centres will be organizing stakeholder engagement and strategy sessions (such as this one) over the next two to three months. Information from these sessions will help inform the design of the funding opportunity.



- There is approximately $25 million available for this competition from Genome Canada.
- In keeping with Genome Canada's mandate to invest in large-scale research, projects of at least $2 million in total budget over a term of up to four years are welcome; there is no maximum budget.
- Applicants will be required to apply for funding through their regional Genome Centre.

- A project’s eligible costs must be co-funded from eligible sources such that the co-funding is at least equal to the Genome Canada contribution.
- The application process will be comprised of three steps: Registration, Pre-Application and Full Application.
- Based on an anticipated January 2020 Competition launch, the deadline for Registrations is expected to be in March, 2020.

Research into the implications of genomics in society (GE^3LS Research)

GE^3LS research investigates the implications of genomics in (and on) society and the factors that may facilitate or hinder the uptake of genomic-based application(s). It aims to inform responsible genomics research and enable uptake of applications.

All projects must include a GE^3LS research component. This can either be the major focus of the project or an integrated component that is shaped by, and helps shape, the overall project by investigating key factors that may facilitate or hinder the uptake of the genomic-based application(s) being developed by the project.

GenomeCanada

Pathway to Success for Integrated GE³LS

Integrated Development – Success Factors

- Finding GE³LS researchers with the right expertise for the problem.
- Pre-existing working relationships and/or familiarity with others' work.
- Early involvement of GE³LS researchers in planning.
- Understanding users' needs and working back from these to help GE³LS deliver results.

Integrated Execution – Success Factors

- Mutual respect to overcome the disciplinary divide.
- Strong communication mechanisms.
- User involvement in project.
- Valuable GE³LS guidance from the Research Oversight Committee.

Challenges in Using Genomics in Ecotoxicology

Gaëlle Triffault-Bouchet, Ph.D, Ecotoxicologist
Centre d'expertise en analyse environnementale du Québec
Ministère de l'Environnement et de la Lutte contre les changements climatiques

November 22, 2019

Votre gouvernement

Québec

Centre d’expertise en analyse environnementale du Québec

Section of the Ministère de l’Environnement et de la Lutte contre les changements climatiques
Gouvernement du Québec

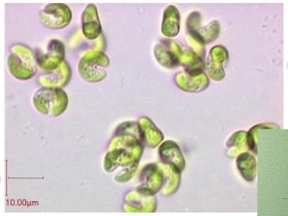
- Mission: Ensure the availability, quality and continuity of **expertise and analytical information** for environmental protection and resource conservation needs.
- Laboratory analysis (chemistry, biology, ecotoxicology, microbiology), field studies, ecotoxicological risk assessment, accreditation of private laboratories and production of reference materials for monitoring these activities,
- 110 employees, in Laval and Québec City

For what purpose do we use the data produced in ecotoxicology?

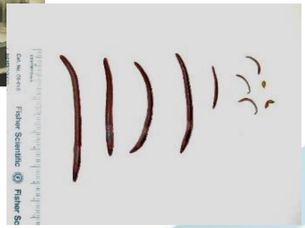
- Hazard potential of chemicals or mixtures (bioavailability, fate, mode of action).
- Ecotoxicological risk assessment (ERA, theoretical or actual).
- Establishing quality criteria.
- Monitoring effluents, lixiviates, residual materials.
- Monitoring the health status of an ecosystem.

What kinds of data are used?

- Most of the time: the results of **monospecific tests**
  - **One organism**, representing a trophic link in an ecosystem,
  - **One contaminant or mixtures**,
  - Conducted in laboratory,
  - Under **simplified standardized** conditions,
  - Internationally recognized methods,
  - **Endpoints**: mortality, growth, reproduction.







- **Data are used individually or with the Species Sensitivity Distribution (SSD) approach**

Advantages of this approach

- This is a **safe approach:**
  - Repeatable and reproducible.
  - Standard experimental conditions are generally set in order to maximize the toxic effects.
  - Many of the selected species are generally sensitive.
  - The safety factors are quite conservative.
- This approach is **realistically** applicable with **moderate effort** and **cost** to a large number of substances and situations.

Some limitations of monospecific tests

- Toxicity tests are often long, which makes it **difficult to react quickly** to contamination.
- Standardized methods allow for the evaluation of a **very small number of endpoints**.
- The sensitivity of a few selected test species may not be **representative** of the distribution of sensitivity among the species of complex biological communities.

Some limitations of monospecific tests

- The standard conditions of laboratory tests may not reproduce the **variability** of physical, chemical, and biological parameters of aquatic and terrestrial ecosystems.

Examples of current needs in ecotoxicology

- **Understanding** what is occurring during toxic exposure to various contaminants:
  - Molecular modes of action (MOAs) of chemicals or other stressors.
  - Discovery of new possible target genes and, consequently, new molecular biomarkers.

- **Predict disruptions** of signaling pathways and cellular functions linked to more integrated processes, such as development and reproduction.

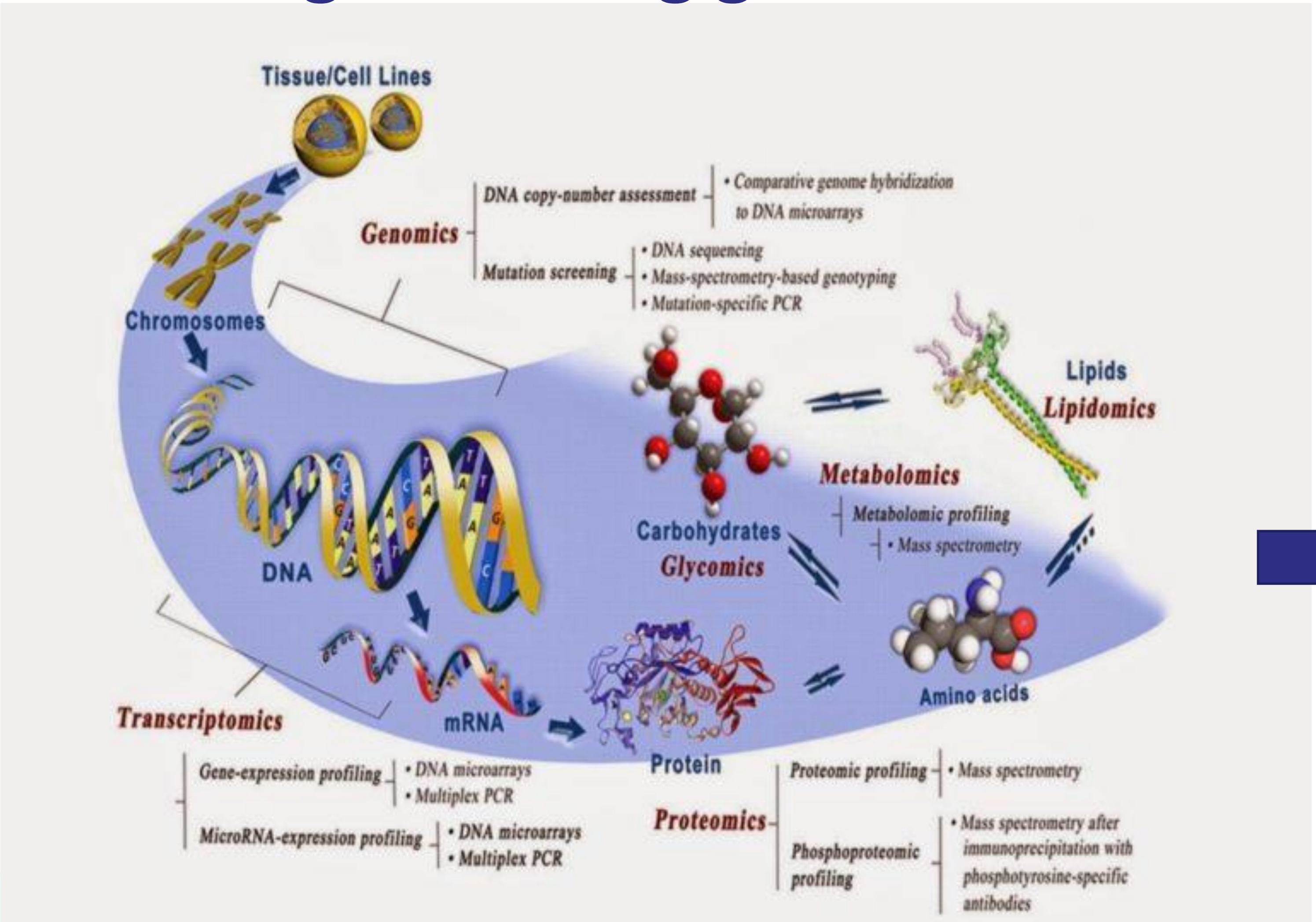
Examples of current needs in ecotoxicology

- Need for **rapid tests**, allowing early detection of contaminants and their effects for management purposes (ex. : *E. coli* and beaches) - Early-warning indicators of exposure to or effect of stress factors.

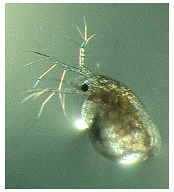
- Need for simple, **lab-based or field tests**, covering effects other than mortality, growth, and reproduction, ex.: endocrine disruption, genotoxicity, etc.

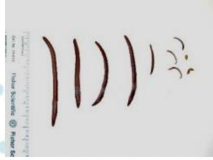
- **Environmental forensic** for microbial and chemical contamination

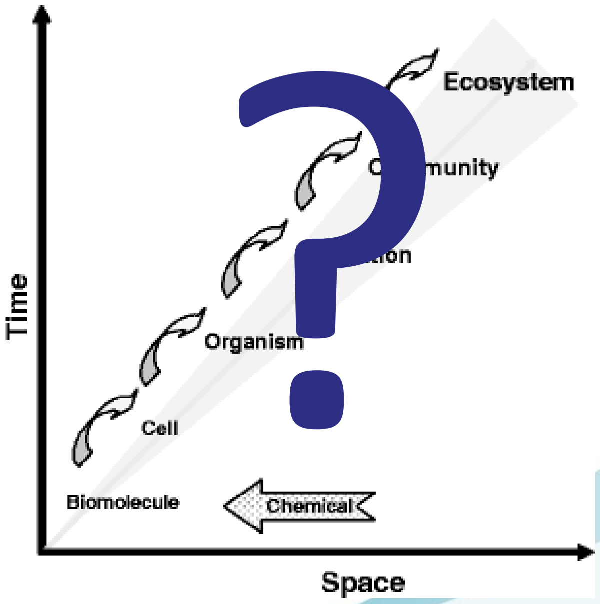
Challenges in using genomics



Wu RD et al. JDR 2011







Challenges in using genomics

- How gene induction/expression can be **linked to effects on organisms** (growth, reproduction, mortality, susceptibility to predation, etc.), populations, communities and ecosystems.
- How to **interpret** genomic expression data from *in situ* studies.
- How to take into account the reversibility of gene induction and repair mechanisms.

Challenges in using genomics

- Need for **integrated studies**, from gene expression to effects (development, reproduction, etc.) that allow us to understand the relationship between those endpoints.
- Need for a **multi-generational approach.**
- Need for **standardized protocols** and approaches.

Thank you for your attention

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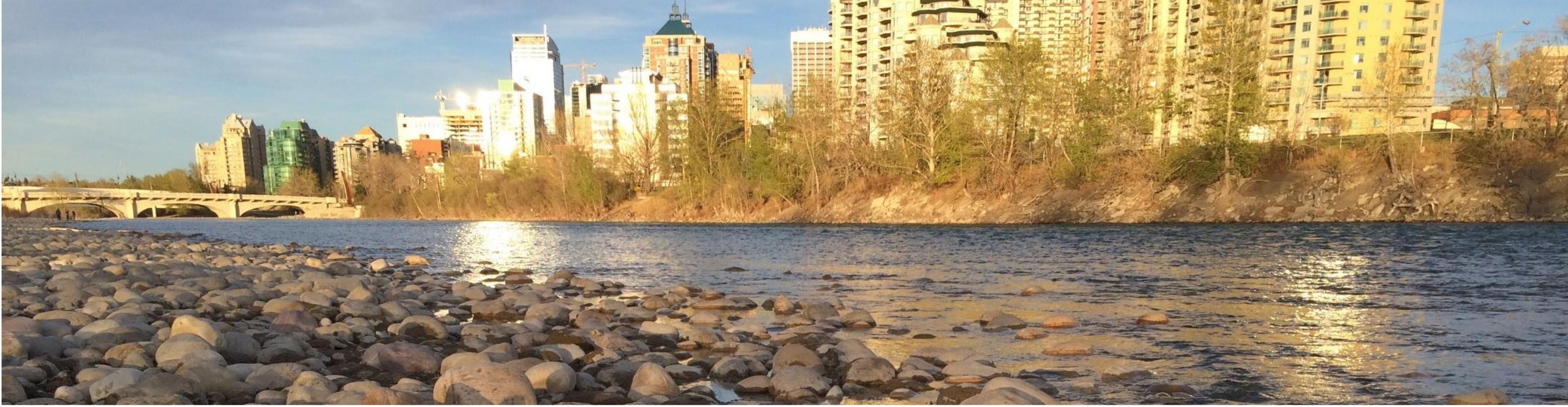


Applied Ecotoxicology and Genomics: practitioner's perspective

Shannon Bard, PhD
Director of Innovation

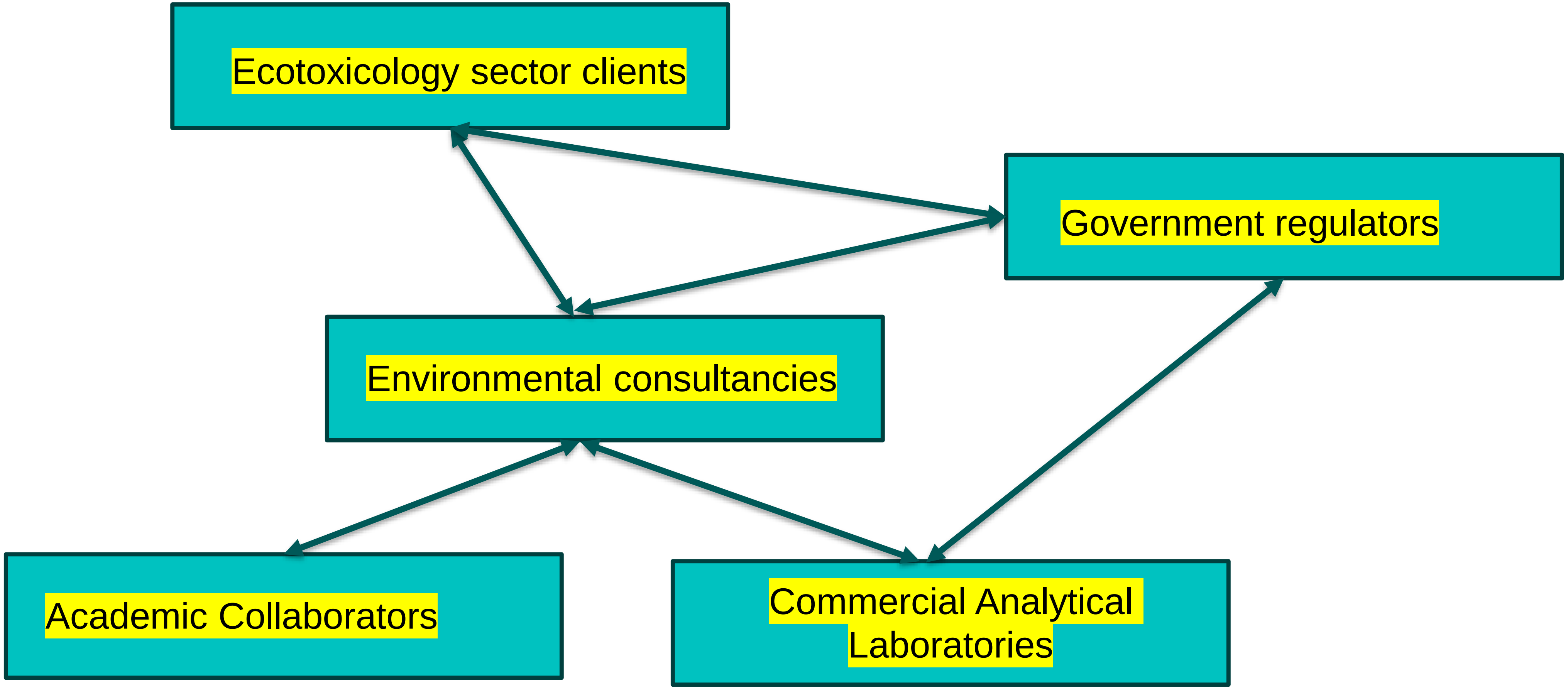
November 22, 2019

Hemmera
An Ausenco Company

Summary

- Applied Ecotoxicology Sector
- Challenges facing sector
- Application of Genomics to overcome sector challenges
- Socio-economic impact of applying genomics to ecotoxicology

Applied Ecotoxicology Sector



Applied Ecotoxicology Clients & Market

Ecotoxicology Sector Clients

- Emit Effluent/Spill
- Historic contamination
- Proponents of new Developments

Diverse Sector: Mining, O&G, energy, ports, transportation (rail/road/ship spills), natural resource extraction, forestry (pulp mills), industrial plants, government (infrastructure), etc.

Market (Services)

- Ecological Risk Assessments
- Environmental Assessments
- Environmental Effects Monitoring (EEM)
- Cumulative Impacts Monitoring
- Emergency Spill Response

Sector Challenges

- Baseline environmental and species at risk surveys
- Contaminated Sites Bioremediation
- Habitat Restoration
- Mining Reclamation
- Effluent biotreatment

Challenges to adoption of Genomic approaches

- Government Guidance/Regulations dictate methodology/best practices
  - New approaches not yet approved – permit

- Access to technology – no commercial lab test yet- limits adoption

- Low tolerance for risk with unproven technology (Mining)

Genomics informs Ecotoxicology

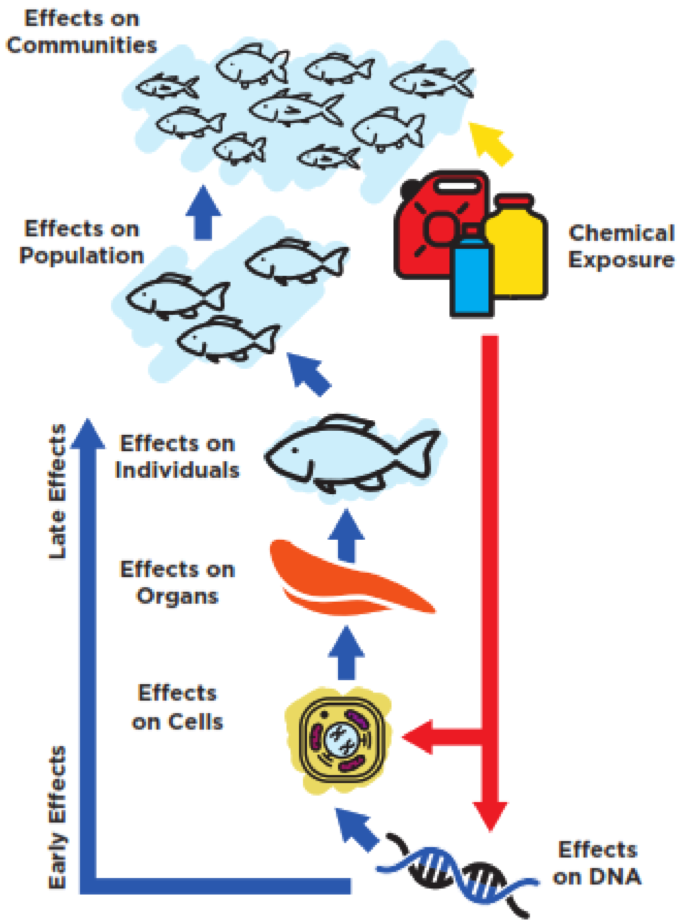


Figure 2. Example of effects, starting at the molecular level and moving up to communities.

<u>Baseline/impacts/restoration monitoring- species identification eDNA</u>

Genomic data replicates traditional information- *comfort/lower risk*

Analogous for microbial communities

- soil reclamation/monitoring
- effluent treatment

<u>'Health indicators' as early warning system</u>

- Sub-lethal effects at sub-organism/molecular level
- Proteomics, metabolomics, transcriptomics, etc.
- *Little adoption at regulatory level*

Source: [SETAC] Society of Environmental Toxicology and Chemistry. 2019. Technical Issue Paper: Omics: Complete Systems, Complete Analyses. Pensacola (FL): SETAC. 4 pp.

Highest Potential for near future widespread adoption: Species identification via eDNA and metabarcoding

Environmental DNA (eDNA)

- naturally occurring genetic materials collected from the environment
- skin cells, gametes, feathers, hair, feces, urine, mucous, egg plasma, etc.

Photos: J Hobbs

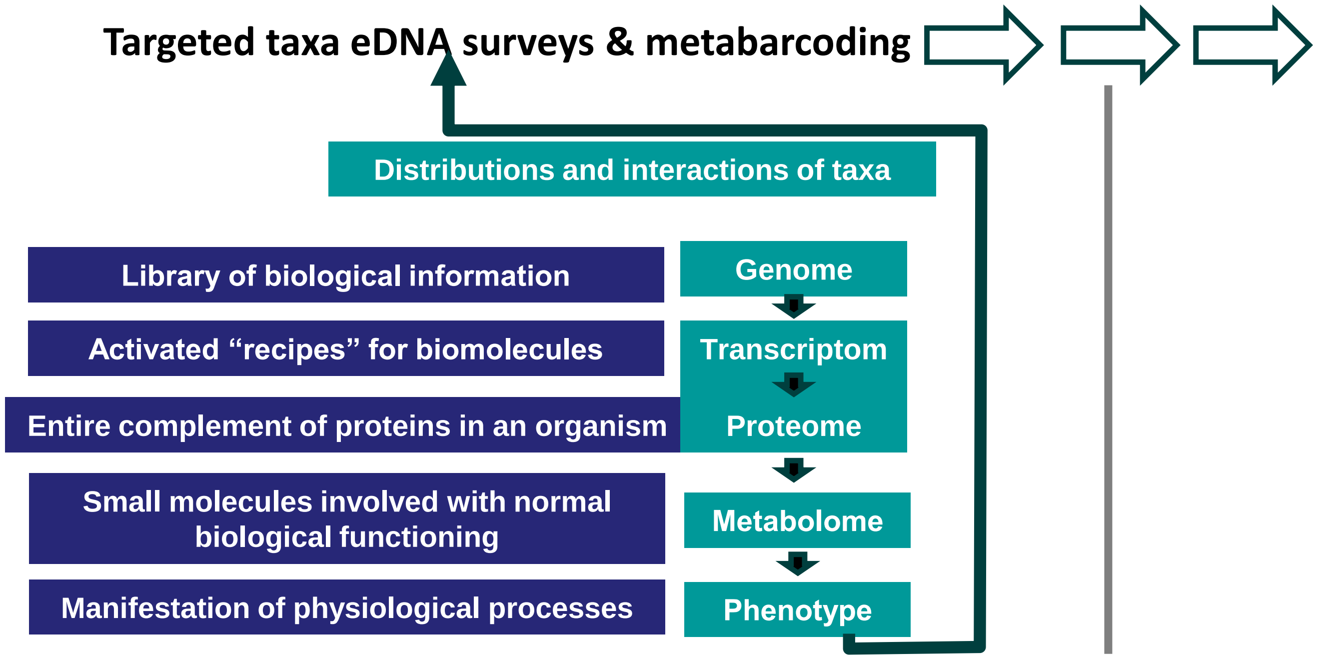


Figure 1. Example of a cascade of interactions among some of the main biological molecules in organisms

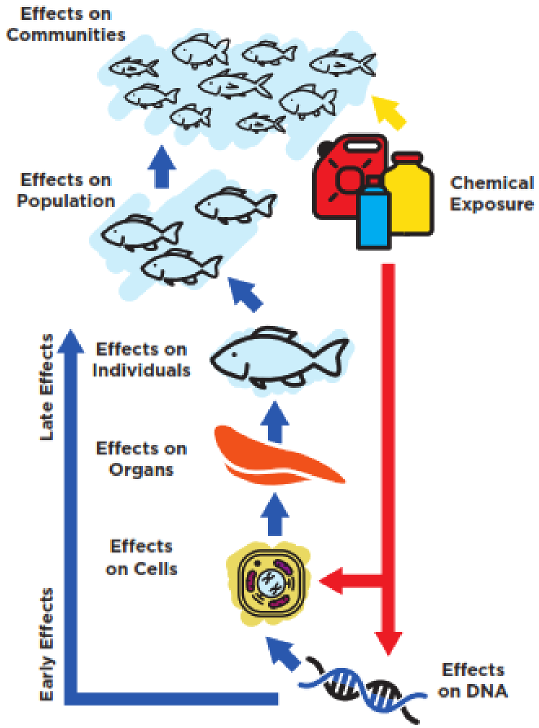


Figure 2. Example of effects, starting at the molecular level and moving up to communities.

Source: [SETAC] Society of Environmental Toxicology and Chemistry. 2019. Technical Issue Paper: Omics: Complete Systems, Complete Analyses. Pensacola (FL): SETAC. 4 pp.

Major Advantages of eDNA from water sample vs traditional

- Less invasive, low risk of pathogen transfer
- More sensitive
- Multiple species simultaneously
- Archive samples
- Faster, cheaper

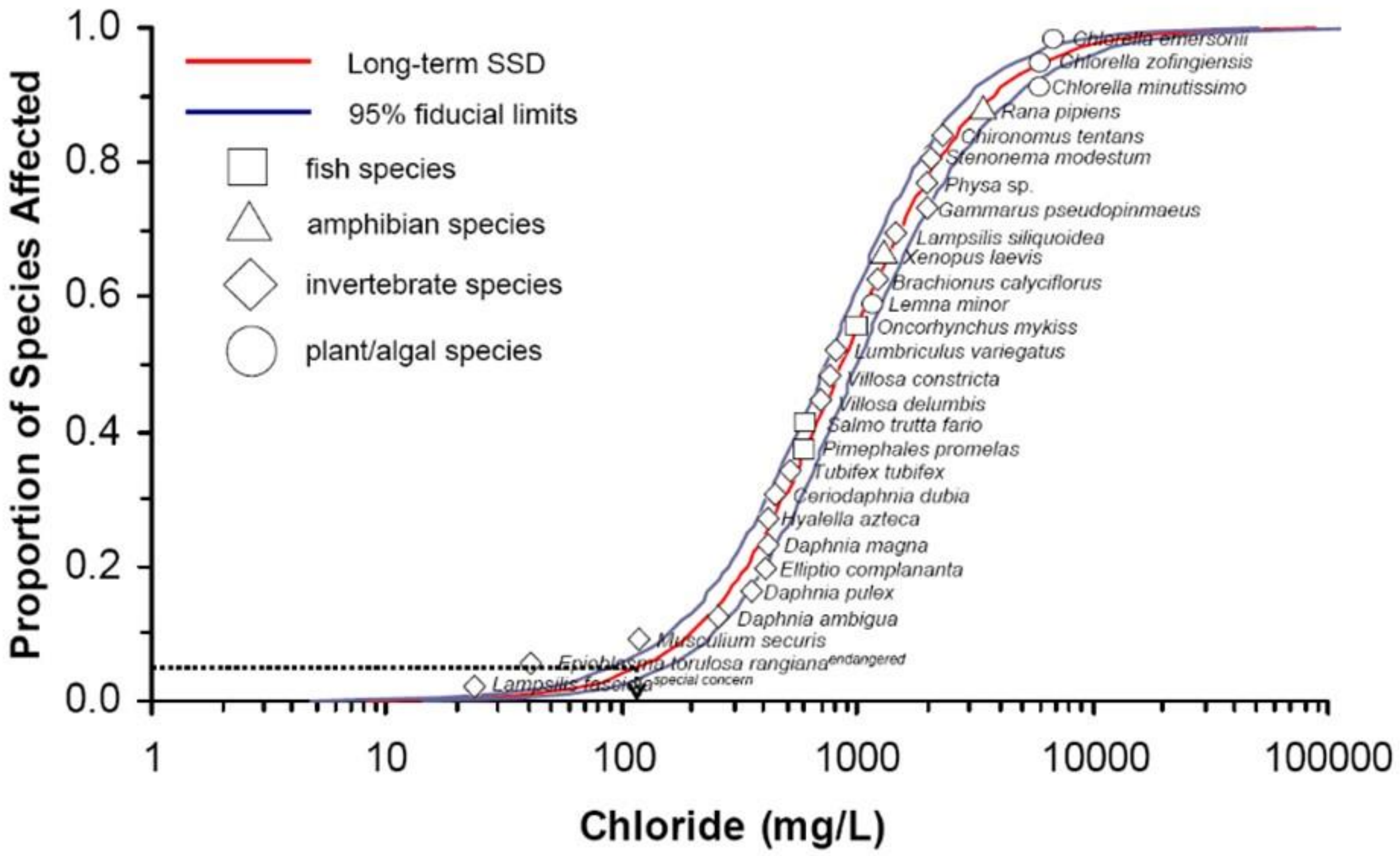
Thus can collect more spatial and temporal data
Better data-> better informed decisions

Photo: J Hobbs

Major Disadvantage eDNA/barcoding

- Presence/absence – species richness data only, **NO abundance**
  - Limits data interpretation
  - Insufficient data for use of certain ecological indices

Species Sensitivity Distribution
Risk-based thresholds of effects

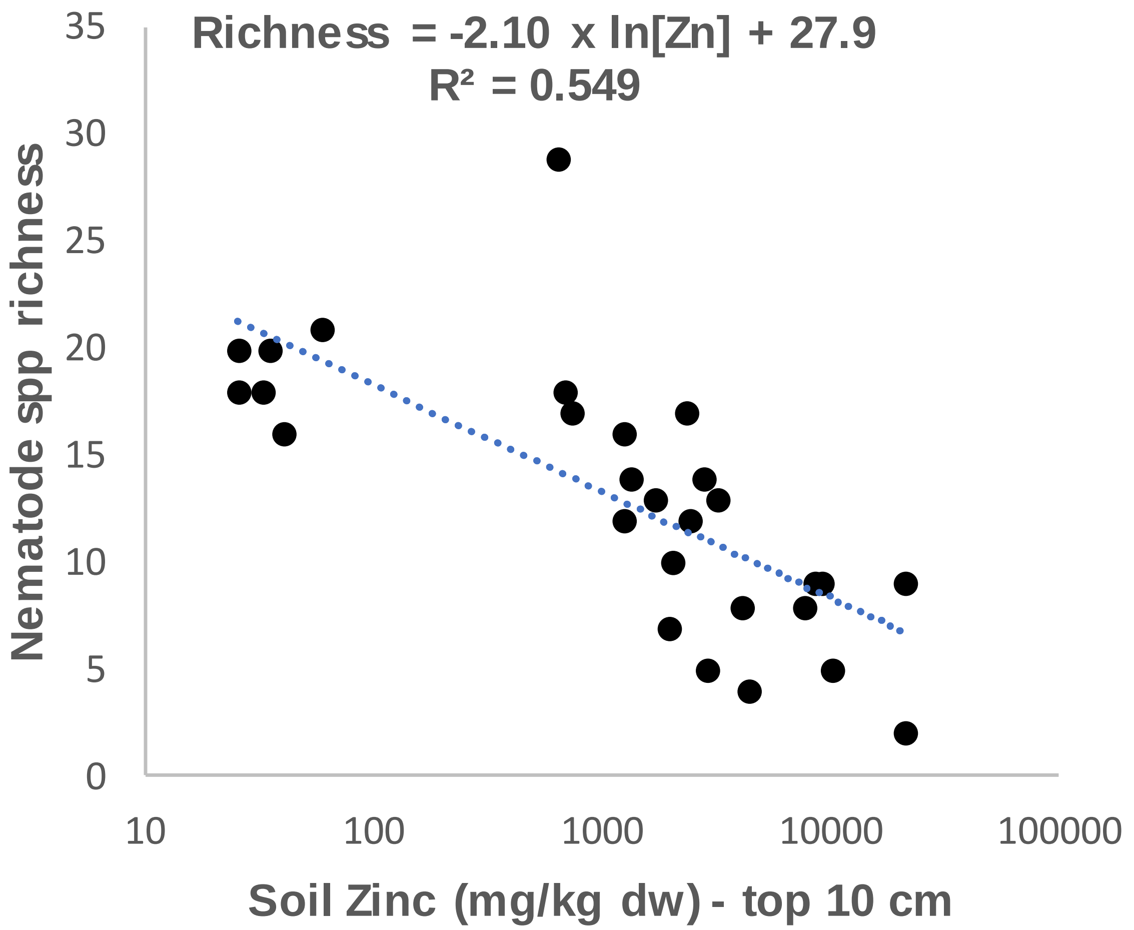


Toxicant-tolerant versus toxicant-sensitive species to assess impacts

Presence/absence spp. data sufficient

Source: [CCME] Canadian Council of Ministers of the Environment, 2011. Scientific Criteria Document for the Development of a CWQG for the Protection of Aquatic Life: Chloride Ion.

Presence data for specific taxa permit rapid bioassessments of ecological risks



Provided by D. Bright

Freshwater stream invertebrate impact metrics

Metric	Reference	Requires Abundance Data?
Multivariate analyses (Reference Condition Approach, …)	Various	YES
Total no. of different taxa	Karr & Chu, 1999	NO
Total no. of Ephemeroptera taxa	Karr & Chu, 1999	NO
% (rel. abundance) of Ephemeroptera	Maxted *et al.* 2000	YES
Total no. of Plecoptera taxa	Karr & Chu, 1999	NO
Total no. of Trichoptera taxa	Karr & Chu, 1999	NO
Total no. of Diptera taxa	Karr & Chu, 1999	NO
No. of long-lived taxa	Karr & Chu, 1999	NO
% Diptera and non-insects	DeShon 1995	YES
% Dipterans	Maxted *et al.* 2000	YES
% non-insects	Maxted *et al.* 2000	YES
Total no. of intolerant taxa	Karr & Chu, 1999	NO
% tolerants	Karr & Chu, 1999	YES
% sediment tolerants or intolerants	Zweig & Rabeni 2001	YES
% oligochaetes	Maxted *et al.* 2000	YES
Hilsenhoff Biotic Index	Maxted *et al.* 2000	YES
% predators	Karr & Chu, 1999	YES
Total no. of clinger taxa	Karr & Chu, 1999	NO
% clingers	Maxted *et al.* 2000	YES
% dominance (top 3 taxa)	Karr & Chu, 1999	YES

Provided by D. Bright

Conclusions

- **Species identification (eDNA & metabarcoding)**
  - Presence/absence data value for ecotox
  - Lack of abundance data greatest limitation

- **Genomic ecosystem health indicators**
  - High potential to inform decision-making
  - Challenges with adoption by sector and regulators

Potential Socio-Economic impact of Application of Genomics to Ecotoxicology

- Timely Informed Decision Making by Environmental Managers & Regulators
  - Genomic approach- less invasive, lower risk alien species introduction, more sensitive, rapid, less expensive, larger geographic area
- Regulations -increased obligation to consult First Nations
  - BC Spill Response Regs 2017
  - Fed and provincial EA process
- Integration of Indigenous communities into Ecotoxicology research team
  - Capacity Building
  - Traditional Knowledge paired with Genomic approaches

Questions

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An Ausenco Company

Challenges and Opportunities for Ecotoxicology in Science and Politics

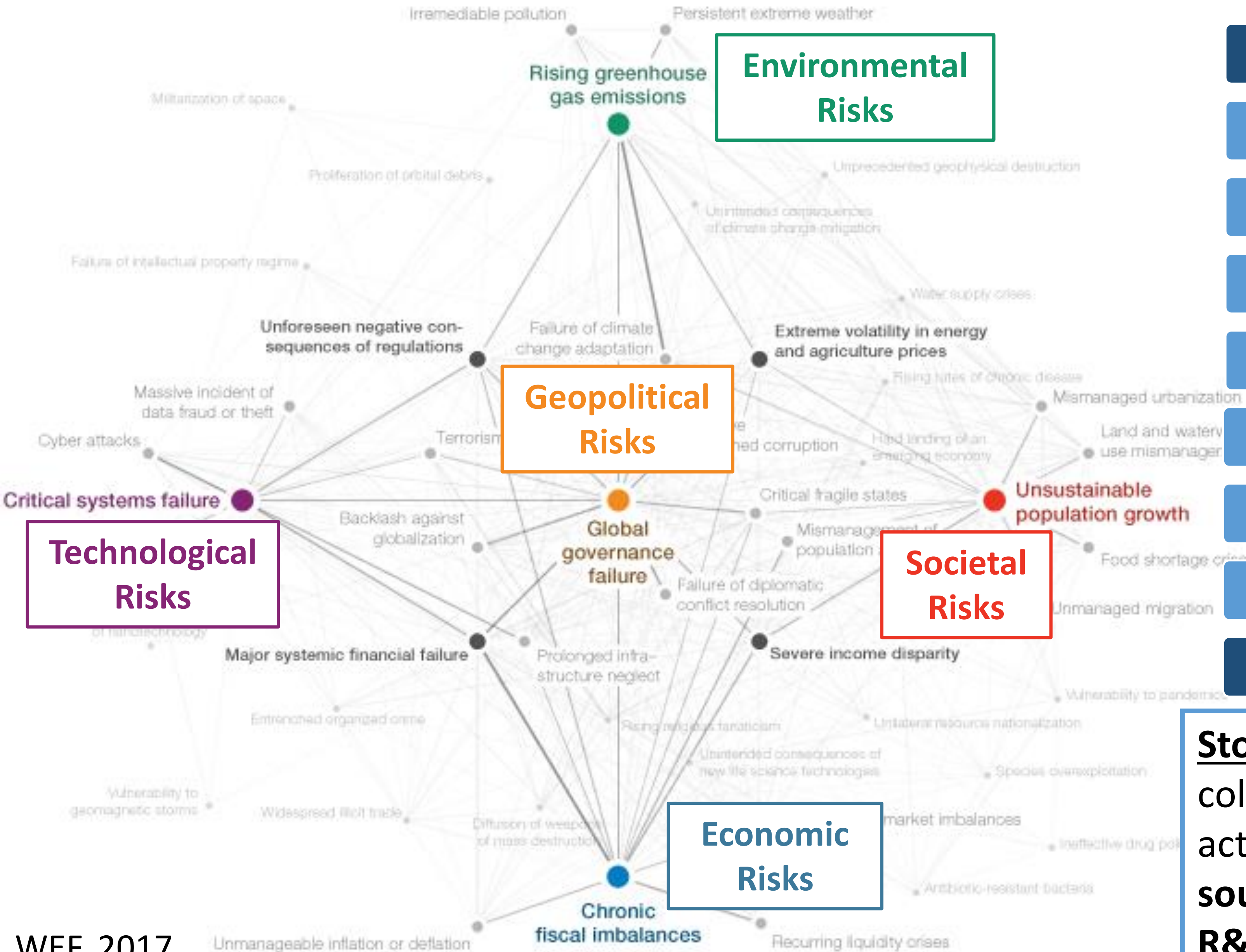
The Honourable Rosa Galvez, PhD, P.Eng, FIC, FCSCE

ParlAmericas

SENATE SÉNAT CANADA

UNIVERSITÉ LAVAL

Global Risks: Cause-Effect Leading to Environmental Problems

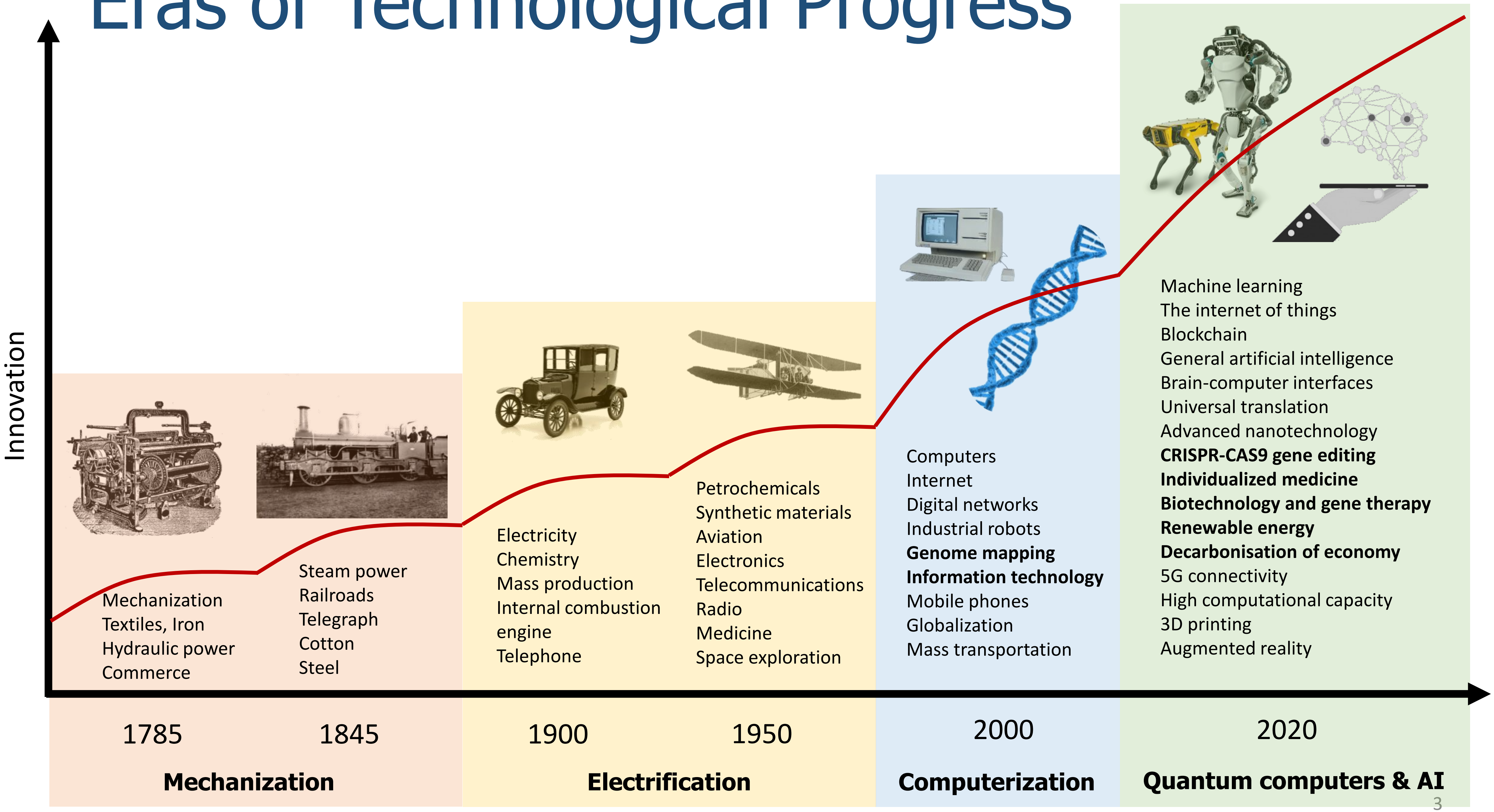


WEF, 2017

- Tax Evasion
- ⬇ Loss of government revenues
- ⬇ Chronic fiscal imbalances
- ⬇ Income disparity, systemic financial failure
- ⬇ Failure in governance
- ⬇ Encourage corruption
- ⬇ Volatility in basic economic sectors
- ⬇ Climate change adaptation becomes more difficult
- ⬇ Increase of GHE, CC & Pollution water, air, soils

Stop the domino effect by organizing collaboration and consolidation of positive actions across all sectors of society - **Tackle sources of problems using SD vision with R&D + Innovation.**

Eras of Technological Progress



Climate Change: Increased Risk to Human and Environmental Health

2017 Fall Reports of the Commissioner of the Environment and Sustainable Development to the Parliament of Canada: Adapting to the Impacts of Climate Change

Human health risks

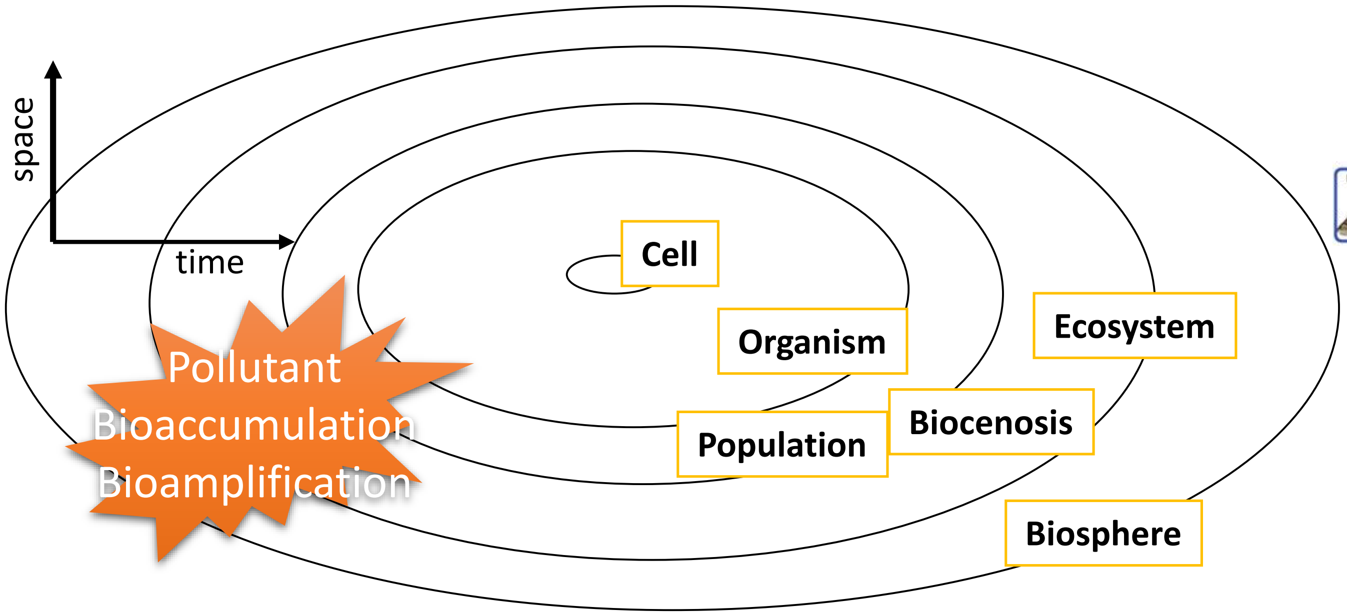
- Dangerous travelling conditions
- Changes in quantity/quality drinking water
- Food security
- Health impacts of changing weather
- Expansion of insect transported diseases
- Respiratory illnesses from forest fires
- Water-born diseases from flood
- Psycho-social impacts from weather disasters
- Heat related illnesses and death

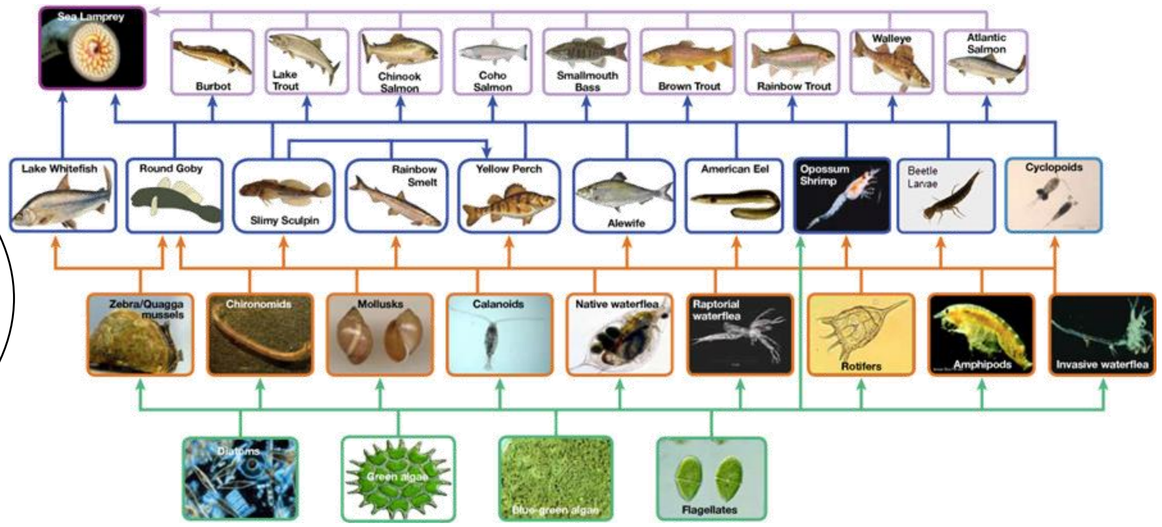
Health Canada, 2008

Wild life risks

- Destruction of habitats by extreme weather events
- Changes in quantity/quality drinking water
- Food security
- Health impacts of warming temperature & precipitation
- New diseases
- Potential for genetic response and adaptation to changes

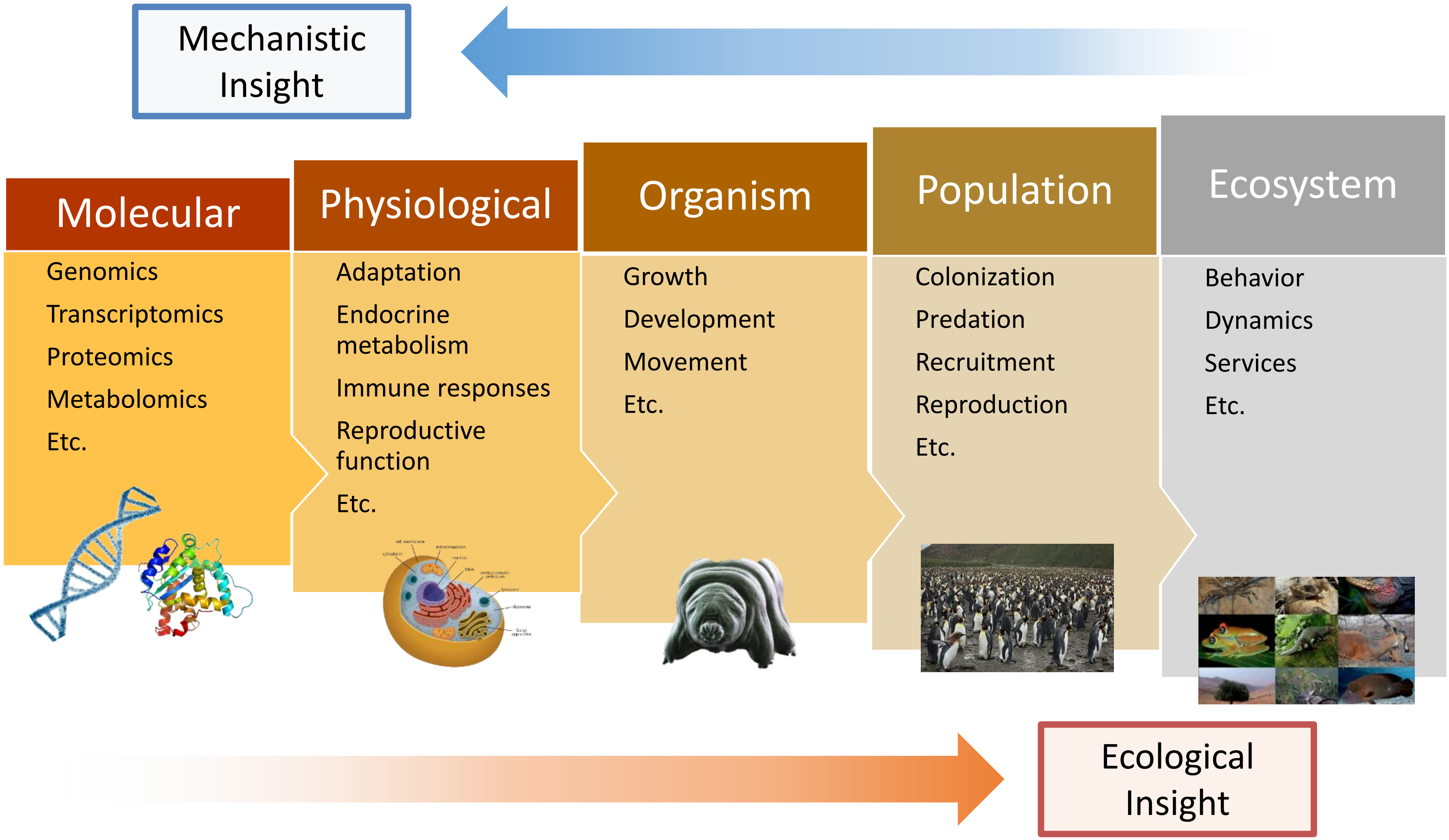
Biological Systems





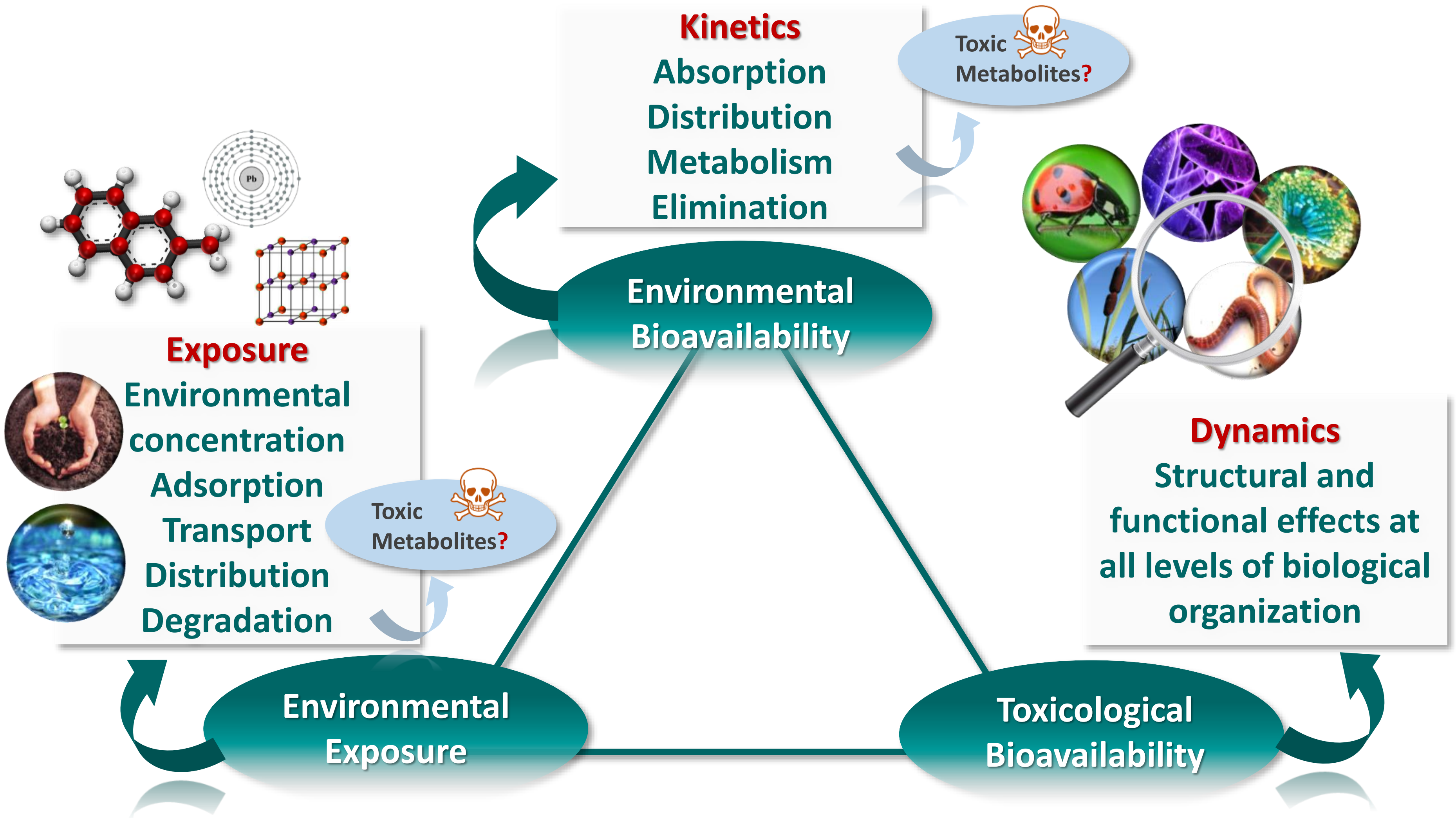
Level	Structure	Function
Cell	tissues, organs	growth, metabolism, detoxification
Organism	species, sex	growth, reproduction, health, behaviour
Population	number, position/chain	fertility, reproduction
Biocenosis	Number of species, dominance, diversity	regulation, equilibrium
Ecosystem	climate, geography	adaptability, stability, reproduction, degradation

Key Opportunities for Genomics in Ecotoxicity



Adapted from Kim et al., 2015

Integrated Evaluation of Ecotoxicology Risks

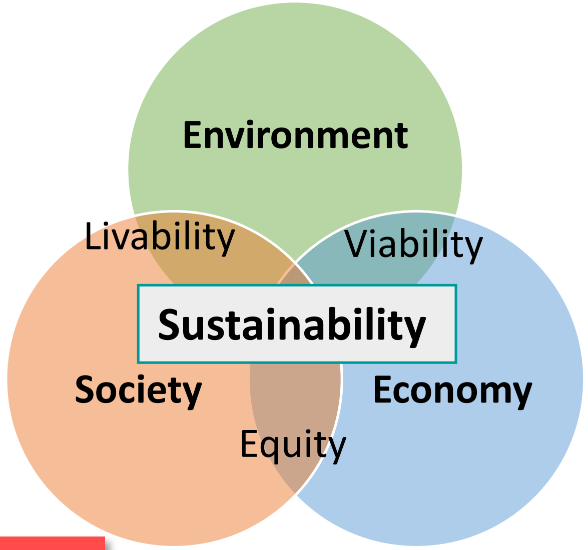


Frische et al. (2003); Peijnenburg et al. (1997)

Research: Remediation of Contaminated Sites in line with the principles of Sustainable Development

Sustainable Development will be (is) at the heart of Government Policy (C-69)

Governments must pay special attention to:
- Harmonious integration of projects in communities where they settle
- Projects made in compliance with environmental guides and criteria
- Consideration of 17 SD Goals



ECOENGINEERING

DESIGN EFFECTIVE AND PRACTICAL METHODS THAT MIMIC NATURAL PROCESSES

BIO LEACHING
Fungal and bacterial mining residues

BIO REMEDIATION
Soils contaminated with hydrocarbons

PHYTO REMEDIATION
With halophytic plants

BIO FILTRATION
Residues of the agri-food industry

<u>My eco-engineering moto</u>:
Learn from nature, work with nature, imitate nature, conserve nature

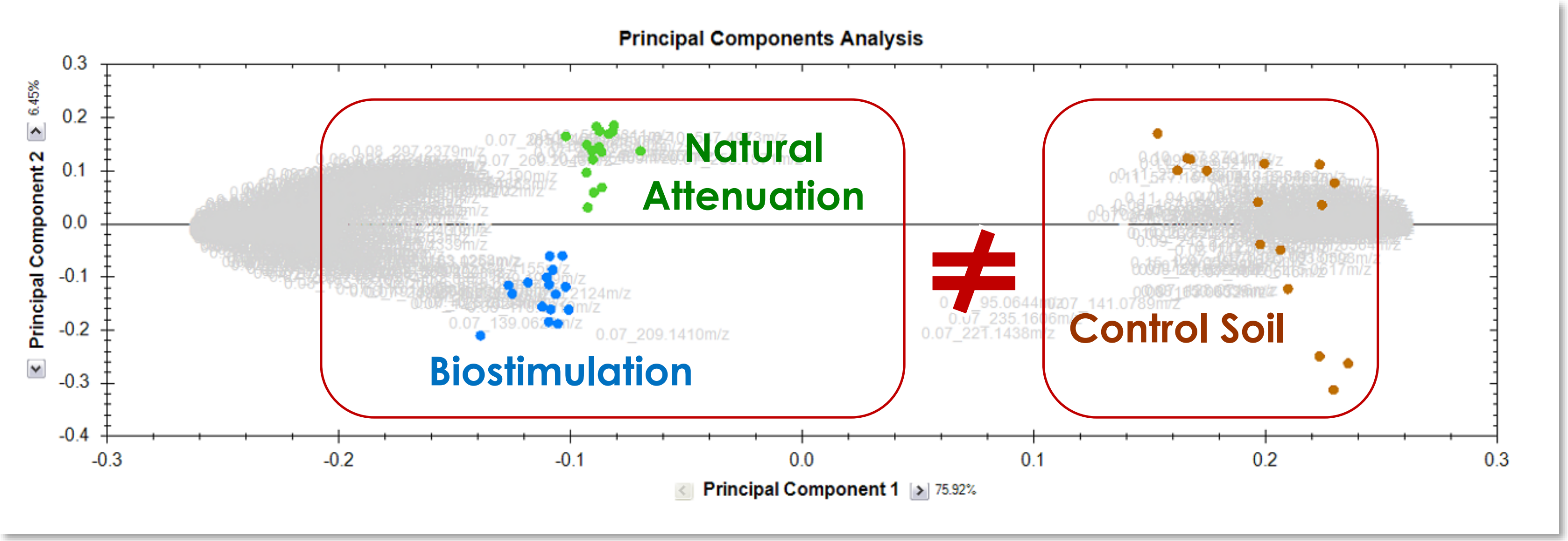
Research: Unconventional Oils – Fate of Pollutants

- The aftermath of multiple accidents and the numerous pipeline projects for the transport of *Dilbit* and *Bakken* oil, highlight the lack of preparedness of cities and governments to deal with unconventional oil emergencies and water sources protection.
- Evidence points out the inability to prevent this type of accident, to timely and efficiently control the hazards, to contain the spread of oil, and to rapidly and efficiently protect the ecosystems and water sources.
- In part this is due to the **physicochemical differences between conventional and unconventional oils** and to **inappropriate spill response and clean-up methods** as oil behavior in the environment is not well understood.

<u>Goal</u>**:** *Develop advanced chemical characterization of unconventional oils, evaluate eco-toxicity and attenuation measures*

Research Example: Metabolomics and Metagenomics

Metabolomic analysis of sequenced soils



Metabolomic analysis allowed differentiation between treatments and control soil but not between natural attenuation and biostimulation, corresponding to that obtained for the TPH degradation rate

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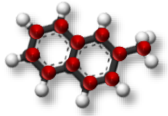
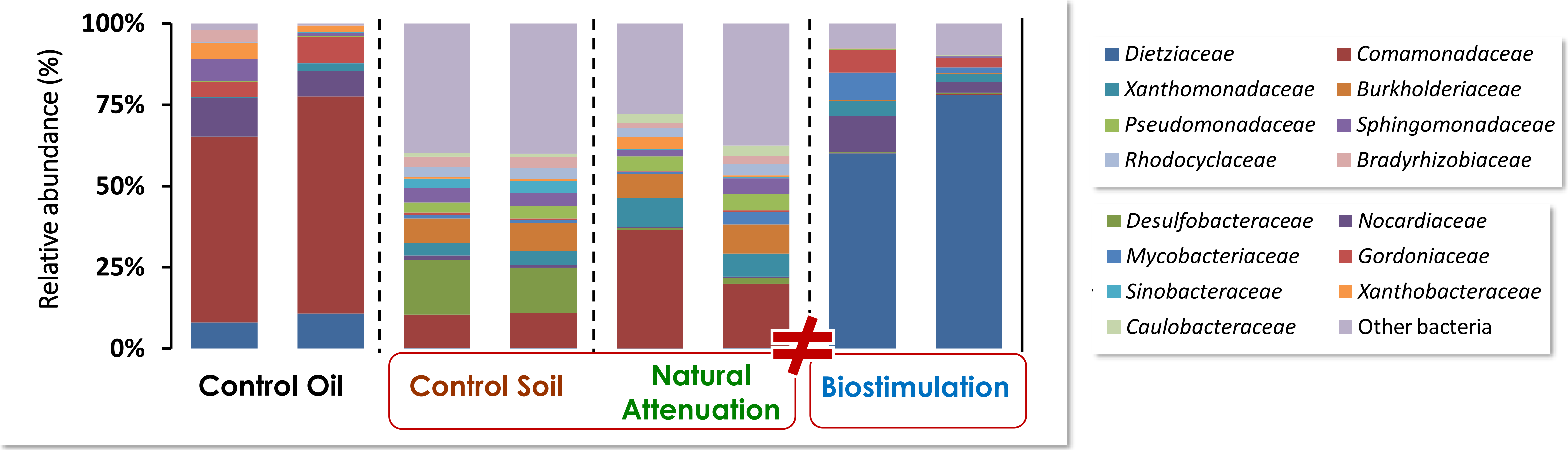
TPH degradation rate



Research Example: Metabolomics and Metagenomics

Bacteria found in soil and oil (Family rank)



- Control soil and natural attenuation showed a similar distribution pattern of microbial families
- Microbial diversity was highly altered during biostimulation process
- This pattern corresponds to that obtained for the CO_2 release

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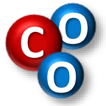
Respirometric analysis



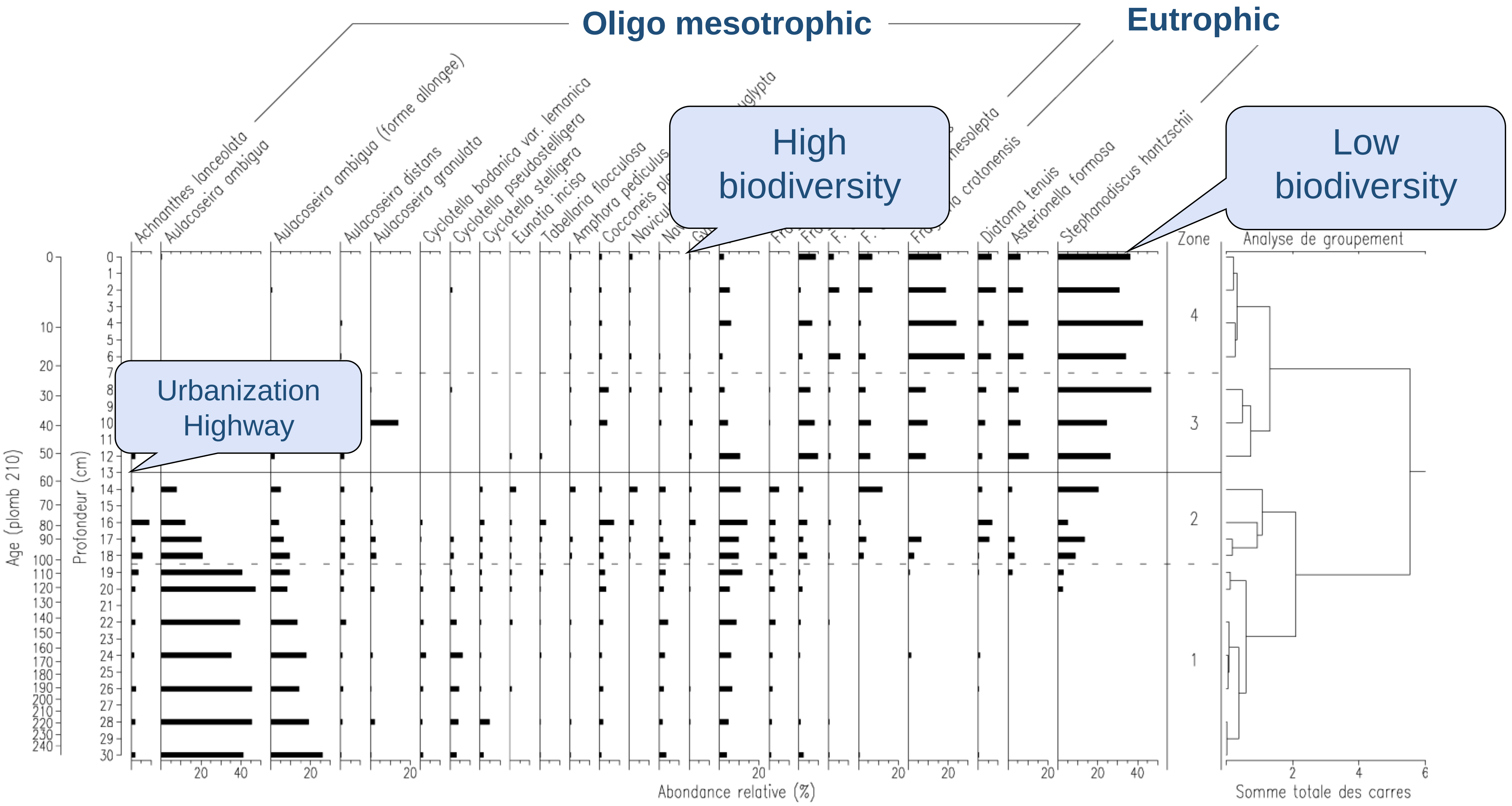
Research example: Increased urbanization and population development around **Lac St-Augustin, Québec City**

Natural environment vs landscaped environment

Historically: Land use has changed from forest to agricultural, from agricultural to urban including a large network of transport.

Today: The lake is in the hyper-eutrophic state, the bottom sediments are contaminated with P and trace metals.

Eutrophication problem - Paleolimnology



Handley, 2019 American Society for Microbiology

Microorganisms can have a profound and varying effect on the chemical character of environments and, thereby, ecological health (Eco-toxicity). Their capacity to consume or transform contaminants leads to contrasting outcomes, such as the dissipation of nutrient pollution via denitrification, the breakdown of spilled oil, or eutrophication via primary producer overgrowth.

Recovering the genomes of organisms directly from the environment is useful to gain insights into resource usage, interspecies collaborations (producers and consumers), and trait acquisition. Microbial data can also be considered alongside the broader biological character of an environment through the co-recovery of eukaryotic DNA. The contributions of individual microorganisms (bacteria, archaea, and protists) to snapshots of ecosystem processes can be determined by integrating genomics with functional methods. This combined approach enables a detailed understanding of how microbial communities drive biogeochemical cycles, and although currently limited by scale, key attributes can be effectively extrapolated with lower-resolution methods to determine wider ecological relevance.

Thank you!

SENATE SÉNAT

CANADA

Genomics in Ecotoxicology:

Defining Canada's strategic opportunities and priorities in the dawn of a future Genome Canada funding competition

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Importance of the ecotoxicology sector to the Quebec's economy

Credit: SDWG

- Ecotoxicology - the study of toxicology within an ecological context
    - Relevant to the "**One Health**" concept – multisectoral approach
    - As both a retrospective study (e.g., identify what are the chemical stressors in the environment) and a prospective study (e.g., predict what the ecological and health effects could be) ecotoxicological research is essential to understanding human impacts on the environment in Canada and elsewhere.
- Ecosystems provide **services of economic value** and preserving their biodiversity allows for ecological resilience to disturbances such as climate change
- E.g., in Canada:
    - Boreal forest - CAN $93 billion in 2006
    - Wildlife- and nature-related activities - CAN $11.4 billion in 1996
    - Fishing, hunting, trapping, and sport-shooting activities CAN $18.9 billion in 2018
    - Example ecosystem: the 54,800 km^2 Manicouagan-Uapishka World Biosphere Reserve (Qc) CAN $1.3 billion per year

Current state of the sector

Credit: TOXMSDT

- **Traditional techniques** - toxic effects from contaminant exposure are evident throughout all levels of biological organization from molecular to population levels

- **Novel high-throughput genomic tools** - assess exposure and effect at the molecular, cellular, and individual levels with a focus on aquatic species

- **Some examples of recent research initiatives:**
  - study the transcriptome anchored in a toxin-induced phenotype
  - link molecular initiating events with adverse outcomes at the population or ecosystem levels
  - identify the mechanism of action for many chemicals across many species with the goal of understanding toxicity and predicting sensitivity (e.g., EcoToxChip)

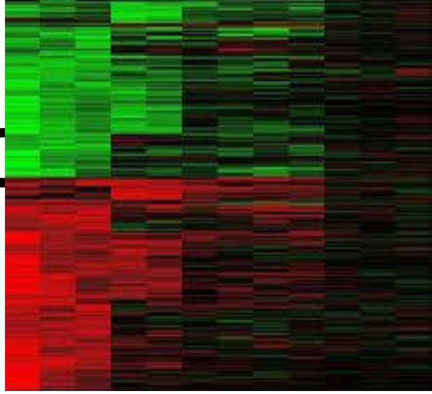
- However, there is still a lack of definite identification of factors responsible for these health effects to relate to ecological aspects

Sector challenges and opportunities

Credit: CPA

- One of the greatest challenges with ecotoxicology in recent years is **how to evaluate and predict the ecosystem response** to environmental contaminants
- We are currently experiencing massive **biodiversity declines** describing the 6th mass extinction with a large driver being **climate change**
  - How will these **multiple stressors** impact ecotoxicological parameters?
  - For example, how will organisms respond to a human impacted event (e.g., pesticide use, oil transport, water quality) in the face of climate change?
- The technology currently available for ecotoxicological research has allowed for the generation of **large amounts of data** to understand how individuals are responding to contaminant exposure

The role of genomics in addressing the sec challenges



- **Ecotoxicogenomics** - using ‘omic tools in an ecological and environmental context to assess the ecosystem’s response to contaminant exposure

- using ecotoxicogenomics in a **regulatory decision framework** is well acknowledged
  - for monitoring purposes (recovery and remediation)
  - in ecological impact and risk assessments

- the **challenge** remains of **linking the changes** we see at the genomics level with adverse outcomes and relaying this information to end-users, including government, regulatory officials, industrial partners, and First Nations communities

- the large amount of molecular data helps to understand the mechanism of action for environmental contaminants.
  - can identify potential biomarkers to predict adverse outcomes to build **AOP**s
  - allows for a high throughput assessment of response in key toxicity pathways and can be a **proactive approach** to help inform **“greener” design in industry** (e.g., for pesticides, pharmaceuticals)

Approach

Credit: WGH

- To continue ecotoxicogenomic research with consideration of biodiversity declines and climate change, there is a need for advancing genomic science to include more ecologically and economically relevant species (e.g., **genome sequencing for non-model species**)
  - studies in the **terrestrial environment** in addition to the aquatic environment to broaden the scope of ecosystem coverage
- To develop and evaluate alternative toxicity methods and **non-invasive sampling** techniques.
  - *in vitro* toxicity testing
  - DNA barcoding or environmental DNA (eDNA)
- To **validate** the new fast-developing genomic tools with old toxicological techniques
  - Curate data into biological databases
  - Develop novel, artificial intelligence-based bioinformatic pipelines to analyze, integrate, and interpret the data
- To improve the **translation** and relevance of ecotoxicogenomic data to end-users through community-driven integration and partnerships
  - First Nations communities, National Parks and Conservation Areas Managers, NGOs, government and industrial partners, and social scientists in the early stage of research development

Conclusion

Credit: GCNDDB

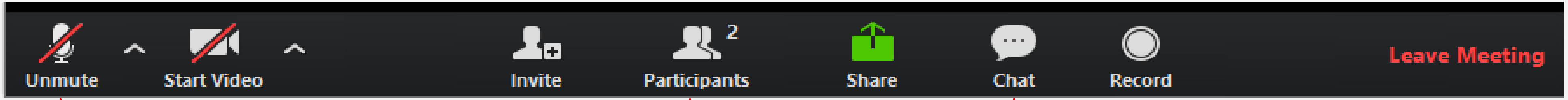
- There is a need to assess the **interactions between genes and the environment**
- There is a need to expand the scope to include the **whole ecosystem**, and in particular ecologically- and economically-important plants and animals
- **Impact and risk management decisions** are continually being made thus advancing genomic research in the context of ecology and the environment can provide evidence to increase confidence and reduce the risk for all of Canada

Discussion Participation

Webinar Participation Instructions

- Please keep yourself on **Mute** during the session unless you would like to contribute.

Zoom Toolbar:

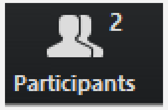


Mute or unmute your microphone

View Participants

Chat box

- To indicate you would like to speak or comment, please **raise your hand** or use the **chat box**. The moderator will go through the list and prompt you to speak. Wait for the cue from the moderator to **Unmute** yourself.

- To **raise your hand**, click on 

in the bottom toolbar. The participant window will open. At the bottom of that window, click the Raise Hand icon.

2020 LSARP Stakeholder Consultation Themes

- Ontario Genomics – BioManufacturing (November 26, 2019)
- Genome Prairie – Conservation and Wildlife Management (November 28, 2019)

Next steps

- Production of a report capturing information generated at CEW and this consultation session
- Compilation of reports from different consultation sessions into one document (to be made public by the end of the year)
- Production of guidelines for the competition: Request for Applications
- Launch of 2020 LSARP competition in the New Year

On behalf of the Genomic Enterprise,

Thank you for your participation in this session!