ECOTOXICOLOGICAL RISK ASSESSMENT OF MICROPLASTICS IN MARINE ARCTIC ENVIRONMENT

by

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A Thesis Submitted to the

School of Graduate Studies

in partial fulfilment of the requirements for the degree of

Master of Engineering

Faculty of Engineering and Applied Science

MEMORIAL UNIVERSITY

Memorial University of Newfoundland

March 2023

St. John's Newfoundland and Labrador.

Abstract

The last few decades have witnessed an exponential increase in plastic production and consumption. The inexorable increase in microplastic accumulation, particularly in the Arctic waters, has become a major environmental concern. Discarded plastics degrade in the environment due to natural forces like wind, waves, and heat into smaller pieces. Plastic fragments produced or decomposed into a size range of 1 μm to 5 mm diameter are termed microplastics. Plastic debris travels through various environmental media before eventually reaching the oceans. In the various oceans, they travel along oceanic currents reaching the Arctic, where they get trapped in the Arctic ice. Moreover, local maritime operations like fishing, tourism, shipping, hydrocarbon exploration, and aquaculture also contribute to the microplastic accumulation in the Arctic waters.

Microplastics are a complex group of pollutants containing plastic polymer, various stabilizing chemicals intentionally added during their production process and numerous other chemicals sorbed while being in the environment owing to their high surface area. These chemicals collectively enhance the toxicity of microplastics. The omnipresent microplastics possess characteristics such as toxicity, long-range mobility, bioaccumulative nature, and environmental persistence. The interaction of such an intricate pollutant like microplastic in the intriguing Arctic environment characterized by a ubiquitous sea-ice presence, extreme light regime, and unique species dwelling in makes them a serious threat to the Arctic marine ecosystem and the biota inhabiting it.

Despite the pressing nature of this concern, there is a paucity of literature on microplastics and a dearth of research on investigating the associated risk. The work presented here assesses the risk posed by microplastics in the pristine and sensitive Arctic region. This thesis comprises two main

contributions. Firstly, it develops an ecotoxicological risk model in polar cod (Boreogadus saida), a pivotal species of the Arctic food web, due to microplastic ingestion. Secondly, it assesses the human health risk due to microplastic prevalence in the Arctic waters. People dependent on the food sources from the Arctic ecosystem, mainly the indigenous people living in the remote Arctic communities, are exposed to higher risk due to limited medical resources and weaker immune systems. The study first identifies all the factors affecting microplastic intake in the polar cod and humans in the Arctic region. Then the response induced is ascertained. Subsequently, Bayesian Network, a probabilistic graphical modeling technique, is employed to assess ecotoxicity.

The study will augment the understanding of the interaction of microplastic with the environment. Further, it will enhance the understanding of ecotoxicological risks in marine life and humans associated with microplastic ingestion. This study will also aid in the development of more effective risk management strategies and policies.

Acknowledgement

In the name of Allah, the Most Beneficent and the Most Merciful. All praise be to Allah alone and many salutations upon His noble prophet Muhammad peace be upon him.

I was able to complete the task as it is presented here with the assistance and ever-going encouragement from my supervisors, Dr. Faisal Khan, Dr. Bing Chen and Dr. Rehan Sadiq. Their vast research expertise and knowledge have inspired me to thoroughly investigate the problem I have addressed in this thesis. They steered me in the right direction at all stages and trained me to conduct successful research while maintaining high standards. I want to thank Dr. Faisal Khan again for inviting me to work at Mary Kay O'Connor Process Safety Centre (MKOPSC) at Texas A&M University.

I would like to acknowledge the financial support provided by the Natural Sciences and Engineering Council of Canada (NSERC) through the CREATE program. I appreciate Dr. Faisal Fahd and Dr. Zohra Halim's encouragement during my research, as well as their conversations with me that gave me new perspectives and insightful opinions. I want to express my gratitude to all the C-RISE and MKOPSC participants who encouraged and supported me during my efforts.

I wish to express my gratitude to my friends for their inspiration and fortitude in trying circumstances. Any work of mine is incomplete without mentioning the contributions of my parents and siblings. I thank them all for the love and affection bestowed upon me.

I dedicate this thesis to my parents for the countless efforts they put in to carve me.

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List of symbols, Nomenclature and Abbreviations

MP	Microplastic
BN	Bayesian Network
CEAC	Contaminants of Emerging Arctic Concern
ROS	Reactive Oxygen Species
EP	Emerging Pollutants
RBSL	Risk - Based Screening Levels
SSTL	Site - Specific Screening Levels
TK	Toxicokinetic
TD	Toxicodynamic
OOBN	Object Oriented Bayesian Network
ADME	Absorption, Distribution, Metabolism, and Elimination
GSH	Glutathione
GST	Glutathione S-transferases enzyme
CYP	Cytochromes P450
EROD	Ethoxyresorufin-O-deethylase
IELCR	Incremental Excess Lifetime Cancer Risk
LADD	Lifetime Average Daily Dose
CSF	Cancer Slope Factor
XME	Xenobiotic Metabolizing Enzymes
UGT	Uridine diphosphate (UDP)-glucuronosyltransferases

1 INTRODUCTION

1.1 Authorship Statement

The principal author of this thesis is Mohammad Sadiq Saeed, who also wrote the first drafts of the two manuscripts incorporated in chapters 2 and 3. The co-author of this thesis, Professor Faisal Khan, provided direction and vetted all the ideas proposed in it. The co-author of this thesis, Professor Bing Chen, offered guidance and technical advice. Professor Rehan Sadiq, another co-author, provided guidance and assistance in addressing technical issues. In addition to the aforementioned, the other co-authors contributed to the review and revision of both manuscripts.

1.2 Overview

Plastics are a diverse group of organic compounds made by the polymerization of monomers derived from fossil fuels such as coal and natural gas (Derraik, 2002). While soft, plastics can be moulded into any rigid shape. The exponential increase in global plastic production and consumption is overwhelming the earth. The rate of plastic production has been the highest among all materials since the 1970s (UNEP). Low prices, coupled with properties like flexibility, longevity, resilience, and durability, have made plastics indispensable. Plastic production witnessed a remarkable 230-fold increase from 1950 to 2019. The figures touched a record 460 million tonnes in the latter year as against 2 million tonnes in the former (Bibas et al., 2022). If the current trends continue, global plastic production is projected to reach 1,100 million tonnes by 2050 (UNEP). The popularity of single-use plastics has made the situation even worse. After being discarded in the environment, they move through various media to eventually reach oceans. According to the UNEP, 2022b, 11 million tonnes of plastics reach the world's oceans each year. Proper handling of this ever-increasing plastic waste, particularly its safe disposal, has thus posed a big challenge.

Plastics are durable and tend to persist for a long time in the environment. The action of various degradation forces, such as sunlight, wind, water currents, temperature gradients etc., fragments them into smaller pieces. When they attain size in between 5 mm to 1 µm, they are termed microplastics (Frias & Nash, 2019). Microplastics are typically composed of three broad groups of pollutants. First is the plastic polymer itself. There are certain stabilizing chemicals added to plastics during their production. Third, the higher surface area due to micro size makes them conducive to sorb various contaminants from the surroundings, including heavy metals and polycyclic aromatic hydrocarbons (PAH), many of which are carcinogens (Amelia et al., 2021). Further, these toxic microplastics have bioaccumulative nature. Their ability of long-range transportation makes them move to remote and uninhabited places like the Arctic, wherein they get trapped in the ice (Bergmann et al., 2019). Immobility due to ice trapping, along with human and animal toxicity, makes them a threat to the whole Arctic ecosystem.

Microplastics are classified as an emerging pollutant (EP) or a contaminant of emerging concern (CEC), particularly threatening the marine ecosystem (Rubio-Armendáriz et al., 2022a). EPs or CECs are described as recently identified chemicals that have the potential to compromise the ecology and induce pernicious effects in humans and animals (UNEP, 2022a). EPs are currently not regulated by any legislative body (Congressional Research Service, 2021). Plastic pollution is thus an exigent environmental concern, particularly in the marine environment, as it jeopardizes the health of species inhabiting it. It also imperils the health of the human communities dependent on the marine ecosystem for food. Hence, assessing the risk posed by them to the marine biota and humans is paramount, particularly in the otherwise unblemished Arctic region.

1.3 Arctic Region

The geographical region circumpassing the north pole is considered the Arctic region in common parlance. It can be defined in multiple ways. In a narrow sense, it is the region above the Arctic circle (66°33’49” N). In terms of temperature, the Arctic region is defined as the area above the $10°C$ isotherm. The Arctic can also be defined as a region along the convergence of salty and warm southern waters with the fresh and cold Arctic waters. Further, the area north of the Arctic treeline boundary is deemed a terrestrial Arctic region. The Arctic treeline boundary is the last northern latitude where trees can grow and sustain (Murray Janine L. et al., 1998).

Historically, the Arctic region had little to no anthropogenic activity, making it one of the most pristine places on the planet. Nevertheless, the buildup of microplastics and several other contaminants flowing from all across the planet has posed a serious threat to the local environment and the species inhabiting it (Bergmann et al., 2022). The surge in human activities in the region in recent years has exacerbated the problem. The Arctic region is crucial for the fragile ecosystem of our planet as it is at the forefront of climate change (Julia Nesheiwat, 2021). Deleterious effects on the environment due to the accumulation of pollutants, including microplastics, are pronounced in the Arctic region (Arctic Council) due to polar amplification., The Arctic region experiences the effects of climate change before the rest of the planet and thus is ideal for studying to predict the planetary future.

The Arctic is characterized by many unique and peculiar features like the presence of sea ice, harsh weather conditions, elongated winters having little to no sunlight and prolonged sunlight during summers (Berge et al., 2015). The species inhabiting the region have very different physiology from their temperate counterparts. These idiosyncrasies of the Arctic region make the feeding behaviour of organisms and the overall functioning of the food chain very eccentric (Andersen et al., 2015; Nahrgang et al., 2010).

1.4 Environmental Risk Assessment

EPA defines risk as the likelihood of developing adverse effects in biota, humans, or ecosystems stemming from exposure to a contaminant. To ensure safety of human and animal life, it is important to assess the associated risk. It entails using a methodical approach to analyze and assess the likelihood and potential consequences of an unwanted event, and then putting methods in place to control or mitigate it. Mathematically, risk is the product of the likelihood of an event times the severity of its consequences (EPA, 2022a).

$$Risk = Exposure\ probability \times Severity\ of\ consequence \qquad \textit{Equation 1.1}$$

Ecotoxicological risk assessment is a process of assessing the potential harmful effects induced by any xenobiotic on an ecosystem and the organisms inhabiting it. This thesis focuses on microplastic as a xenobiotic in the Arctic ecosystem. The induced detrimental effects of microplastics in the organisms within the Arctic ecosystem are ascertained by estimating the cytotoxicity in polar cod and carcinogenicity in humans. The thesis attempts to present risk assessment models due to microplastic exposure that are attuned to the environmental and geophysical conditions of the Arctic region. Ecotoxicological risk assessment is a four-step process involving hazard identification, exposure assessment, response assessment and risk characterization (EPA, 2022b).

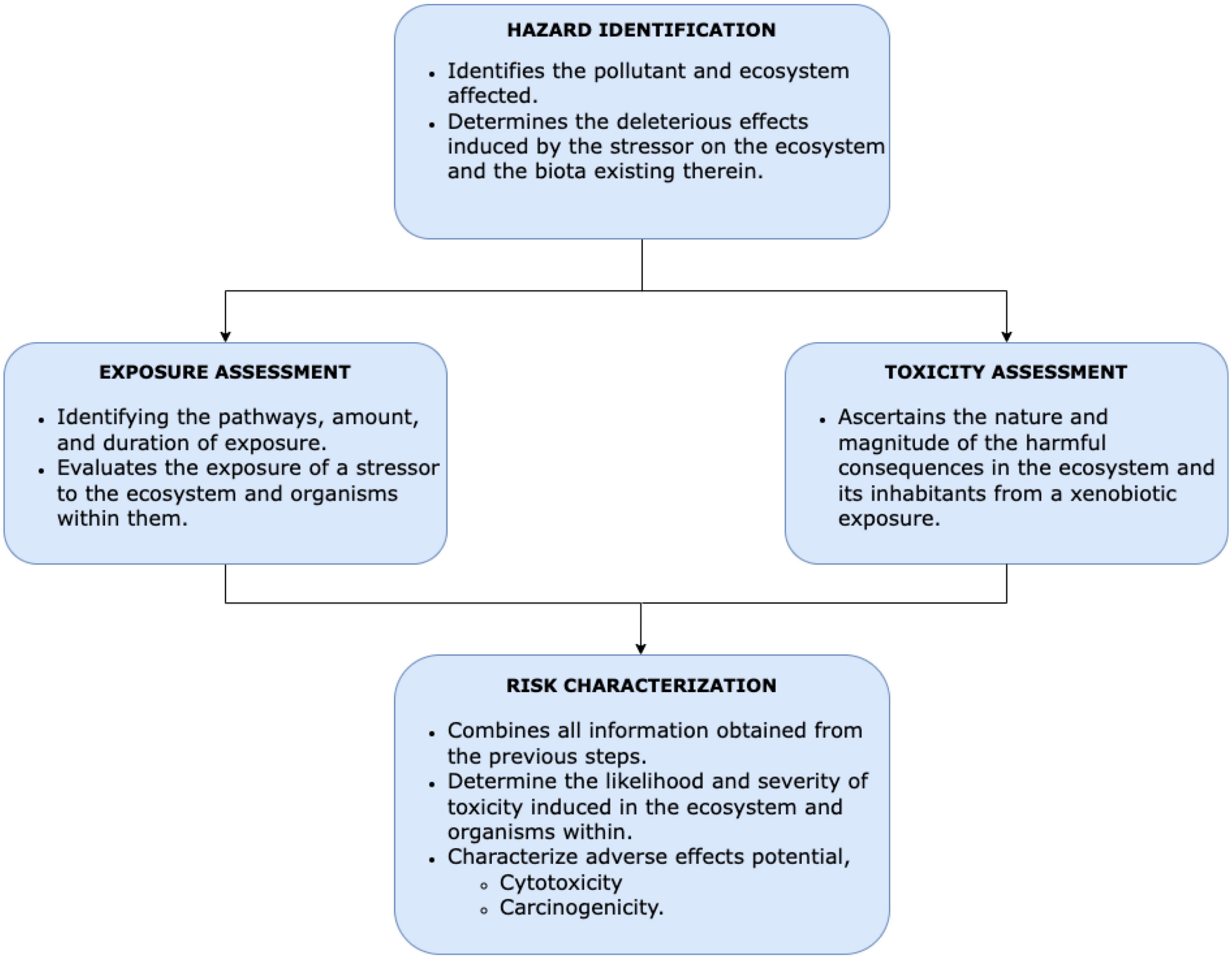

Figure 1.1 Components of ecotoxicological risk assessment

Hazard Identification: This step involves determining the deleterious effects, such as cell death and formation of cancer cells induced by a stressor on the ecosystem and the biota existing therein.

Exposure Assessment: This step evaluates the exposure of a stressor to the ecosystem and organisms within them by identifying the pathways, amount, and duration of exposure.

Toxicity Assessment: This step ascertains the nature and magnitude of the harmful consequences in the ecosystem and its inhabitants from xenobiotic exposure.

Risk Characterization: This step combines all the information obtained from previous steps to determine the likelihood and severity of harmful responses induced in the ecosystem and organisms. It also tries to identify any uncertainties associated with the assessment.

Ecotoxicological risk assessment helps better manage a pollutant by aiding in developing the safe regulation policies of a given chemical stressor. It also guides in formulating risk mitigation strategies. This study assesses the ecotoxicological risk in polar cod and human beings inhabiting the Arctic region due to the exposure of microplastics using Bayesian Network technique. A Bayesian Network is a directed acyclic graph which satisfies Markovian condition. In simple words, a Bayesian Network is a probabilistic graphical model that depicts variables and their conditional dependencies via a directed acyclic graph.

1.5 Research Motivation and Objective

The motivation for this work stems from the meagreness of research on microplastic toxicity on marine biota and humans, particularly in the limpid Arctic waters. The objective of the study is to investigate the toxic effects induced by microplastics in the Arctic marine biota and human communities dependent on local food sources, mainly indigenous people of the Arctic. Traditionally such an objective can be achieved by performing toxicity assays. However, the toxicity data on Arctic biota are thin on the ground (Chapman & Riddle, 2003). Also, there are no reference values for microplastics such as Chronic Reference Dose (RfD), risk-based screening levels (RBSLs), or Site-specific target levels (SSTLs) values (Rubio-Armendáriz et al., 2022b; Zuccarello et al., 2019). The complex chemical and biochemical properties of microplastic, idiosyncratic environmental features of the Arctic, and unique physiological properties of the species inhabiting the region further compound the problem. Additionally, the scarcity of dose-response relationships and little to no toxicity data availability makes toxicological modelling a daunting task. The thesis aims at addressing the above identified challenges by accomplishing two key research goals:

- Investigating the cytotoxicity in polar cod (Boreogadus saida) due to microplastic exposure without the use of toxicity assays.
- Assessing the carcinogenic risk in humans consuming food from microplastic infested Arctic ecosystem, particularly those living in the remote Arctic communities, i.e., indigenous people of the Arctic.

The objective is achieved by proposing a comprehensive stochastic modelling approach to assess microplastic toxicity by circumventing the traditional route of toxicity assays. Polar cod is identified as a vital species that best indicates the microplastic risk in the Arctic food web. Risk in polar cods is evaluated in terms of cytotoxicity. Subsequently, the human health risk is assessed as the microplastic moves up the food web to eventually reach humans. Health risk in humans is assessed in terms of carcinogenicity.

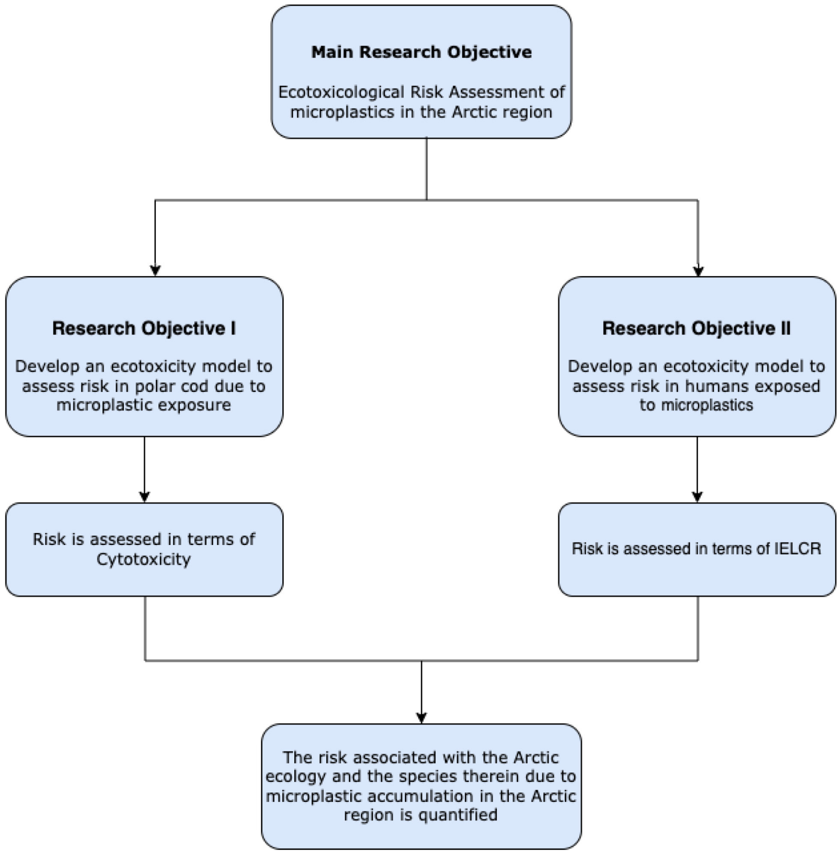

Figure 1.2 Pathway of the research objectives

1.6 Organization of Thesis

The thesis follows the style of a manuscript-type thesis. It incorporates two manuscripts. The first manuscript published in the Environmental Pollution journal is presented in chapter 2. Chapter 3 details the second manuscript and is submitted to the Science of The Total Environment Journal.

Chapter 2 addresses the first research objective. It proposes a comprehensive probabilistic model to estimate the cytotoxicity in Boreogadus saida (polar cod), a vital species of the Arctic food web due to microplastic accumulation in the Arctic waters. This is done by first identifying all the factors impacting microplastic intake by polar cod, which includes environmental and geophysical parameters of the Arctic region, microplastic properties, and the physiological characteristics of the polar cod. The effects of seasons, ice-thickness, and water salinity, along with the microplastic size and density, on the microplastic intake are detailed. Subsequently, the distribution and biotransformation of the ingested microplastic are considered by tracking the changes in relevant biomarker values. Finally, a Bayesian Network that accounts for all the aspects affecting polar cod's ecotoxicity is developed.

Chapter 3 is based on the second objective. It submits a novel stochastic modelling approach to assess the carcinogenic risk in humans, mainly indigenous people of the Arctic, exposed to microplastic through the Arctic food and water sources. To achieve this, first, the major route of microplastic to humans is identified. Then the factors affecting microplastic intake, such as environmental and geophysical parameters and microplastic properties like size and density, are identified. Subsequently, the microplastic distribution and metabolism are ascertained. Lastly, a Bayesian Network is developed to assess human carcinogenicity.

Chapter 4 summarizes the thesis with research findings. It presents the conclusions that can be drawn from the study, detailed in chapters 2 and 3. Additionally, it offers suggestions and directions for further research.

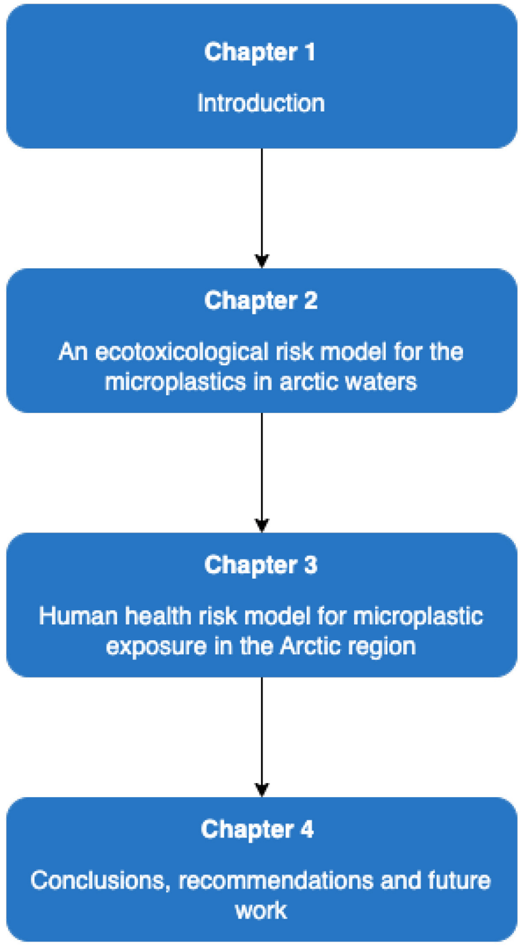

Figure 1.3 Thesis organization

1.7 Output of Thesis

The thesis delivers two peer-reviewed journal papers. The first paper is published in Environmental Pollution Journal while the second one is submitted to the Science of The Total Environment Journal.

Table 1.1 Research outcome: Journal papers published as part of the thesis.

Journal Paper	Title	Authors	Journal, Volume, Article
1	An ecotoxicological risk model for the microplastics in Arctic waters.	Mohammad Sadiq Saeed, Syeda Zohra Halim, Faisal Fahd, Faisal Khan, Rehan Sadiq, Bing Chen.	Environmental Pollution, 315, 120417.
2	Human health risk model for microplastic exposure in the Arctic region.	Mohammad Sadiq Saeed, Faisal Fahd, Faisal Khan, Bing Chen, Rehan Sadiq.	Science of The Total Environment Journal, submitted.

A version of chapter 2 has been published in Environmental Pollution Journal. I am the primary author of this manuscript, along with co-authors Syeda Zohra Halim, Faisal Fahd, Faisal Khan, Rehan Sadiq and Bing Chen. I developed the proposed framework of the model and its application using a case study along with the analysis of the result. I prepared the first draft of the proposed framework and revised it based on the co-author's feedback. The co-author Faisal Khan proposed the framework concept and helped develop the framework, revising and testing the application of the model. The co-authors Rehan Sadiq and Bing Chen supported in giving constructive feedback to improve the application of the model and also assisted in reviewing and improving the presentation of the proposed framework in the manuscript. The co-authors Syeda Zohra Halim and Faisal Fahd helped implement the feedback other co-authors provided in revising and finalizing the manuscript.

A version of chapter 3 is submitted under the Science of The Total Environment Journal. I am the primary author of this manuscript, along with co-authors Faisal Fahd, Faisal Khan, Bing Chen and

Rehan Sadiq. I developed the proposed framework of the model and its application using a case study along with the analysis of the result. I prepared the first draft of the proposed framework and revised it based on the co-author's feedback. The co-author Faisal Khan proposed the framework concept and helped develop the framework, revising and testing the application of the model. The co-authors Bing Chen and Rehan Sadiq supported in giving constructive feedback to improve the application of the model and also assisted in reviewing and enhancing the presentation of the proposed framework in the manuscript. The co-author Faisal Fahd helped implement the feedback other co-authors provided and also assisted in revising and finalizing the manuscript.

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2 AN ECOTOXICOLOGICAL RISK MODEL FOR THE MICROPLASTICS IN ARCTIC WATERS

Abstract

The risk posed to Arctic marine life by microplastics, a Contaminants of Emerging Arctic Concern (CEAC), is poorly known. The reason is the limited understanding of the dose-response relationship due to the region's peculiar environmental and geophysical properties and the unique physiological properties of the species living there. The properties of microplastics in the region and their distribution across the oceanic profile further complicate the problem. This paper addresses the knowledge gap by proposing a novel comprehensive ecotoxicity model. The model uses oxidative stress caused by the Reactive Oxygen Species (ROS) to assess cell mortality. Cell mortality has been used as an indicator of ecological risk. The model is implemented in the Bayesian Network (BN) framework to evaluate the cytotoxicity, measured as the probability of causing mortality. The work enhances the understanding and assessment of the cytotoxicity of microplastics in polar cod and associated risks.

***Keywords**:* microplastic pollution, ecological risk analysis, Bayesian Network, Object-Oriented Bayesian Network, Arctic risk.

2.1 Introduction

Plastics are a wide class of organic compounds. They are polymers of fossil feedstock like natural gas, coal, and oil that can be moulded into any shape when soft and then set into a rigid shape. The commonly used plastics are - polypropylene, polystyrene, low-density polyethylene (LDPE), high-density polyethylene (HDPE), and Polyethylene terephthalate (PET). Plastics are used widely for various reasons, primarily convenience (Hahladakis et al., 2018). At present, more than 5000 different types of plastics are available in the market. Industrial production of plastic has skyrocketed since the mid-20th century, reaching an annual production of 368 million tonnes by 2019 (Plastics Europe, 2020). COVID-19 witnessed a meteoric rise in plastic consumption in various forms like face masks, testing materials, and personal protective equipment. An increase in the consumption of take-away food from restaurants packed with plastic utensils and an uptick in online purchases resulted in greater plastic waste generation (Ammendolia et al., 2021).

Plastic debris or microplastics are found everywhere, in oceans, freshwater systems, and soil globally (Andrady, 2017; Dris et al., 2016; Ivar Do Sul & Costa, 2014; Liu et al., 2018; Talbot & Chang, 2022; Xu et al., 2022). It is also an integral part of municipal waste everywhere. Around 19-23 million metric tonnes of plastic waste flow annually from terrestrial sources to oceans (Borrelle et al., 2020). Apart from land sources, maritime operations like fishing, aquaculture, shipping, and offshore fishing and oil and gas extraction also contribute significantly to ocean plastic accumulation.

Plastic is generally very durable, and thus, tends to persist for a very long time in the environment. Also, its ability of long-range transportation clubbed with the property of bioaccumulation makes it even more detrimental to animals, human beings, the environment, and the whole ecosystem. Plastics being released into the environment are exposed to several natural processes like decomposition by microbes, mechanical forces (wind, water currents, animals), chemical weathering, UV exposure, temperature variations, and photo-oxidation. This leads to the disintegration and fragmentation of plastic fibers into smaller pieces (Hidalgo-Ruz et al., 2012; Kubowicz & Booth, 2017). When the fibers reach the size of less than 5mm, they are called microplastics (MPs). Plastic fibers in the range of 1 μm to 5 mm are referred to as microplastics (Frias & Nash, 2019). MPs are very heterogeneous when it comes to their physical and chemical properties. MPs travel through various media into the Arctic Ocean. The cold environmental conditions of the Arctic are conducive to its accumulation. (Peeken et al., 2018) reports that certain regions in the Arctic, like Fram Strait, have some of the world's highest microplastic deposition. Here, it gets introduced to the Arctic food chain. Arctic communities at the topmost trophic level of the food chain are eventually exposed to these microplastics.

Microplastics have been found in Arctic surface water (Kanhai et al., 2018), sub-surface waters (Morgana et al., 2018), the seafloor (Bergmann et al., 2017), and even ice (Obbard et al., 2014). (Huntington et al., 2020) has reported that the amount of microplastics or other anthropogenic particles is 90% for surface water and zooplankton samples and 85% for sediment samples. (Cole et al., 2011) categorizes these sources into primary and secondary sources. Primary sources are those where the plastics were originally produced as microplastics, while secondary sources are those where the large plastic fibres degrade into smaller fragments (<5mm), thereby converting them to microplastics. Ocean currents eventually fragment the larger plastic debris dumped in oceans into microplastics. To understand the gravity of this degradation, (Koelmans et al., 2017) state that 99.8% of the plastic that entered the oceans from 1950 has already degraded into microplastics or even nano plastics.

Broadly, three types of compounds can be associated with marine plastic litter. First is the plastic polymer itself. Second are chemicals like plasticizers, antioxidants, and flame retardants that are added intentionally during their production for example, polybrominated diphenyl ethers (PBDEs), chlorinated paraffin, polychlorinated biphenyls (PCBs) and polychlorinated naphthalene (PCNs). The third class is hydrophobic chemicals sorbed by the microplastics from the surroundings. These include endocrine disrupting chemicals (EDCs) like polychlorinated biphenyls (PCBs), hydrophobic organic compounds (HOC) like polycyclic aromatic hydrocarbons (PAHs), heavy metals like Pb, Fe and persistent organic pollutants (POPs). All three chemicals together make microplastics very toxic to the exposed organisms (Li et al., 2018).

It is critical to assess the ill impacts of this microplastic accumulation, particularly in the pristine and sensitive Arctic region. MPs are ingested or inhaled by marine species, and thus they get into the food chain and food web of the region. (Avio et al., 2020) demonstrated the presence of microplastics in various benthic, demersal, and benthopelagic or pelagic organisms. Studies like (Jiang et al., 2020) and (Gerstenbacher et al., 2022) studied and reviewed the toxicological effects of microplastics on organisms.

Microplastics contain certain harmful chemicals like additives, flame retardants and colourants. Also, they have a tendency to attract other pollutants and harmful micro-organisms from the surroundings onto themselves. Thus, they become even more dangerous on being ingested by living beings.

2.1.1 Microplastics in the Arctic Region

The Arctic region is the area surrounding the north pole. There is no consensus on the southern boundary of the region. However, mostly it is understood as the region above the arctic circle, which is at 66°33’49’’ N. As the Arctic is sparsely populated, low plastic accumulation in the region would be expected. However, extensive microplastic deposition is observed in the region. In fact, Fram Strait in the Arctic has reported very high microplastic concentration, at $1.2 \times 10^{-7}\ m^{-3}$ (Peeken et al., 2018). Most of the microplastic in the Arctic originates from remote sources. The Arctic receives more than 10% of the global river discharges even though it contains a little over 1% of the global ocean water (Holmes et al., 2012). This makes it more prone to plastic input. Recently, due to human intervention in the region, local sources of microplastics have also contributed to it. Maritime activities like aquaculture, hydrocarbon exploration, and ship traffic contribute as local microplastic sources. Fishing gear is a primary local microplastic source in regions like Greenland, Norwegian and Barents Seas (Linnebjerg et al., 1991), Kara Sea (Benzik et al., 2021) and subarctic North Atlantic (Buhl-Mortensen & Buhl-Mortensen, 2017) and North Pacific oceans (Polasek et al., 2017). (Rist et al., 2020) identified Nuuk, the capital of Greenland, as a major local source. Fisheries are a significant source on the beaches of Svalbard, Novaya Zemlya, Franz Josef Land, and Barents Sea. Domestic sources from Arctic communities also contribute to microplastic accumulation. Plastic particles exuviate from ship paint, and skidoos are also a potential microplastic source. Greywater released from vehicles operating in the region also leads to microplastic deposition (UNEP 2016, 2016). Southwest Greenland and Tasiujarjuaq, Nunavut, have reported paint-derived microplastic fragments (Liboiron et al., 2021). Figure 2.1 summarizes all the sources of microplastic in the Arctic region.

It is vital to assess the risk of this pathway of microplastics through the food chain and understand the factors affecting the risk so that proper mitigative and preventive measures can be taken to reduce or eliminate the risk to animals, humans, and the environment. Polar cod is an important part of the ecosystem. They reside in the Arctic, where concentrations are high, they rely on organisms that are in the lower food chain, and they are consumed by upper levels and play a critical role in the entire food chain.

2.1.2 Polar cod

Aquatic life is susceptible to illness and even death from microplastic exposure (Wright et al., 2013). Polar cod, or *Boreogadus saida*, is a circumpolar marine fish found in abundance in the fast-changing Arctic ecosystem. They produce antifreeze glycoproteins which help them adapt to subfreezing temperatures (Osuga & Feeney, 1978). Polar cod is the most vital species of the short and simple Arctic food chain. It has a strong relationship at every trophic level. Polar cod is a forage fish and preys upon lower trophic species like krill, copepods, amphipods and other arctic zooplanktons, and is in turn preyed upon by higher trophic species such as polar bears, seals, birds, beluga whales, and Arctic fox. Seals, polar bears, walrus and many avian species rely primarily on polar cod for their survival. It is to the credit of polar cod that in the high arctic food web, almost three-quarters of the zooplankton production is channeled through them to the higher predatory species (Bakke et al., 2016; Benoit et al., 2014; Hop & Gjøsæter, 2013a). This unique positioning of polar cod in the Arctic food web makes it an excellent selection for this study. Many studies like (Christiansen et al., 2014; Tomy et al., 2014) have also identified polar cod to be an excellent indicator of the associated risk in the food chain.

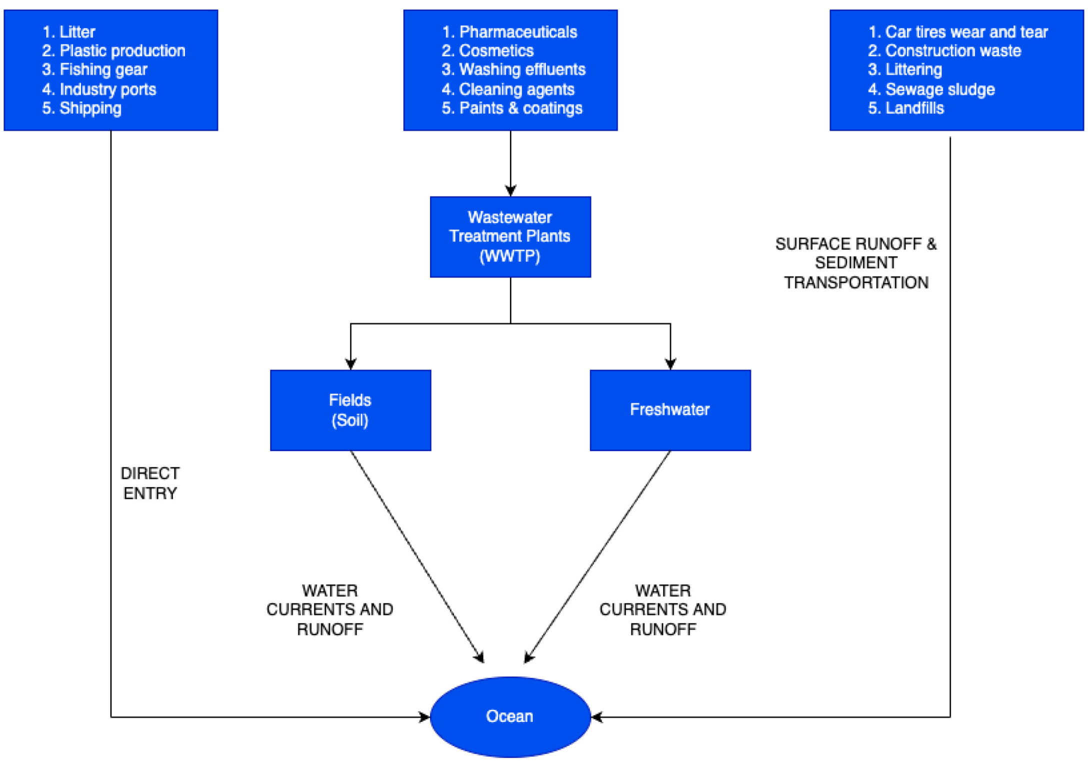

Figure 2.1 Sources of microplastics in Arctic Region.

The knowledge gaps or challenges in the ecotoxicological risk assessment of microplastics in the Arctic region are:

1) Paucity of literature on microplastics toxicity modelling, particularly in ice-infested Arctic waters. Ice cover traps the microplastics. Thus, MPs intake varies greatly from one species to another. Species like seals take food from ice-cover regions; thus, they are overexposed, while others like capelin are less exposed.

2) Lack of reference data – Reference values like Chronic Reference Dose (RfD), RBSLs, SSTLs value for microplastics are not available. Also, toxicity data on Arctic species is rare. The lack of data is generally compensated by using the data of temperate species. However, the practice is highly questionable owing to the many environmental, and geophysical distinctions in both the regions and physiological differences between the species.

3) Behaviour of Arctic species and food chain features: the Arctic food chain has some interesting features. Many species rely mostly on one prey to meet their energy requirements. For instance, whales mostly eat small fish, like polar cod, whereas polar bears' diet is mainly composed of seals. This feature of the aquatic food chain has a cascading effect on the next trophic level (Nevalainen et al., 2017).

This study aims to overcome these limitations by developing a comprehensive ecotoxicity risk assessment model for polar cod exposed to microplastics in the Arctic region. It appraises the likelihood of cell death in polar cod after microplastic ingestion. The developed model circumvents the traditional use of toxicity assays by adopting a Bayesian-based approach that projects the probability of cell death in the cod after ingestion. The study aims to graphically represent the Toxicokinetic (TK) and Toxicodynamic (TD) processes in polar cod. Various environmental, geophysical, and physiological parameters influencing the TK and TD processes in polar cod are identified. A cause-effect relation is then established between these parameters to develop a BN. This complex BN is then transformed into an Object-Oriented Bayesian Network (OOBN) for simplification to determine the cell death likelihood, which further studies can subsequently use to evaluate the organism fatality.

2.2 Toxicokinetic Mechanism

Toxicokinetics (TK) describes how species respond to toxicants inside their bodies. It covers the overall description via four key concepts, i.e., absorption, distribution, metabolism, and elimination (ADME). The contaminant is absorbed and distributed in the whole body via systemic circulation. It gets metabolized in the liver and then eliminated via feces and gills. TK models quantize the xenobiotic distribution across the various organs in the species.

2.2.1 Absorption and Distribution

Microplastic, owing to its small size, finds its way into amphipods, copepods and other zooplanktons easily (Cole et al., 2013). These zooplanktons are eaten by polar cod. Moreover, while foraging, polar cod often mistakenly consume microplastics particles. Microplastic intake is also observed via water ingestion (Kohlbach et al., 2017; Lonne & Gulliksen, 1989). The ingested microplastics reach the liver, from where they are distributed to the whole body through the systemic circulation.

2.2.2 Metabolism and Elimination

Microplastics reach the liver of the polar cod through the intestine, where it is acted upon by enzymes, causing biotransformation. From the liver, some part of it reaches the systemic circulation, which also leaks small amounts to fats and other depositions. Biotransformation occurs in the liver in two phases. In phase I, the CYP1 group of enzymes acts on the microplastic xenobiotics to form water-soluble metabolites. The phase I process is characterized by the addition of polar atoms to the xenobiotics to form hydrophilic metabolites that are either easily eliminated or result in toxification or inert presence in the body (Santana et al., 2018). Oxidation is concomitant to processes like biotransformation. Hence, a balance should be there to counter its negative effects. This is what occurs in phase II reactions. The phase II process is a conjugation reaction of the oxidized metabolite with glutathione (GSH) and is facilitated by the Glutathione S-transferases (GST) enzyme, thereby acting as an antioxidant defence in cod (Giulio & Hinton, 2008).

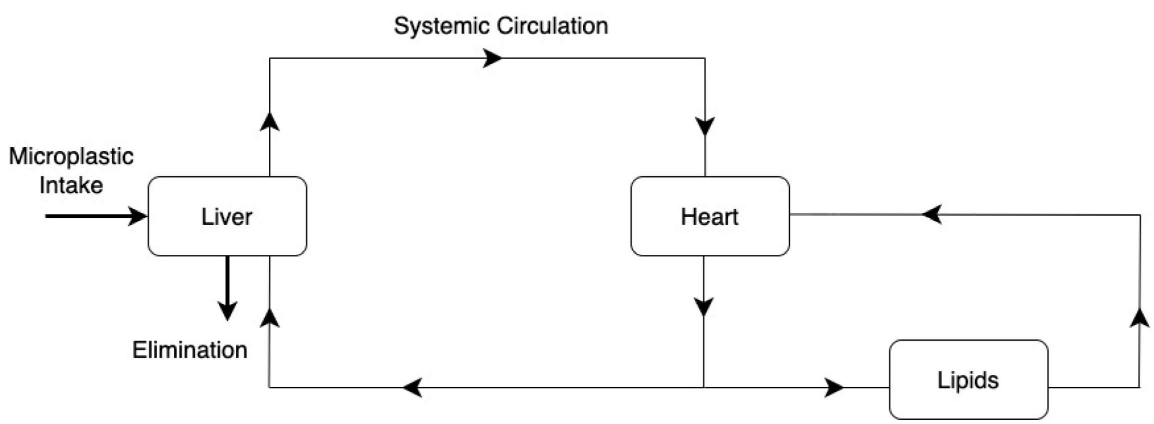

Figure 2.2 Route of microplastic in polar cod after oral ingestion.

Metabolites formed because of phase I reactions lead to cytotoxicity if they are not conjugated by the phase II process. So, cell death occurs when the concentration of toxic metabolites produced after phase I reaction exceeds the conjugating capacity (Banni et al., 2009). Cells, however, possess an innate ability to repair themselves but only up to a threshold. If a greater number of cells than the threshold dies, the organ fails. Apart from the oxidative stress due to biotransformation, peroxidation of lipids is also a cytotoxicity mechanism. However, it is not considered in our analysis. To quantify the metabolite concentration in polar cod, Ethoxyresorufin-O-deethylase activity (EROD) assay is used as a phase I biomarker while glutathione-S-transferase (GST) assay is used as a phase II biomarker.

The metabolized microplastics are then eliminated via the hepato-biliary tract. Gills also act as another source of xenobiotic removal, but this is not considered in this study.

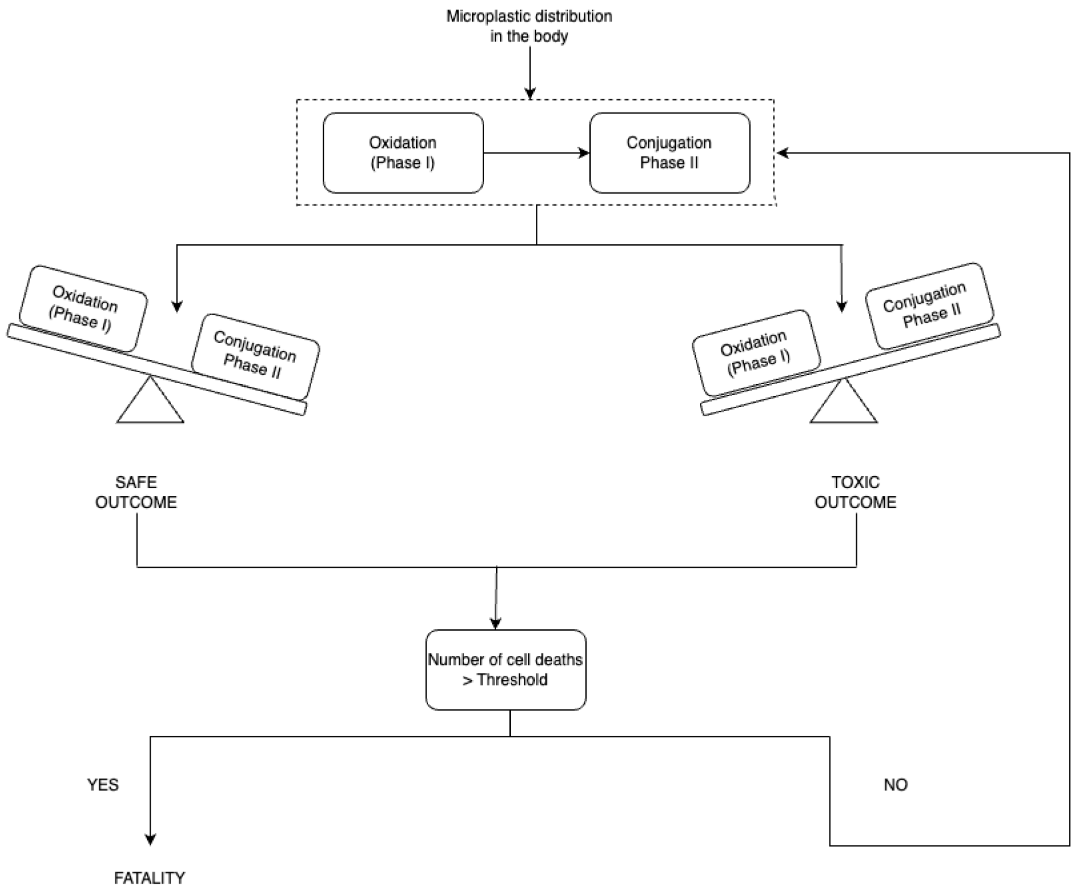

Figure 2.3 Toxicity mechanism in polar cod.

Phase I mechanism:

The microplastics ingested by polar cod get oxidized in the presence of Cytochrome P450 oxidase. Polar groups get attached to them to form reactionary intermediary metabolites.

$$Microplastic + O_2 + Reducing\ agent \xrightarrow{CYP450\ enzyme} MP = O^- + H_2O$$

Phase II mechanism:

The reactionary intermediary metabolites produced in the phase I mechanism are now acted upon by glutathione in the presence of the GST enzyme. If the GST activity is high, all of the reactionary intermediary metabolites are detoxified to glutathione conjugated metabolites. If the GST activity is low, superoxide (O_2^-) is produced, which is converted to H_2O_2 via SOD enzyme activity and eventually to OH^- by the Fenton reaction. This damages cell DNA and also leads to lipid peroxidation, resulting in cell death. GST activity depends on the liver microsomes and the baseline phase I and II activities.

2.2.3 Deleterious effects of microplastic intake

Studies by (Alomar et al., 2021; Choi et al., 2022; Maaghloud et al., 2021; Nanninga et al., 2020; Rist et al., 2020) have investigated microplastic ingestion on various zooplanktons and fish. Microplastic intake results in reduced feeding behaviour, false satiation sense, growth inhibition and fecundity inhibition in polar cod. Microplastic debris blocks the intestinal tract, which causes injury to its internal system and pseudo-satiation sense (Kühn et al., 2018). Very fine microplastic particles pave their way to cells and organs, with consequences still under research (Brennecke et al., 2016; Browne et al., 2008). (Sun et al., 2016) shows the presence of various absorbed persistent organic pollutants on the deployed samples of polyethylene in western Svalbard. The adsorbed chemicals are transferred to the organisms upon consumption, which leads to many health problems (Chen et al., 2017).

2.3 Ecological Risk Methodology and Application

The steps in the methodology, as shown in Figure 2.4, are as follows:

1) Identify factors (environmental, geophysical, physiological factors and microplastic properties) affecting microplastic intake and distribution in the polar cod.
2) Identify the temporal (seasonal) changes in the enzymatic activity affecting the microplastic toxicity to polar cod.

3) Determine the baseline values of the identified environmental, geophysical, physiological factors and microplastic properties.
4) Identify the cause-and-effect relationship between the identified factors.
5) Develop the structure of a Bayesian network using these identified factors.
6) Collate data from the available literature and expert elucidation.
7) Use Object Oriented BN to simplify the BN for better realization.
8) Determine changes in biomarker values due to microplastic intake.
9) Determine the cell death probability from the developed BN model.

These steps offer an ecological risk model aimed at determining the likelihood of cell fatality due to microplastic intake in polar cod using the cause-and-effect relationships established in the Bayesian network.

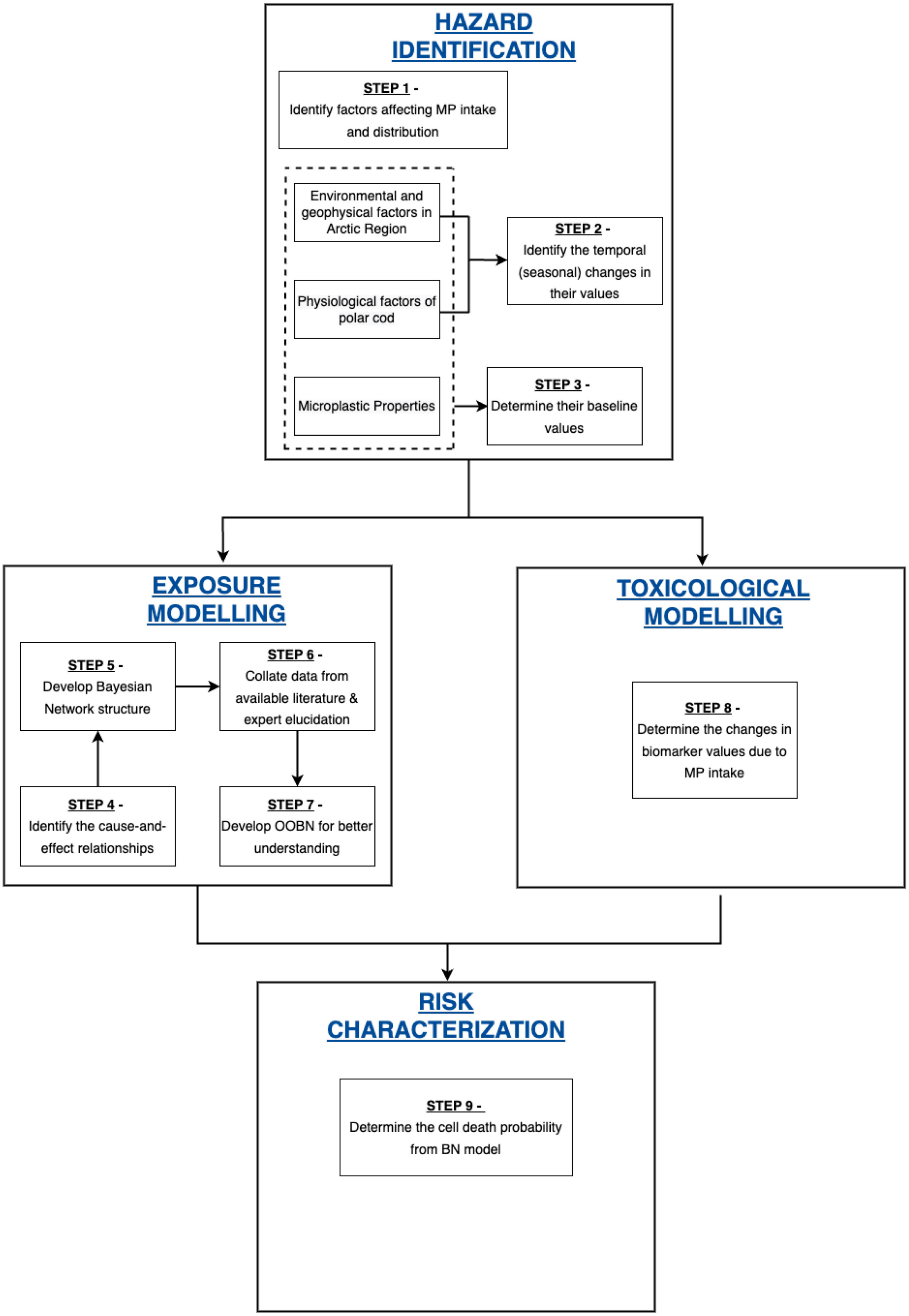
HAZARD IDENTIFICATION
STEP 1 - Identify factors affecting MP intake and distribution
Environmental and geophysical factors in Arctic Region
Physiological factors of polar cod
Microplastic Properties
STEP 2 - Identify the temporal (seasonal) changes in their values
STEP 3 - Determine their baseline values
EXPOSURE MODELLING
STEP 5 - Develop Bayesian Network structure
STEP 6 - Collate data from available literature & expert elucidation
STEP 4 - Identify the cause-and-effect relationships
STEP 7 - Develop OOBN for better understanding
TOXICOLOGICAL MODELLING
STEP 8 - Determine the changes in biomarker values due to MP intake
RISK CHARACTERIZATION
STEP 9 - Determine the cell death probability from BN model

Figure 2.4 Methodology of the developed ecotoxicity model.

2.3.1 Factors affecting microplastic intake and distribution in polar cod

There are three categories of factors that determine the microplastic intake in polar cod. The first one is the region-specific environmental and geophysical factors. Another is physiological factors of the polar cod, and the last one is the properties of the microplastic particle. The Arctic region is uniquely characterized by harsh weather conditions, the presence of a thick ice layer and an extreme light regime, including periods of midnight sun and polar night (Berge et al., 2015). Along with these unique physical characteristics, the transfer of energy along the various trophic levels of the food chain is also idiosyncratic (Werner, 2006). Thus, the environmental and geophysical factors identified are season, sea-ice thickness, and salinity. The polar cod's physiological factors are liver microsomes and baseline enzymatic activity in both the phases. Also, properties of microplastics like their size and density influence their intake and distribution.

2.3.1.1 Environmental and geophysical factors in the Arctic

The Arctic undergoes three seasons, namely, winter, summer, and autumn. In winter, ice-thickness increases, which in turn increases the salinity as the formed ice pushes the brine deep into the seawater. Ice-melt and lower salinity in summer facilitate the increased availability of sunlight in the ocean, which enhances the algal activity. Algae are consumed by amphipods and copepods, which are then eaten by polar cod, thereby increasing the feeding activity (Berge et al., 2015).

2.3.1.2 Microplastic particle properties

The properties of microplastic, like its shape, size, density, and composition, influence its intake by all species in general and polar cod. For this study, microplastic size and density are considered. Lower microplastic size and higher density lead to higher feeding activity. (Rist et al., 2020) noted that the concentration of microplastic increases with decreasing particle size.

2.3.1.3 Physiological factors of the polar cod

Physiological parameters like liver microsomes and the baseline enzymatic activities affect the biotransformation, cell response and distribution. Around one-fifth of the cell area is the smooth endoplasmic reticulum, where phase I CYP1A enzymes are present. Approximately 2% of the cytosolic protein in polar cod are phase II activity enzymes (Moore, 1992).

The elevated baseline enzymatic activity enhances the corresponding phase activity, which eventually determines the cell damage probability.

2.3.2 Temporal (seasonal) changes in enzymatic activity

Enzymatic activity of polar cod is directly contingent on food availability. During the summer season, a reasonable amount of sunlight enters the Arctic ecosystem. This sets the phytoplankton in action through photosynthesis and thus energy comes into the ecosystem. This is less prominent during the winter season. Thus, a feeding outburst is observed in the summer season, which leads to fat reserves in polar cod. These fat reserves are crucial during spawning in the following months of early winter (Hop & Gjøsæter, 2013b). Hence, enzymatic activities are enhanced during the summer season and gradually decrease as the feeding activity changes.

2.3.3 Baseline data of environmental, geophysical and physiological factors

The Arctic region experiences four seasons, of which three are considered in this study, namely winter, summer, and autumn. Winter lasts the longest, from December to June, followed by summer from July to September and the remaining months of October and November are autumn. So, the prior probabilities of winter, summer, and autumn are 0.58, 0.25 and 0.17 respectively.

The data of ice-thickness are taken from Fram Strait (Werner, 2006) and the Kongsfjord region (Nahrgang et al., 2010). The only deep-water connection between the Arctic and Atlantic is Fram

Strait, which lies between Svalbard and Greenland (Thiede et al., 1990). The ice thickness varies between 0.8 m to 3.5 m throughout the year. Ocean salinity ranges from 16.7 psu to 34.6 psu. Liver microsomes are taken to vary from 5% to 25% in polar cod. The baseline phase I activity is measured in increase in folds of the CYP1A enzyme activity and the baseline phase II activity is measured in increase in folds of the GST activity. Baseline phase I activity and baseline phase II activity range from 3-13 pmol/min/mg to 200-250 pmol/min/mg respectively. (Nahrgang et al., 2010; Rodd et al., 2017).

Plastic deposition in the Fram Strait has exhibited a meteoric rise during the last few years (*Parga Martínez et al., 2020*). Previous studies have also established that Fram Strait has the highest microplastic concentration in the whole Arctic and that the size of most particles is smaller than 50 µm (Peeken et al., 2018). The studies (Hänninen et al., 2021; Tekman et al., 2020) have shown the presence of microplastic across the Arctic water column, with their values ranging from 0.012 N/m^3 to 1287 N/m^3. Also, they come in all sizes, from 5 mm to 1 µm.

2.3.4 Develop an OOBN using available literature and expert elucidation

Bayesian networks (BN) are directed acyclic graphs (DAGs) containing nodes and arcs that satisfy the Markovian condition. A BN uses known quantitative information to determine the posterior probability. When there are many nodes in the BN, it becomes visually unpleasant and difficult to understand. In such a case, an Object-oriented Bayesian network (OOBN) is developed as a hierarchy of sub-networks with desired abstraction levels to simplify the otherwise complex BN (Kjaerulff & Madsen, 2008). Similar usual nodes are clubbed together as one instance node, which is then the input of the next sub-network.

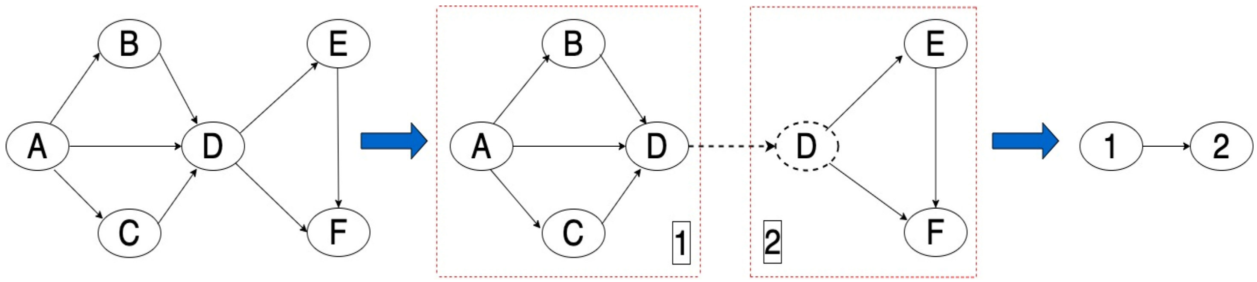

Figure 2.5 Conversion of a BN to OOBN.

The instance nodes of the object-oriented Bayesian network of the study conducted are in Figure 2.6, Figure 2.7, Figure 2.8 below.

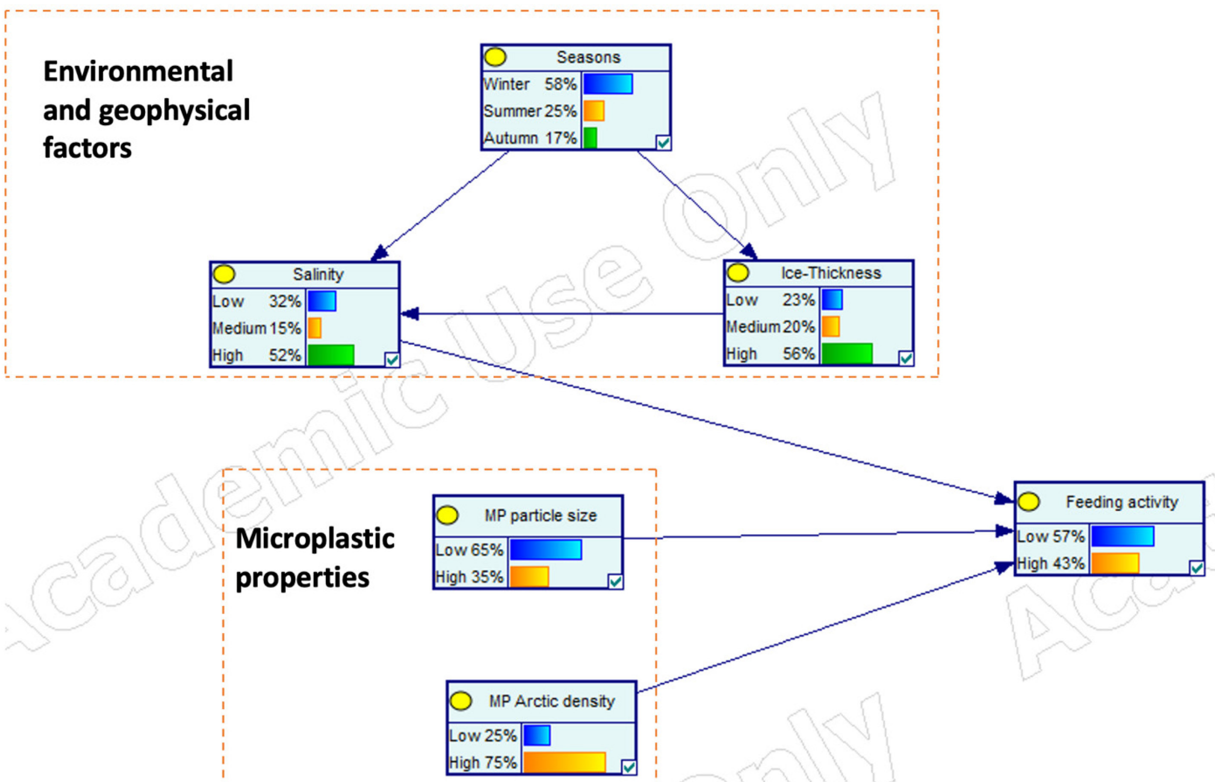

Figure 2.6 Feeding activity instance node of the developed OOBN.

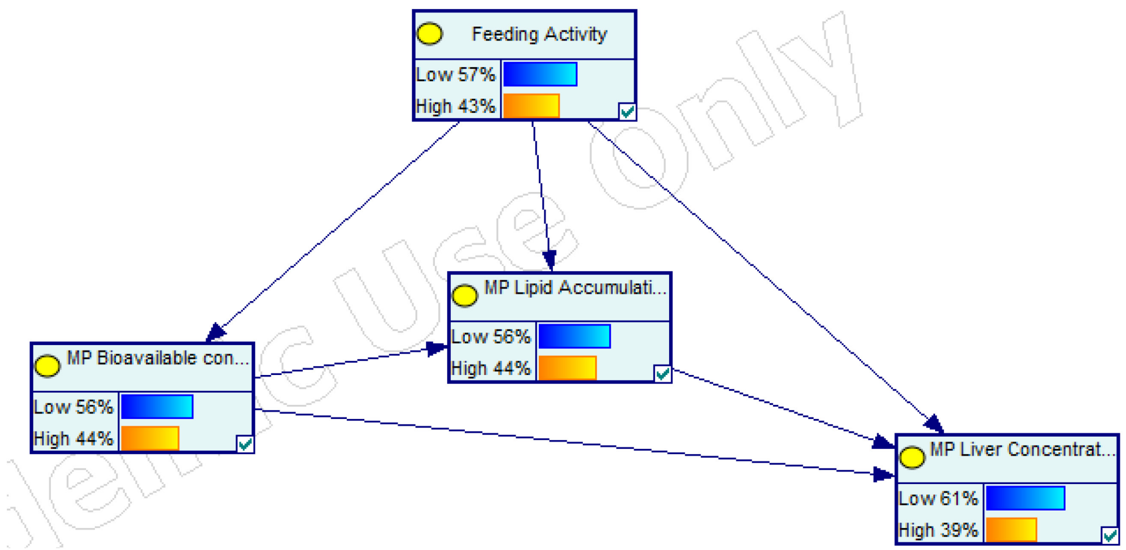

Figure 2.7 Microplastic concentration reaching liver instance node of the developed OOBN.

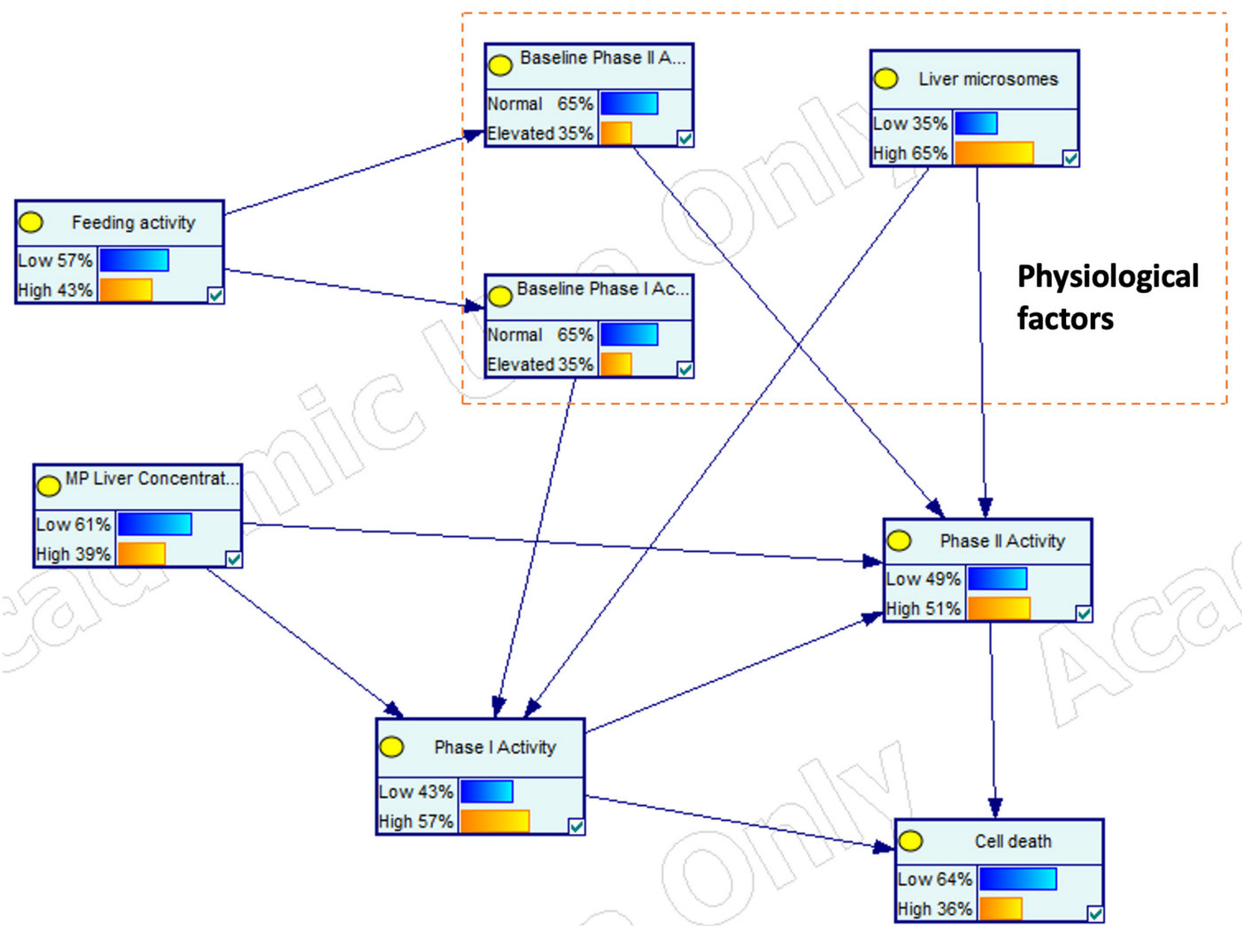

Figure 2.8 Cell death instance node of the developed OOBN.

Table 2.1 Nodes of BN, their states and description

Nodes	States	Description	References
Season	Winter Summer Autumn	Winter spans from December to June (0.58) Summer spans from July to September (0.25) Autumn spans from October to November (0.17)	
Arctic ice thickness	Low Medium High	Ice thickness in the Fram Strait in Arctic region varies from 0.8 m to 3.5 m. Low – 0.8 - 1.5 m Med – 1.5 - 2.5m High – 2.5 - 3.5m	(Werner, 2006)
Salinity	Low Medium High	Salinity increases with drop in temperature. As ice forms at the top, it pushes the salts to the bottom. Low – < 10% Med – < 25% High – < 40%	(Fahd et al., 2020)
Microplastic Particle Size	Low High	MP size ranges from 1 μm - 5 mm Low – < 2.5 mm (0.65) High – 2.5 – 5mm (0.35)	(Frias & Nash, 2019)

Nodes	States	Description	References
Microplastic Particle Density	Low High	MPs are present throughout the water column in the Arctic. They decrease as we go down the water column before increasing drastically at the sediments. 0.012 N/m^3 to 0.144 N/m^3 when measured using 335µm mesh. 9 N/m^3 to 1287 N/m^3 when measured using 32µm mesh. 4356 MP pieces weigh 1 kg in the Fram Strait. Low – < 700 N/m^3 or < 161 gm/ m^3 High – 700–1300 N/m^3 or 161–298 g/m^3	(Hänninen et al., 2021; Tekman et al., 2020) (Bergmann et al., 2017)
Feeding activity	Low High	Feeding is high during autumn and summer and low during winter. Low – < 15% High – > 15%	(Cusa, 2016)
MP lipid accumulation	Low High	The concentration of MP and associated toxicants are trapped in the lipids, particularly in liver lipids, expressed as percentages. Low – < 25% High – < 25%	(Hop & Gjøsæter, 2013b)

Nodes	States	Description	References
MP Bioavailable concentration	Low High	Gills remove major portion of toxicants. The states in the node are defined as: Low – < 70% High – > 70%	Expert Opinion
MP liver Concentration	Low High	More than three-quarter of the xenobiotic intake in the fish is metabolized in the liver. The states in the node are defined as follows: Low – < 70% High – > 70%	(Banni et al., 2009)
Liver microsomes	Low High	About 15-20% of the liver area is taken by endoplasmic reticulum. The states of the node are defined as: Low – 5-12% (0.35) High – 12-25% (0.65)	Expert Opinion
Baseline Phase I activity	Normal Elevated	The baseline phase I activity ranges from 3-13 pmol/min/mg. Normal < 8 pmol/min/mg Elevated > 8 pmol/min/mg	(Rodd et al., 2017)

Nodes	States	Description	References
Baseline Phase II activity	Normal Elevated	The baseline phase II ranges from 200-250 pmol/min/mg. Normal < 350 pmol/min/mg Elevated > 350 pmol/min/mg	(Nahrgang et al., 2010)
Phase I activity	Low High	The phase I activity is measured increase in folds of the EROD activity (Ethoxyresorufin-O-deethylase) Low – ≤ 8 High – ≥ 10	(Rodd et al., 2017)
Phase II activity	Low High	The Phase II is measured in fold increase in GST activity (Glutathione S-transferase) Low – ≤ 4 High – ≥ 7	(Nahrgang et al., 2010)
Cell damage from biotransformation	Low High	Low – 5-15% High – 15-30%	Expert Opinion

2.3.5 Model testing and benchmarking

The OOBN-based ecotoxicity model is tested using a study by Mahadevan & Valiyaveettil, 2021. The study assesses the impact on BHK-21 cells or baby hamster kidney cells on being exposed to very small plastic particles of polyvinyl chloride (PVC) and polymethyl methacrylate (PMMA). The induced cellular biochemical changes in BHK-21 cells like cell morphology, cell fatality and concentrations of reactive oxygen species (ROS) were monitored at various concentrations of the plastic dose over a period of time. Results exhibit a substantial decrease in cell viability, or in other words, an increase in cell death, at $40.3 \pm 0.1\%$ for PVC and $61.3 \pm 4.0\%$ for PMMA when 200 μg/mL is the exposed concentration for 120 hours. The developed OOBN model also shows similar results. In the model, high feeding activity is an outcome of high microplastic concentration, which is defined as 161–298 g/m^3 or 161–298 μg/mL. This means that when the exposed concentration is 200 μg/mL, cell death is high.

2.4 Results and Discussion

Seasonal variations in the Arctic region affect the sea ice thickness and water salinity. The latter is influenced by the former, and the microplastic properties like size and density shape most species' absorption or feeding activity, including polar cod. Feeding activity determines the xenobiotic distribution in the systemic circulation and lipids, which collectively decides the pollutants' concentration reaching the liver. Feeding activity induces changes in baseline enzymatic activity, which affects phase I and phase II activities. Xenobiotic concentration in the liver and physiological factors like liver microsomes and baseline enzymatic activities also influence phase I and phase II activities. The developed model identifies the causal dependencies between all the associated variables to determine the outcome in the form of cell death likelihood.

The cell death likelihood gives an idea of the toxicity of microplastics to polar cod and can be used to assess organ failure and organism fatality further. It can also be extended to estimate the impact across the Arctic food chain. In GeNie software by BayesFusion LLC, sensitivity analysis of the node ‘cell death’ is performed (Figure 2.9). Sensitivity analysis is done to identify the most important factors that affect cell death. The results show that the phase I and phase II activities have the highest effect on cell death, followed by the concentration of microplastics reaching the liver and feeding activity.

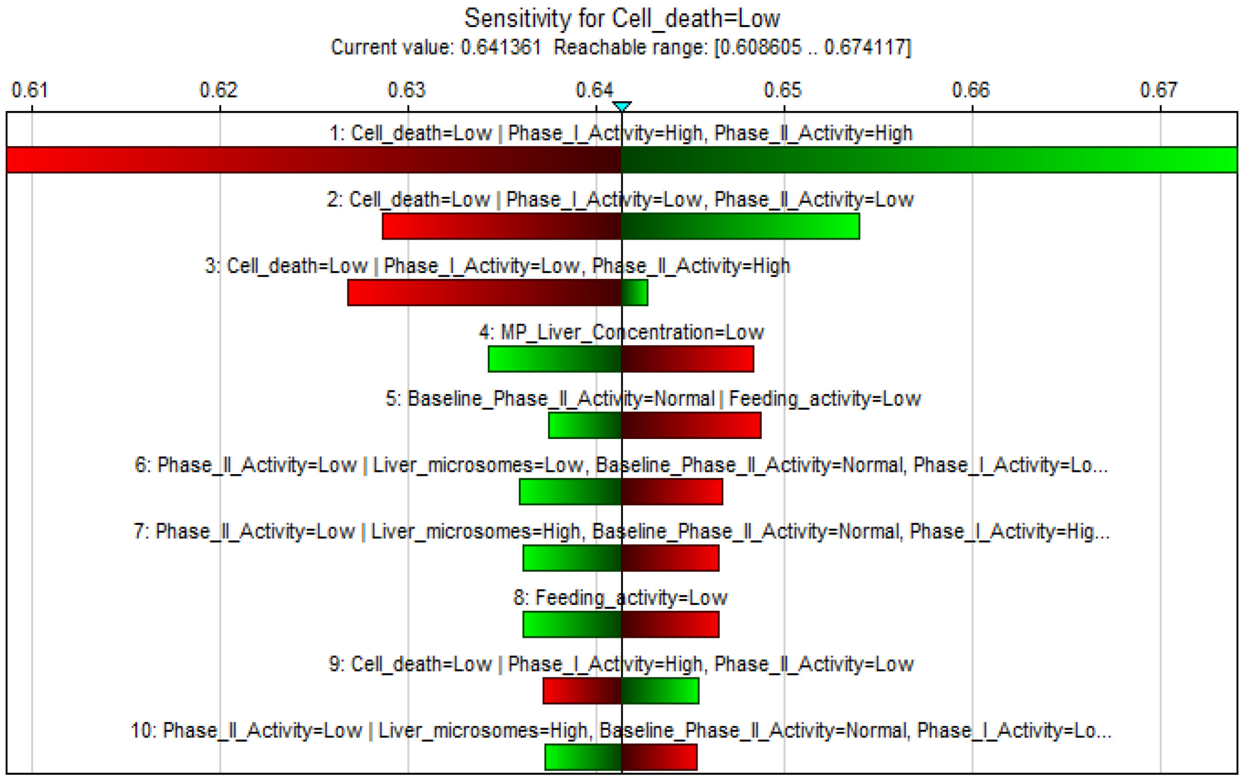

Figure 2.9 Sensitivity tornado for cell death.

The unchecked plastic waste is a serious threat to the Arctic ecosystem. The proposed model presents a stochastic approach to estimate the microplastic toxicity in polar cod without toxicity assays. This is achieved by identifying the various factors that influence the TK and TD processes in polar cod, establishing the cause effect relationship between them and then developing a Bayesian belief network to estimate the cell death likelihood. For clarity, the BN is simplified into OOBN. The model shows how the microplastic in the Arctic region facilitates cell fatality in polar cod, which will eventually lead to organ failure and organism death. The sensitivity analysis further identifies the most crucial factors which impede cell viability.

The study, however, is not free from limitations. It assumes the temporal static nature of the ice-thickness and salinity within a season, i.e., variations within a season are not considered. Data available from literature and expert opinions were considered for the probabilities of various nodes of the Bayesian Network. Also, some assumptions were made in the conditional probabilities of the Bayesian Network. Giulio & Hinton, 2008 detail the various pathways of biotransformation, which are very complex, and subjected to numerous factors. For the sake of simplicity, only the major pathway, i.e., CYP1A, is considered in this study.

In future, as more information is available, the probabilities in the BN model can be updated to get better results. Additionally, a time variable can be incorporated for more accurate risk probabilities. Moreover, extending the probability of cell death to organism fatality is another challenge for future work. Also, the organism fatality, in turn, can be extrapolated using a suitable population model to develop an understanding of the health of colonies of species. While considering other possible biotransformation pathways, the phase I and phase II activity should be replaced by relevant biomarkers. Cell death from lipid peroxidation and DNA damage due to biotransformation can also be considered using suitable biomarkers. Biomarkers sensitive to phase 1 and phase II activities, in addition to EROD and GST after identification, can be incorporated into the developed model. Biomarkers for other biotransformation pathways, once identified, can also be added to the model to produce more accurate results. As new information and data in the field of genomics become available, they can be considered in the model to estimate more precise trends in polar cod.

2.5 Conclusions

The present study proposes a comprehensive model to assess the risk posed by microplastics to polar cod in the Arctic environment. The physiological factors of the polar cod and the environmental and geophysical factors of the region affecting microplastic intake, distribution, and biotransformation in polar cod are considered. A cause-effect relationship between all the factors is established to develop an Object-Oriented Bayesian Network that determines the cytotoxicity.

The biotransformation of microplastics and their metabolites results in oxidative stress, which leads to cytotoxicity. On being exposed to microplastics, changes in cell metabolic activity and antioxidant defence activity are measured using Ethoxyresorufin-O-demethylase activity (EROD) assay and glutathione-S-transferase (GST) as biomarkers.

The traditional approach, which is used extensively to measure the toxicity of a xenobiotic to a temperate fish, is often challenged for Arctic species. This is because it fails to encompass the sui generis features of the Arctic region. The developed model addresses this issue effectively by creating an all-encompassing and holistic model using a Bayesian Network. The model evaluates changes in the homeostatic functioning of polar cod by predicting cell toxicity.

The risk deemed in this study is the death of a cell in polar cod. This occurs when the phase I activity outcome (ROS) is not conjugated by phase II activity. Fahd et al. (2020) propose that when 35% of cells in an organ die, a fatality occurs. Using this observation and the OOBN presented in the current study, a detailed stochastic ecological risk model for microplastic is developed. The developed model will serve as an essential tool to establish arctic risk management policies and strategies.

Acknowledgments

The authors thankfully acknowledge the financial support provided by the Natural Sciences and Engineering Council of Canada (NSERC) through the CREATE program and the Mary Kay O'Connor Process Safety Centre at Texas A&M University.

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3 HUMAN HEALTH RISK MODEL FOR MICROPLASTIC EXPOSURE IN THE ARCTIC REGION

Abstract

Microplastics enriched with carcinogens like heavy metals, polycyclic aromatic hydrocarbons (PAHs), and their derivatives are ubiquitous in the Arctic waters. They contaminate the local land and sea-based food sources, which is a significant health hazard. It is thus imperative to assess the risk posed by them to the nearby communities, which primarily rely on locally available food sources to meet their energy requirement. This paper proposes a novel ecotoxicity model to assess the human health risk posed by microplastics. The region's geophysical and environmental conditions affecting human microplastic intake, along with the human physiological parameters influencing biotransformation, are incorporated into the developed causation model. It investigates the carcinogenic risk associated with microplastic intake in humans via ingestion in terms of incremental excess lifetime cancer risk (IELCR). The model first evaluates microplastic intake and then uses reactive metabolites produced due to the interaction of microplastics with xenobiotic metabolizing enzymes to assess cellular mutations that result in cancer. All these conditions are mapped in an Object-Oriented Bayesian Network (OOBN) framework to evaluate IELCR. The study will provide a vital tool for formulating better risk management strategies and policies in the Arctic region, especially concerning Arctic Indigenous peoples.

Keywords: Microplastic, Risk, Arctic, Cancer risk, Indigenous communities, Human health.

3.1 Introduction

The plastic generated globally gets transported to the oceans through wind, water currents and animals. (Isobe et al., 2021) estimates that 24.4 trillion microplastic pieces are present in the world's upper oceans. They have now reached all parts of oceans affecting nearly 88% of the aquatic species. The gravity of this pollutant can be highlighted by the fact that microplastic levels will exhibit 50 times increase by 2100, even if all plastic contamination ceases today (World Wide Fund for Nature Inc, 2022). In the process of reaching and moving in the ocean, they disintegrate into small fragments upon being exposed to solar heat, temperature gradients, and oceanic waves. When they degrade to a size smaller than 5mm, they are called microplastics (Gigault et al., 2018; Talbot & Chang, 2022). Some plastic fragments are manufactured in this microscopic dimension and are termed primary microplastics, whereas those plastic particles which attain this size range after degradation are called secondary microplastic (Frias & Nash, 2019).

A considerable amount of these oceanic microplastics also move towards Arctic waters, where these tiny fragments get trapped in the sea ice and thus remain for a prolonged duration. Further, the cold climate provides stability to them, and thus, they tend to stay there for a very long period. Microplastics have been reported across the whole Arctic water column. (Tošić et al., 2020) has reported microplastics in surface Arctic water, (Morgana et al., 2018) in sub-surface Arctic waters, and (Bergmann, Wirzberger, et al., 2017) at the seabed of the Arctic Ocean. (Bergmann, Wirzberger, et al., 2017; Y. Lin et al., 2022; Ramasamy et al., 2021) have shown microplastic presence in the Arctic sediments, and (Obbard et al., 2014; von Friesen et al., 2020) proved them in sea-ice. These microplastics are consumed by marine plants and animals, from where they travel across the food web, eventually reaching humans (Avio et al., 2020). Microplastics are found in vivo in many Arctic species like arctic Calanus copepods (Rodríguez-Torres et al., 2020). The existence of this pollutant in Arctic fish is evidenced by (Morgana et al., 2018; Rummel et al., 2016). (Trevail et al., 2015) has confirmed them in seabirds, while (Carlsson et al., 2021) manifested them in walruses. (Moore et al., 2020) and (Hallanger et al., 2022) established them in beluga whales and Arctic foxes respectively. Recently, plastic debris was discovered in the body of an Arctic seal pup (Pinzone et al., 2021). Plastics create lesions and blockages in the gastrointestinal tract hampering feeding activity (Foekema et al., 2013; Moore et al., 2020). Their small particle size provides a large surface area leading to increased bioavailability and chemical toxicity (Bradney et al., 2019; Chen et al., 2019; Cózar et al., 2014; Kedzierski et al., 2018).

The microplastic deposition and accumulation in the Arctic biota has not only imperiled them but also made the humans living in the indigenous Arctic community settlements vulnerable. Species at each trophic level of the Arctic food chain are exposed to an otherwise unassessed health risk. The Arctic food chain is unique and intriguing. This is because the phytoplankton at the ice edge is exposed to sunlight for a minimal duration in summer while they remain under icecaps for the rest of the year (Janout et al., 2016). The idiosyncratic nature of the Arctic food chain makes it even more challenging to evaluate the risk. The lower trophic level organisms are exposed to microplastics through ingestion which then moves up the food chain, finally reaching humans. The indigenous communities in the Arctic have traditionally relied only on the locally available food and water sources. Microplastics get bioaccumulated and biomagnified at each trophic level before it reaches humans.

Plastics contain many carcinogenic additives like plasticizers, photostabilizers, and flame retardants (Do et al., 2022). Also, microplastics enrich many other environmental pollutants, like heavy metals, polycyclic aromatic hydrocarbons (PAHs), phenanthrene (PHE) and their derivatives (Li et al., 2018; Liu et al., 2019). These microplastics induce inimical effects in humans and other organisms upon intake (Bakir et al., 2016; Ito et al., 2022; Varg et al., 2021). Various deleterious health effects of microplastics have been documented, including oxidative stress (Hsieh et al., 2021; Yu et al., 2021), changes in gene expression (Carrasco-Navarro et al., 2021;

Dolar et al., 2022), inflammation (Cao et al., 2023; Dong et al., 2020; Jin et al., 2018), reproduction rates (Sussarellu et al., 2016), and impeded growth (Kaposi et al., 2013). Recent studies have detected microplastics in human respiratory tract (Prata, 2018), human blood (Leslie et al., 2022), human placenta (Ragusa et al., 2021), and human breast milk (Ragusa et al., 2022). Studies like (Hu et al., 2022; Sharma et al., 2020) have established the human carcinogenicity of these enriched microplastic polymers. No study however has assessed the cancer risk in humans due to microplastic intake in the Arctic region.

The indigenous communities of the Arctic face severe food insecurity due to the high transportation and logistics costs of food items. Food insecurity is prevalent among the Inuit population, with studies showing that it affects as much as 80% of their population (Richmond et al., 2020). These communities rely mostly on traditional food available in the surroundings. So, people here are more vulnerable, and thus, proper risk analysis needs to be done to safeguard their interests (Marushka et al., 2021). The human communities inhabiting the circumpolar North have the staple diet of Arctic animals like polar bears, polar foxes, seals, narwhals, and polar cods. So, they are most susceptible to the detrimental impacts induced by all toxicants, including microplastics (Stimmelmayr & Sheffield, 2022).

The above discussion highlights the importance of biota health risk assessment, especially human health risk in the Arctic. However, only a few studies have tried addressing it. (Fahd et al., 2020) and (Fahd et al., 2019) assesses the risk polar cod in the Arctic waters are exposed to due to oil spills. (Fahd et al., 2021) investigates the ecological risk assessment in the Arctic food chain on exposure. The Arctic human communities are highly vulnerable to microplastic consumption, which results in many genetic, reproductive, and immune-related problems. It also leads to the development of cancerous cells. Lack of medical facilities in these communities further exacerbates the problem (Gibson et al., 2016). (Saeed et al., 2022) estimates the risk of microplastic intake in a vital Arctic species, polar cod. (Xin et al., 2022) analyses the effects induced by polybrominated diphenyl ethers adsorbed on small polystyrene particles in Arctic Cyanobacteria. (Prata et al., 2020) reviews the human health risk associated with microplastic exposure. The motivation for this study derives from the paucity of work on the carcinogenicity of microplastics. Few studies, like (Sharma et al., 2020), have captured the cancer risk associated with humans due to microplastic exposure, but none tried hands in the limpid Arctic region and food-insecure indigenous settlements.

This study is the first attempt to investigate the carcinogenic risk in humans living in remote Arctic communities, mainly indigenous people of the Arctic, due to microplastic accumulation in the Arctic waters. It advances a stochastic modeling proposition that alludes to an in-silico approach to estimating the microplastic toxicity in humans as it moves across the food chain. It is achieved by first identifying the pathway of microplastic from Arctic waters to humans. Then, all the factors influencing their consumption and biotransformation, like Arctic environmental, geophysical, and human physiological, are ascertained. The limited availability of the toxicity data and paucity of dose-response relationships is a challenge in toxicological modeling. The intake determines the Toxicokinetic (TK) and Toxicodynamic (TD) parameters at the human cellular level. TK focuses on the distribution of microplastics in different body parts, whereas TD oversees the effects induced in an organism. The TK and TD parameters are used to evaluate the cell mutations induced due to the unconjugated reactive metabolites production, which are expressive of the carcinogenic slope factor. Finally, the carcinogenic risk is assessed using the reckoned dose and cancer slope factor.

3.2 Proposed Methodology

The methodology proposed to develop a stochastic ecotoxicological model for human health risk assessment due to any xenobiotic in the Arctic region is shown in Figure 3.1. The developed model propounds a novel approach in which various factors adding to the toxicity model are first identified, and then a cause-and-effect relationship between all these factors is established in a Bayesian Network to evaluate the carcinogenic risk in human beings living in the Arctic communities.

The methodology assesses the carcinogenic effects induced in terms of incremental excess lifetime cancer risk (IELCR). IELCR is a measure of the incremental increase in the likelihood of developing cancer in a population exposed to a carcinogen over what would have occurred in the absence of exposure. It can be calculated mathematically as follows (Bleam, 2017).

$$IELCR = LADD \times CSF \qquad \textit{Equation 3.1}$$

LADD is the lifetime average daily dose.

CSF is the cancer slope factor.

LADD is the dose calculated by averaging the total exposure over an individual's lifetime of 70 years. CSF is a parameter representative of developing cancer due to lifetime exposure to a carcinogen. It is expressed as the population affected per unit weight of carcinogen per unit body weight per day.

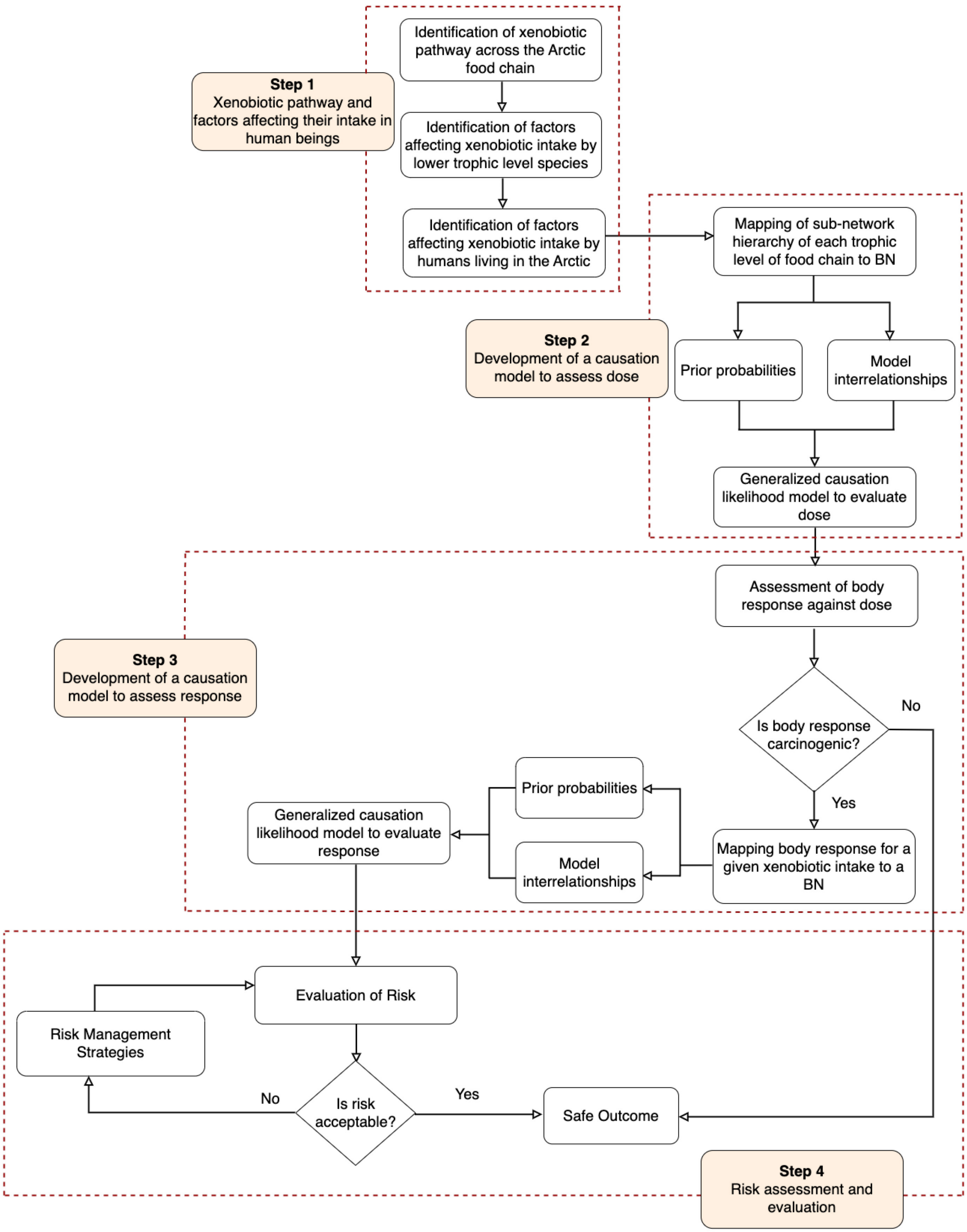

Figure 3.1 The proposed methodology for the cancer risk assessment in humans exposed to microplastics.

3.2.1 Xenobiotic pathway and factors affecting their intake in human beings

Any xenobiotic present in the environment enters the animals in the food web and travels up the food chain culminating in the top predator, i.e., humans. Other exposure routes could be inhaling polluted air and dermal contact with contaminant. However, the main source is the intake of locally available food, called country or traditional food, which comprises of the land and sea animals. These animals constitute the Arctic food chain which is unique and simple. Around 21,000 known species and many unknown species call the Arctic home. Many peculiar species, such as the polar bear, beluga whales, seals, and polar cod are found here. The sui generis nature of the biodiversity in the region can be ascribed to cold and harsh conditions. (Nordström, 2017). The major pathway of a toxicant from the environment to the human body is through the animals in the food chain. Biomagnification is also observed as the contaminant moves from lower trophic levels to higher trophic levels (Farrell & Nelson, 2013; Ortega-Borchardt et al., 2023; Saley et al., 2019). The pathway for microplastic, for instance, is detailed in the application section below.

In the identified food chain, all the factors affecting xenobiotic intake by species across all trophic levels are ascertained. The local environmental and geophysical conditions like season, sea-ice thickness and salinity of the water influence the feeding activity (Fahd et al., 2019), which determines the contaminant intake. Xenobiotic consumed via feed is then exposed to the physiological situation of the species, where it gets transformed. Thus, environmental and geophysical factors of the region and the physiological parameters of species in the food chain are paramount in modeling.

3.2.2 Development of causation model to assess dose

The factors influencing xenobiotic intake at each trophic level of the food chain are mapped into a directed cyclic graph, and then a cause-effect relationship is established between them.

Subsequently, it is updated with prior and conditional probabilities to predict the consequence likelihood. The mapping of the sub-network hierarchy of each trophic level to a Bayesian Network, as shown in Figure 3.2 is inspired by the work of (Kamil et al., 2023).

A Bayesian Network is a stochastic approach to modeling a scenario from cause to consequence. It is a directed acyclic graph respecting Markovian conditions, i.e., non-descending nodes are not influenced by a parent node (Rahman et al., 2020). A very complex nodal structure is formed if there are many causal factors which is challenging to decipher. Therefore, to simplify, it is fragmented into a sub-network hierarchy called Object-Oriented Bayesian Network (OOBN). The factors affecting microplastic intake are mapped and split into OOBN in the application section below.

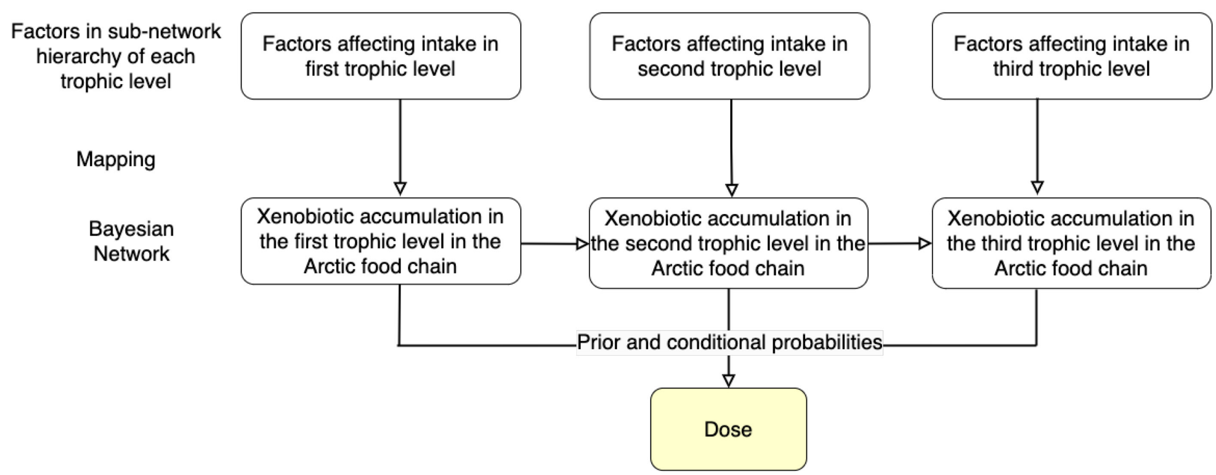

Figure 3.2 Mapping of the *sub-network hierarchies of each trophic level to a Bayesian Network.*

3.2.3 Development of causation model to assess response

A xenobiotic undergoes absorption, distribution, metabolism, and elimination (ADME) upon ingestion. Systemic circulation facilitates absorption and distribution in the body, whereas the liver metabolizes it into waste which is eventually eliminated via the excretory system.

The human body responds to a carcinogen in different ways. Carcinogenic xenobiotics activate xenobiotic metabolizing enzymes (XMEs), mainly cytochrome P450s (CYPs) (Zanger & Schwab, 2013), glutathione S-transferases (GST) (Huang et al., 2018), and uridine 5'-diphospho-glucuronosyltransferases (UGT) (Tourancheau et al., 2017). Metabolic enzymes like CYP oxidases in phase I activate pro-carcinogens largely by oxidizing them and converting them to unstable, reactive metabolites (RMs) which then attach themselves irretrievably to macromolecules like DNA, lipids, and proteins, leading to cell mutations which are often cancerous (Guengerich, 2008). In phase II, XMEs such as GSTs and UGTs inactivate the toxic RMs to glutathione conjugated metabolites. Low phase II activity leads to superoxide (O_2^-) production, which later converts to hydroxide (OH^-) in the presence of SOD enzyme. It causes DNA damage and lipid peroxidation, resulting in higher cancer susceptibility. It also means a higher concentration of toxic reactive metabolites and activated carcinogens remaining in the body, which are precursors to malignancy and cancer development (Beyerle et al., 2020; Nebert et al., 2013; Saeed et al., 2022; Tamási et al., 2011).

Cell mutations are an indicator of carcinogenic response (Barnes et al., 2018; Broustas & Lieberman, 2014). A causation model is developed considering all the parameters discussed above by establishing a cause-effect relationship between them and updating them with prior and conditional probabilities available in the literature and expert elucidation to estimate the response of an individual exposed to a carcinogen.

3.2.4 Risk assessment and evaluation

Risk assessment involves the estimation of the likelihood of the potential hazard, which is the outcome of causal factors in the mapped Bayesian Network. Subsequently, an acceptable risk criterion is upheld based on the available literature. If the acceptance risk criterion is unavailable in the literature, then based on the nature of the study, it can be defined using literature data and expert judgment. Recent research accessed objective risk from textual data by defining risk criteria (Kamil, Taleb-Berrouane, et al., 2023). Thereupon comparing the estimated risk value from the model to the acceptable risk criterion, it is determined whether the risk is acceptable or not. Unacceptable risk values are linked to risk management strategies to reduce them to an acceptable value (Krishnasamy et al., 2005).

3.3 Applications of Methodology: A Case Study

3.3.1 Xenobiotic pathway and factors affecting their intake in human beings

The indigenous people of the Arctic have long relied on the country food partly because of food insecurity and partly to preserve their culture and lifestyle. Their diet mainly comprises the locally available sea and land animals. It includes Arctic Char, polar cod, various pinnipeds like seals, walruses, caribou, narwhal, beluga, sea birds, polar bears, polar foxes and so on (Geographic, 2018; Procter & Natcher, 2012).

Microplastic, on reaching the Arctic waters make their way into all Arctic species through the food web. In this complex food web, it is imperative to identify the major route of microplastic to humans. Based on the works of (Steiner et al., 2019), and (Bluhm & Gradinger, 2008) the following food chain is identified for the purpose of this study, as depicted in Figure 3.3.

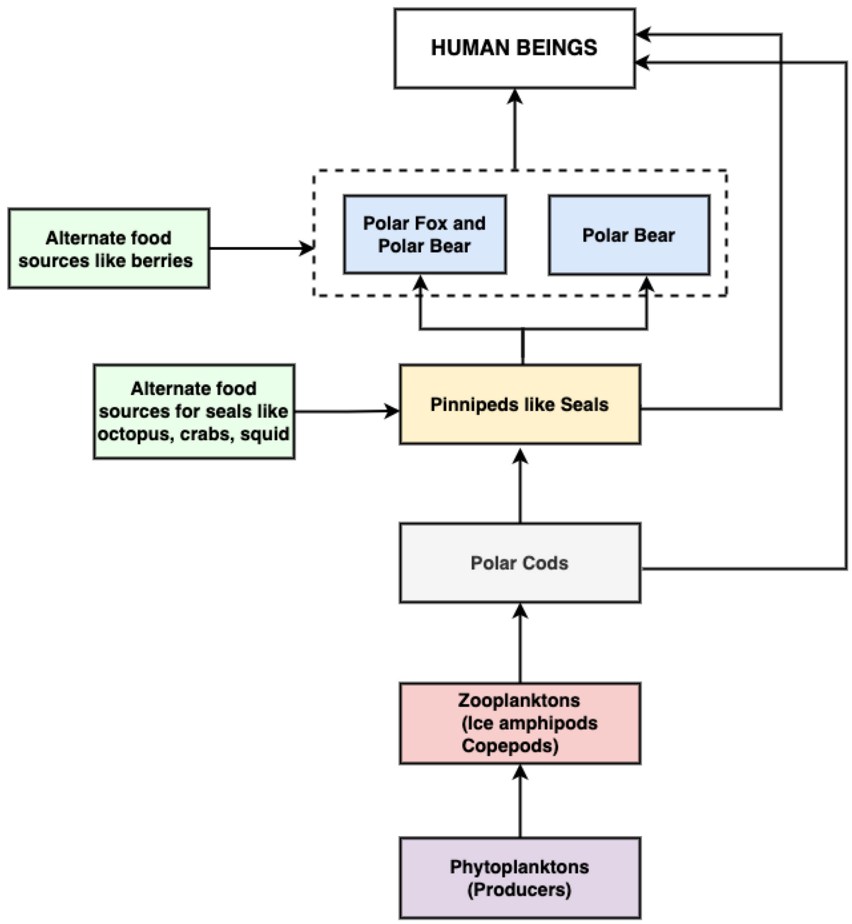

Figure 3.3 Considered Arctic food chain.

Once the pathway is determined, it is indispensable to investigate the factors that affect microplastic intake. Regional environment and geophysical conditions such as season, sea ice thickness and water salinity are considered. Also, microplastic properties like their size and concentration are taken into account for this study.

3.3.2 Development of causation model to assess dose

A causation model is developed from the identified factors affecting microplastic intake by species at the lowest/first trophic level in the considered food chain (Figure 3.3).The model is furthered by prior and conditional probabilities of each node to predict the microplastic accumulation in it, which acts as an input to the next trophic level species. The process is iterated again for the second and the third trophic level species. Finally, the sub-network hierarchy of all trophic levels is mapped into a Bayesian Network to estimate the lifetime average daily dose (LADD) likelihood in apex predator, i.e., humans, as shown in Figure 3.4.

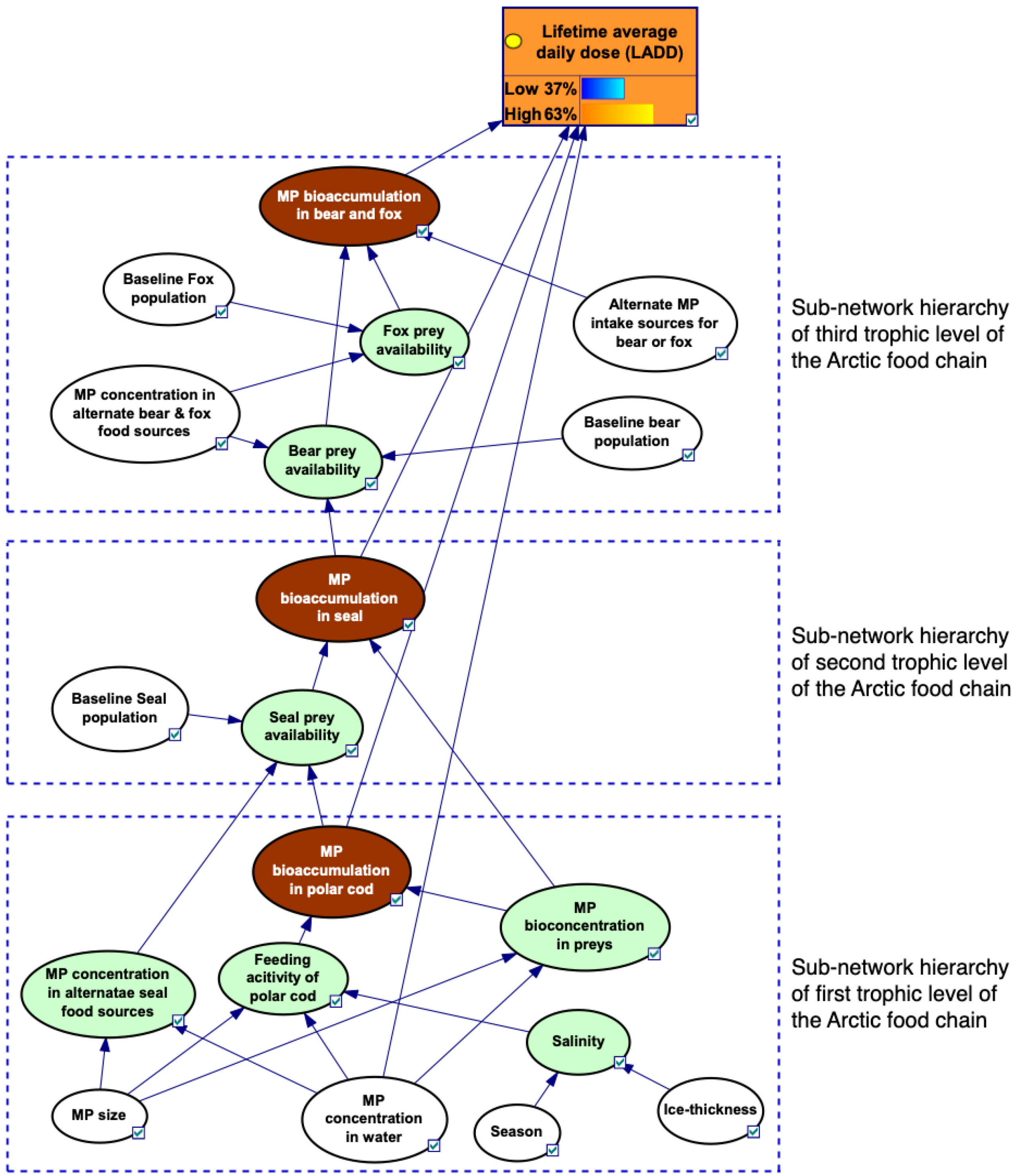

Figure 3.4 Assessment of microplastic lifetime average daily dose (LADD) in humans.

3.3.3 Development of causation model to assess response

Small microplastic fragments sorb various carcinogens while in the environment. (Bakir et al., 2012) establishes persistent organic pollutants presence on the surface of microplastic debris in the marine environment. It also provides a medium for heavy metal deposition on its surface (Brennecke et al., 2016). Thus, microplastics enriched with carcinogens enter the food chain and induce a carcinogenic response in humans.

The ingested microplastics get distributed inside the human body. The study considers a three-compartment model, wherein the ingested microplastic divides in three chambers via the systemic circulatory system, as shown in Figure 3.5. The liver is where biotransformation occurs. Some part of it is then eliminated from the body through the excretory system in the form of urine, sweat and feces.

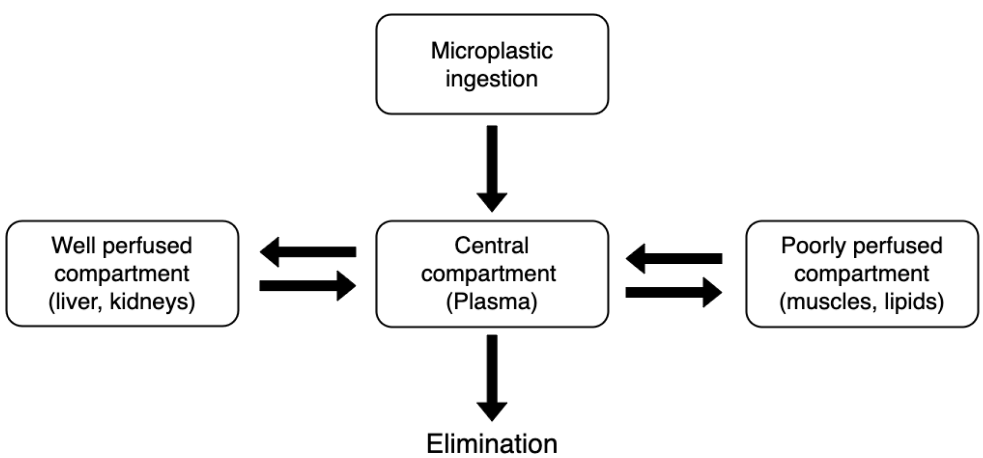

Figure 3.5 Distribution of microplastic in human body.

In the liver, carcinogens supplemented microplastics are absorbed from the gastrointestinal tract and metabolized into hydrophilic or water-soluble chemicals, which are easily eliminated from the body in urine or bile. The biotransformation of microplastics is mediated by CYP enzymes sourced from the liver microsomes derived mostly from the membranes of the endoplasmic reticulum of the liver. Microplastics proliferate the smooth endoplasmic reticulum of the liver, an intracellular organelle to enhance CYP enzymes production. The smooth endoplasmic reticulum consists of a continuous and complex network of smooth tubules active in xenobiotic detoxication. Once microplastics are removed from the liver, proliferating endoplasmic reticulum returns to normal levels to achieve homeostasis. Biotransformation of microplastics in the liver is a two-phase process: phase I involves activation of pro-carcinogens, converting them into unstable, reactive metabolites in the presence of cytochrome p450 oxidase and phase II detoxifies these intermediary carcinogenic reactive metabolites via GST enzyme into stable glutathione conjugated metabolites, which is eliminated from the body via excretory system. The remaining unconjugated metabolites attach themselves to macromolecules like proteins and DNA, causing mutations which indicate a carcinogenic response as discussed in the methodology section above. All the factors resulting in cell mutations are identified and mapped into a Bayesian Network to predict the carcinogenic response, as shown in Figure 3.6.

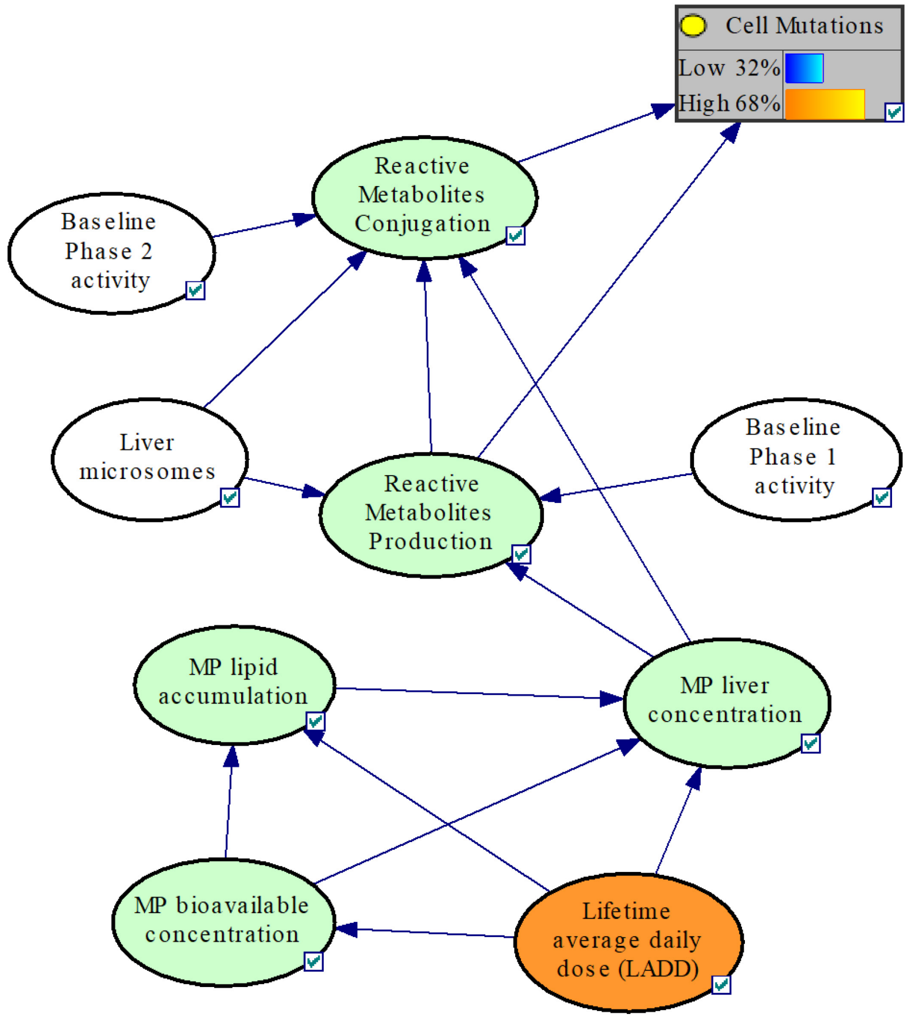

Figure 3.6 Assessment of cell mutations in humans on microplastic intake

3.3.4 Risk assessment and evaluation

The cancer risk assessment framework is based on an Object Oriented Bayesian Network modeling approach which is used to simplify a complex Bayesian Network and make it easy to follow. It is a hierarchy of sub-networks which represents the Bayesian Network with a desired level of abstraction (Khakzad et al., 2013; Sarwar et al., 2018). Figure 3.7 below illustrates the conversion of the Bayesian Network into Object Oriented Bayesian Network.

The likelihood of incremental excess lifetime cancer risk (IELCR), as evaluated by the model, is depicted in Figure 3.8. (Health Canada, 2021) recommends risk values in the range of 10^{-6} and 10^{-5} as tolerable risk. In other words, cancer cases in the range of 1 to 10 or lower in a million population are deemed acceptable. The developed model predicts risk higher than the acceptable value.

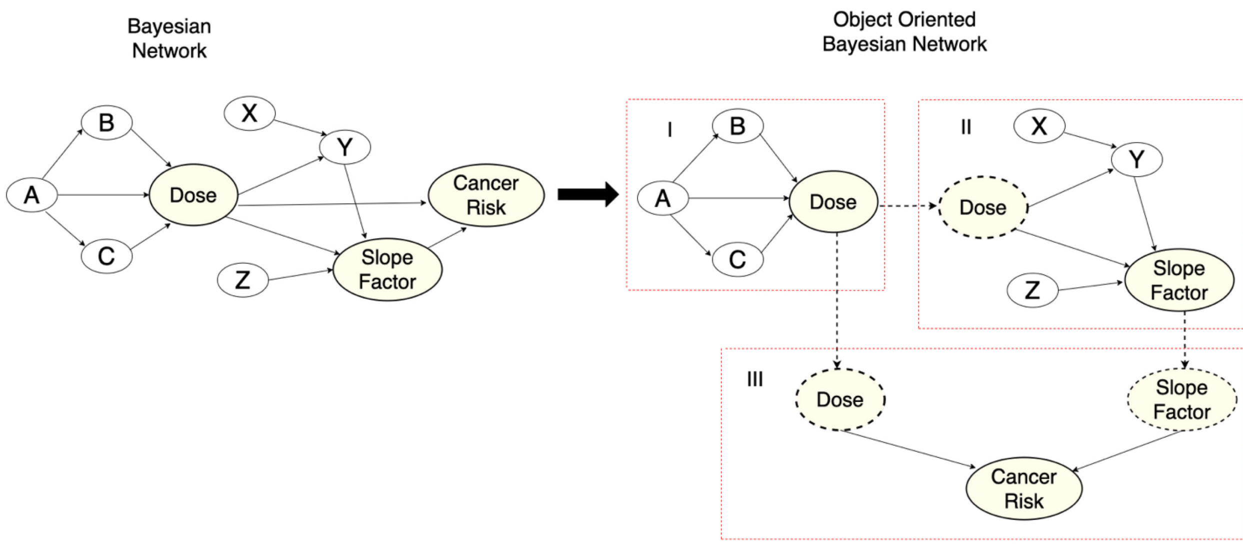

Figure 3.7 Conversion of Bayesian Network into Object Oriented Bayesian Network.

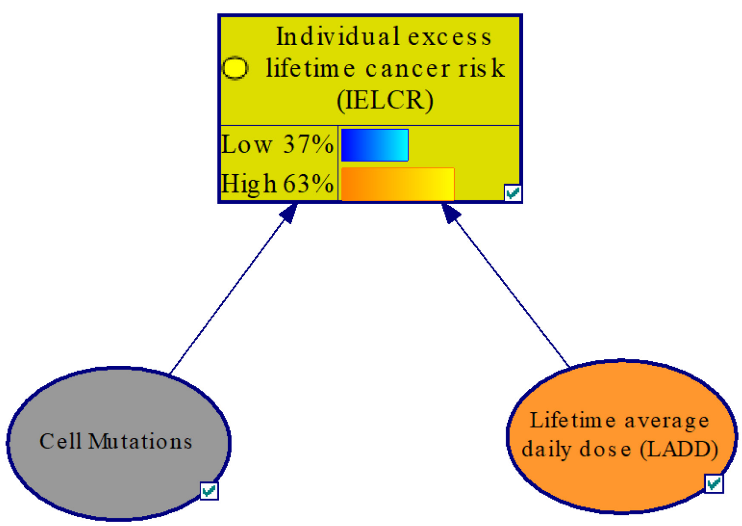

Figure 3.8 Assessment of individual excess lifetime cancer risk (IELCR) in humans on microplastic intake.

3.4 Results and Discussions

Microplastics are complex pollutants and thus upon ingestion cause various health problems in humans. They are composed of plastic polymers, additives added during their production process and chemicals sorbed from the environment. Some plastic monomers like vinyl chloride are known human carcinogens. Additives like benzene, cadmium and 1,3-butadiene are also proven carcinogens (Conti et al., 2021). Certain chemicals sorbed by microplastics such as few PAHs like Benzo[a]anthracene, Chrysene, Benzo[a]pyrene etc. are recognized as cancerogenic compounds (Robin & Marchand, 2022). The developed model thus considers the carcinogenic effects of microplastics by assessing the incremental excess lifetime cancer risk (IELCR) in humans living in the Arctic communities due to microplastic exposure from Arctic waters.

The Arctic region is peculiar for its distinct environmental and geophysical properties. The eccentric nature of the species inhabiting the region adds more to its enigma. Seasonal variations influence the water salinity as ice thickness fluctuates across the year. The microplastic fragments' properties, such as their size and concentration, along with water salinity, affect the feeding activity of lower trophic level species which determines the accumulation of microplastics in them. This accumulated microplastic in first trophic level species shapes its accumulation in second and third level species along with other factors like their respective baseline population. Microplastic amassed in species at all three levels of the food chain, and concentration in the water together decide the lifetime average daily dose in human beings.

The ingested microplastic gets distributed in three chambers inside the body via systemic circulation. The concentration reaching the liver along with liver microsomes and baseline phase

I and phase II activities govern their metabolism. The reactive metabolites remaining after conjugation determines cell mutations which are indicative of carcinogenic response. The lifetime average daily dose, in conjunction with cell mutations, estimates the IELCR. The developed causation model is equipped with prior and conditional probabilities to assess the human carcinogenic risk.

The model evaluates the high lifetime average daily dose (LADD) likelihood in humans exposed to microplastics from Arctic waters at 63%. High LADD is considered as lifetime microplastic intake higher than 40.7 ng per capita Appendix 1. High carcinogenic slope factor, which means more than 5% cell mutations (Appendix 1), is estimated to be 68%. In other words, the likelihood of less than 5% cellular mutations is assessed to be 32%. Finally, the model predicts the high likelihood of IELCR at 63%. High likelihood is defined as risk values in between 10^{-5} to 10^{-3} and low IELCR likelihood is defined as risk values lower than the acceptable value of 10^{-5} (Appendix 1). The low likelihood of IELCR stands at 37%. It indicates that humans in the Arctic settlements exposed to microplastic are highly susceptible to developing cancer cells. Thus, proper management policies should be formulated to protect the health of the population living in the remote Arctic regions, mainly the indigenous peoples. Various independent bodies and organizations should be set up to oversee the fair implementation of these strategies, and due importance should be paid to the health and overall hygiene of these communities.

3.4.1 Model testing

The developed causation model is tested by creating a few scenarios. Five scenarios are generated to test the model in which scenarios 1 and 2 represent the lower bound and upper bound of the carcinogenic risk model. Scenarios 3, 4 and 5 correspond to in between cancer risk likelihood values. Table 3.1 illustrates all the generated scenarios, their description, and the IELCR estimated by the model.

Scenarios 1 and 2 represent the variability in the results predicted by the model. Scenario 1 is based upon an extreme winter condition with small sized microplastic prevalence having a low concentration in the Arctic waters. It further considers the high baseline population of organisms in the food chain. It also assumes low CYP enzyme activity in the human liver. The model predicts a high likelihood of IELCR at 42% in this case. The upper bound condition depicted in scenario 2 is based on environmental conditions when enhanced feeding activity is observed. The parameters are set such that the foraging activity of species is conducive and the CYP enzyme activity is high. The results show a high likelihood of IELCR at 74%.

Other scenarios are based on intermediate milieux. Scenario 3 represents sparse big microplastic debris in the cold winter season with a high baseline population of food chain organisms and elevated phase I and normal phase II activity. The Bayesian Network estimates 55% high likelihood of IELCR. Scenario 4 takes into account a harsh winter situation with abundant microplastics, low prey population, and elevated phase activities. The outcome observed is 70% high IELCR likelihood. Scenario 5 considers the autumn season with a high microplastic size, low microplastic concentration, and low population of species at all three trophic levels. It further assumes high liver microsomes and elevated enzymatic activities. The study shows a 70% probability of high IELCR. The model predictions of all scenarios considered are graphically represented in Figure 3.9.

Table 3.1: Generated scenarios for model testing with their respective incremental excess lifetime cancer risk (IELCR) likelihood.

Scenarios	**Lifetime average daily dose (LADD) parameters conditions**	**Cell mutations parameters conditions**	**IELCR likelihood**
1	Season (*Winter*) Ice-thickness (*High*) MP size (*High*) MP concentration (*Low*) Organisms Baseline population (*High*)	Liver microsomes (*Low*) Baseline phase I activity (*Normal*) Baseline phase II activity (*Elevated*)	High *(42%)* Low *(58%)*

Scenarios	Lifetime average daily dose (LADD) parameters conditions	Cell mutations parameters conditions	IELCR likelihood
2	Season (*Summer*) Ice-thickness (*Low*) MP size (*Low*) MP concentration (*High*) Organisms Baseline population (*Low*)	Liver microsomes (*High*) Baseline phase I activity (*Elevated*) Baseline phase II activity (*Normal*)	High *(74%)* Low *(26%)*
3	Season (*Winter*) Ice-thickness (*High*) MP size (*High*) MP concentration (*Low*) Organisms Baseline population (*High*)	Liver microsomes (*High*) Baseline phase I activity (*Elevated*) Baseline phase II activity (*Normal*)	High *(55%)* Low *(45%)*
4	Season (*Winter*) Ice-thickness (*High*) MP size (*High*) MP concentration (*High*) Organisms Baseline population (*Low*)	Liver microsomes (*High*) Baseline phase I activity (*Elevated*) Baseline phase II activity (*Elevated*)	High *(70%)* Low *(30%)*

Scenarios	Lifetime average daily dose (LADD) parameters conditions	Cell mutations parameters conditions	IELCR likelihood
5	Season (*Autumn*) Ice-thickness (*High*) MP size (*High*) MP concentration (*Low*) Organisms Baseline population (Low)	Liver microsomes (*High*) Baseline phase I activity (*Elevated*) Baseline phase II activity (*Elevated*)	High *(60%)* Low *(40%)*

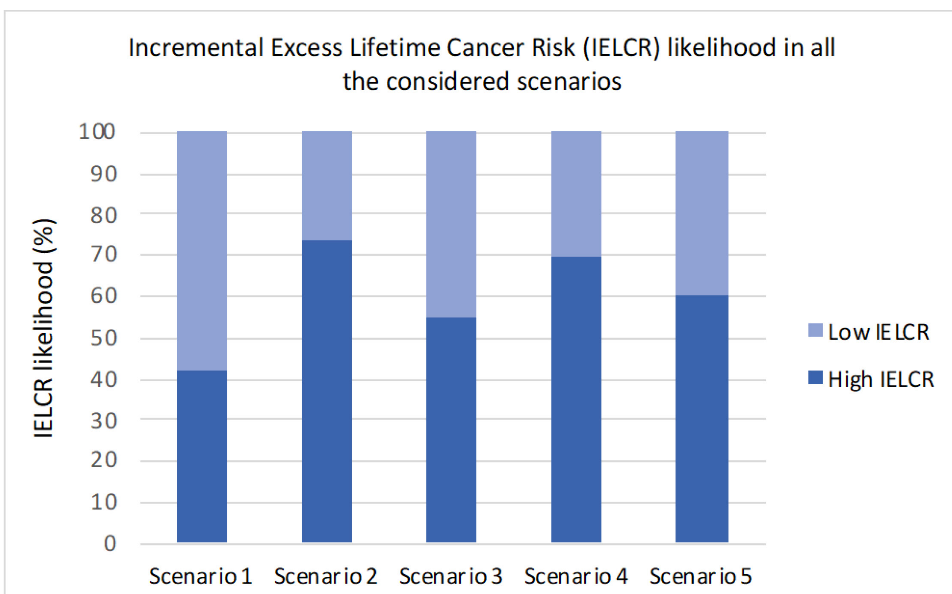

Figure 3.9 IELCR likelihood estimated by the developed model for all scenarios considered.

3.4.2 Model verification

A study published by (Sharma et al., 2020) is used to test the results produced by the developed ecotoxicity model. The study calculates the mean incremental lifetime carcinogenic risk of PAH enriched microplastics in humans at 1.11×10^{-5}. The mean risk associated with children is even higher at 1.46×10^{-5}. The ecotoxicity model developed also predicts similar results. The study considers a high likelihood of incremental lifetime carcinogenic risk as values ranging from 10^{-5} to 10^{-3}. Results estimate the high likelihood of incremental lifetime carcinogenic risk at 63%, which verifies the model.

3.4.3 Limitations of the study

The study, however, is not devoid of limitations. The sex and age of humans and other species at all trophic levels are not considered. Sex and age are critical paraments that influence the feeding, hunting and rearing activities. They also impact the biotransformation process, which determines the cellular mutations. Additionally, some assumptions were made in the prior and conditional probability values of the Bayesian Network. The Arctic food web consists of many species. The study deals with only a few of them in the examined food chain. Biotransformation is a very complex process in microplastics enriched with carcinogens involving multiple pathways and numerous affecting factors (Xin et al., 2023). Only the major pathway of Cytochrome P450 enzyme is considered in the analysis.

3.5 Conclusions

The study advances a novel approach to comprehensively determine the deleterious effects of microplastic accretion in the clean Arctic waters on human beings. This is achieved by evaluating the incremental excess lifetime cancer risk (IELCR) in the apex predator, considering the cascading effects up along the Arctic food web. Risk is assessed as IELCR because many carcinogens leach inside human body upon microplastic ingestion.

This research will enhance the understanding of the risks humans in the Arctic communities are exposed to and will facilitate the policymakers to come up with programs and strategies to combat the imminent risk. The study will help formulate risk management strategies to minimize the microplastic risk to humans. The results of the study will provide the necessary impetus to safeguard the health and interests of indigenous communities. The Arctic Council publishes an agreement among the eight Arctic states titled Arctic Environmental Protection Strategy (AEPS), which addresses the issues of the region. The developed comprehensive marine risk model will also serve as a vital tool for Arctic environmental protection and conservation.

In future, as more research is done, the model can be updated with more detailed and scrupulous information to obtain better and precise results. Knowledge of hunting behaviours of different communities in the region, characteristics of more species in the Arctic food web, and their foraging behaviour, along with the details of microplastic response among species at various trophic levels, could be included in the mode to predict more realistic results.

Acknowledgement

The authors thankfully acknowledge the financial support provided by the Natural Sciences and Engineering Council of Canada (NSERC) through the CREATE program and the Mary Kay O'Connor Process Safety Centre at Texas A&M University.

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Appendix 1: Nodes of the Bayesian Network with their states and description.

Some elements of the table have been adapted from the work of (Saeed et al., 2022).

Table 3.2 Arctic geophysical and environmental factors and microplastic properties

Sr. No.	**BN Nodes**	**Nodal States**	**Characterization of the nodes**
1.	MP size	Low High	(Frias & Nash, 2019) defines microplastic as a plastic fragment smaller than 5mm in size. Low: $<2.5\ mm$ High: 2.5 $mm - 5mm$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
2.	MP concentration in water	Low High	Microplastic concentration measured with 335µm mesh in the Arctic varies from 0.012 N/m^3 to 0.144 N/m^3. However, on using 32µm mesh, 9 N/m^3 to 1287 N/m^3 is the reported concentration (Hänninen et al., 2021; Tekman et al., 2020). (Rist et al., 2020) quantified microplastics in the West Greenland region of the Arctic in the range of 142 N/m^3 to 0.12 N/m^3. Low: <700 N/m^3 High: 700 N/m^3 – 1300 N/m^3
3.	Season	Winter Summer Autumn	The Arctic region experiences – Winters for 7 months, i.e., December to June, Summers for 3 months, i.e., July to September, Autumns for 2 months, i.e., October to November.
4.	Ice-thickness	Low High	In the Fram Strait, thickness of sea ice layer ranges from 0.8 m in summers to 3.5 m in winters (Werner, 2006). Low: *0.8 m – 2.0 m* High: *2.0 m – 3.5 m*

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
5.	Salinity	Low High	Sea ice thickness is directly proportional to salinity. As ice thickness widens on the Arctic surface, salts are squeezed deep in the ocean, increasing salinity (Fahd et al., 2020). Low: $< 18\%$ High: $18\% - 40\%$

Table 3.3 Food chain species and their associated factors

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
1.	Feeding Activity of polar cod	Low High	In summers, phytoplanktons receive sunshine and thus energy flows in the Arctic food chain, enhancing feeding activity of organisms (Cusa, 2016). Low: $<15\%$ High: $>15\%$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
2.	MP concentration in alternate seal food sources	Low High	In addition to polar cods, seal preys on fish, cephalopods, crustaceans and bivalves, crabs, zooplankton and small fish like caplin. Samples of Atlantic cod and Atlantic salmon collected from Newfoundland, Canada reports the microplastic frequency of occurrence at 1.4% with 0-1 per individual and others have reported 1.68% with 0-2 MP per individual. Microplastic concentration in Bigeye sculpin from Northeast Greenland is between 0-1 MPs per positive organism with frequency of occurrence of 34% (Bergmann, Wirzberger, et al., 2017; Kögel et al., 2022; Liboiron et al., 2019; Saturno et al., 2020; Savoca et al., 2021). Low: <$0.015\ N/fish$ High: >$0.015\ N/fish - 0.0336\ N/fish$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
3.	MP concentration in preys (lower trophic species)	Low High	Samples of various primary consumers collected from Norwegian fjord have reported MP concentration of 1.4 MPs per positive organism with frequencies of occurrence between 20 – 41.1% (Bour et al., 2018). Low: <$0.42\ N/organism$ High: >$0.42\ N/organism$
4.	MP bioaccumulation in polar cod	Low High	Microplastic concentration in polar cod sample from Northeast Greenland is between 1-2 microplastics per positive organism with frequency of occurrence of 18% (Morgana et al., 2018). Low: < $0.20\ N/fish$ High: > $0.20 - 0.36\ N/fish$
5.	Seal prey availability	Low High	Average annual gross energy requirement by seal = 4.6×10^9 Joules Gross energy per kg fish = 8.10×10^6 Joules (Dyck & Kebreab, 2009; RYG & ØRITSLAND, 1991) Low: <$1.56\ kg\ fish/day$ High: >$1.56\ kg\ fish/day$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
6.	Baseline Seal population	Low High	Population of seals in the Barents Sea is between few thousands in certain areas to 7 million (Laidre et al., (2015). Low: > 3 $million$ High: 3 $million - 4$ $million$
7.	MP bioaccumulation in seal	Low High	Microplastics have been reported in the gastrointestinal tract (GIT) and stomachs of the seals. 11.2% seal stomachs contained plastic with an average weight of 0.0929 gm per seal stomach (Bravo Rebolledo et al., 2013; Hernandez-Milian et al., 2019; Nelms et al., 2019; Pinzone et al., 2021). Low: > $0.0929\ gm/seal$ High: < $0.0929\ gm/seal$
8.	Baseline bear population	Low High	Population of polar bear in the Baffin Bay, Barents Sea and Davis Strait lies between 2059 - 3593, 1899 – 3592 and 1833-2542 respectively (Laidre et al., (2015). Low: < 2800 High: > 2800

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
9.	Bear prey availability	Low High	An average polar bear (500kg) requires 1 kg of seal blubber or 4 kg fish in a day for body mass maintenance (Dyck & Kebreab, 2009). Low – < 1 kg seal/day or 4 kg fish/day High – > 1 kg seal/day or 4 kg fish/day
10.	MP concentration in alternate bear and fox food sources	Low High	Samples of various secondary consumers collected from Norwegian fjord have reported Microplastic concentration of 2.3 MPs per positive organism with frequencies of occurrence between 5.9 – 65% (Bour et al., 2018). Low: $< 0.69\ N/organism$ High: $> 0.69\ N/organism$
11.	MP bioaccumulation in the Arctic fox	Low High	An average of 0.36 plastic fragments or 0.17 g per Arctic fox is reported (Skúladóttir, 2019; Technau et al., 2022). Low: $< 0.17\ g/organism$ High: $> 0.17\ g/organism$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
12.	Baseline fox population	Low High	The population of Arctic fox is estimated up to few hundred thousand. In Scandinavian mainland, it is endangered. The total population estimate in Finland, Norway and Sweden is a mere 120 adult individuals (World Wide Fund for Nature, n.d.). Low: < 2800 High: > 2800
13.	Alternate MP intake sources for bear and fox	Low High	Samples of various primary consumers collected from Norwegian fjord have reported microplastic concentration of 1.8 MPs per positive organism with frequencies of occurrence between 25 – 55% (Bour et al., 2018). Low: < 0.66 $N/organism$ High: > 0.66 $N/\ organism$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
14.	MP bioaccumulation in bear and fox	Low High	A study on a polar bear population in Alaska showed that one-fourth of them had microplastics in their stomachs. It was also reported in the GITs of the polar bears in Nunavut, Canada. Feces of polar bears in Franz Josef Land contain microplastics. However, no quantification study has been carried out yet (Lusher et al., 2022). Low: < $0.05\ N/organism$ High: > $0.05\ N/\ organism$
15.	Food availability for humans	Low High	The locally available food for the humans living in the Arctic is also a source of microplastic intake. The average seafood consumption for a healthy adult man in the Arctic is approximately 24.4 g/capita/day while for a woman it is 11.4 g/capita/day (Marushka et al., 2021). The MP parameterization Low: < $18\ g/capita/day$ High: > $18\ g/capita/day$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
16.	MP lifetime average daily dose (LADD)	Low High	(Hazimah et al., 2021) estimates human microplastic accumulation at 40.7 ng/capita until the age of 70 years. Low: < $40.7\ ng$ High: > $40.7\ ng$

Table 3.4 Factors of microplastic biotransformation in human beings

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
1.	MP lipid accumulation	Low High	Microplastics trapped in the lipids are expressed as percentage (Tan et al., 2020). Low: < 25% High: < 25%
2.	MP bioavailable concentration	Low High	The maximum microplastic concentration reported in human blood is $7.1\ \mu g/ml$ (Leslie et al., 2022). Low: < 70% High: > 70%

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
3.	MP liver Concentration	Low High	The major xenobiotic metabolism site is the liver, as the highest concentration of biotransformation enzymes is found here here (Gu & Manautou, 2012). Low: < 70% High: > 70%
4.	Liver microsomes	Low High	Endoplasmic reticulum accounts for roughly one-fifth of liver. Low: < $5\% - 12\%$ High: > $12\% - 25\%$
5.	Baseline Phase I activity	Normal Elevated	Values of baseline phase I activity is reported to be in between 0.06-0.22 pmol/min/mg (Quinney et al., 2013). Normal: < $0.15\ pmol/min/mg$ Elevated: > $0.15\ pmol/min/mg$
6.	Baseline Phase II activity	Normal Elevated	The baseline phase II activity in human liver can reach up to a maximum level of 228 pmol/min/mg (C. C. Lin et al., 2006). Normal: < $210\ pmol/min/mg$ Elevated: > $210\ pmol/min/mg$

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
7.	Phase I activity	Low High	Increase in folds of EROD (Ethoxyresorufin- O-deethylase) activity is an expression of phase I activity. It varies in human hepatocytes between 33.2 to 171.2 after incubating for 24 hours with DB(a,h)A, a PAH inducer (Roberts et al., 1994). Low: ≤ 60 High: ≥ 60
8.	Phase II activity	Low High	Increase in folds of GST (Glutathione S-transferase) activity expresses Phase II activity (Cauchi et al., 2006). Low: ≤ 4 High: ≥ 7
9.	Cell mutations	Low High	Low: < 5% High: > 5%

Sr. No.	BN Nodes	Nodal States	Characterization of the nodes
10.	Incremental excess lifetime cancer risk (IELCR)	Low High	The acceptable IELCR value is less than 1 to 10 in a million or in between 10^{-6} to 10^{-5} (Health Canada, 2021). Low: < 10^{-5} High: $10^{-5} - 10^{-3}$

4 SUMMARY, CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE WORK

4.1 Summary

Plastic accumulation, due to its unprecedented consumption over the last few decades is recognized as a potential threat to all marine ecosystems. Plastics are distributed across the water column in different size variations, including microplastics which pose a greater risk to the ecosystem health than the larger plastics. Microplastics are also pervasive in the pristine Arctic waters, where they pose a significant threat to the Arctic ecosystem and the people therein, particularly the indigenous people of the Arctic. To investigate the risk associated with microplastics in the Arctic ecosystem, this thesis proposes two quantitative risk assessment models. The first model estimates the risk in polar cod, while the other investigates the human health risk due to microplastic ingestion.

This thesis incorporates three primary Chapters. The first chapter introduces microplastics, the Arctic region, its fragile ecosystem, and ecotoxicological risk analysis. It describes the complex nature of microplastic as a pollutant and the risk they pose to the organisms that inhabit the Arctic region. It also provides a background on how microplastics travel across the food web to eventually reach humans, particularly those living in remote Arctic communities. Further, it accentuates the scarcity of available literature on microplastic risk assessment. Lastly, it highlights the importance to estimating the risk posed by microplastics to the Arctic ecosystem and the humans therein.

The second chapter establishes polar cod as a species of paramount importance to the Arctic food web. Subsequently, all the factors affecting the microplastic intake in polar cod are identified, and the response induced is determined through changes in relevant biomarker values. The cause-effect relationship is then established in a Bayesian Network framework to evaluate cytotoxicity in polar cod.

The third chapter presents a stochastic modelling approach to assess the human health risk due to microplastic exposure. First, it identifies the pathway of microplastic across the Arctic food web. Then it identifies the factors affecting microplastic intake in humans. Subsequently, the toxicological effects are identified. Finally, a Bayesian Network is developed to assess the carcinogenic risk. Lastly, this chapter concludes by summarizing the study and highlighting the successes of this investigation.

4.2 Conclusions

Microplastics are fast gaining prominence in the Arctic waters. They pose a serious health risk to the whole Arctic biota and humans deriving their food from the region, particularly the nearby indigenous Arctic community settlements. The lower trophic level organisms are exposed to microplastics through ingestion which then moves up the food chain, eventually reaching humans. Microplastics get bioaccumulated and biomagnified at each trophic level before it reaches humans, making them most vulnerable.

Little to no work has been done to assess the ecotoxicological risk in humans and Arctic species due to microplastic exposure. This thesis accomplishes this knowledge gap by developing two novel models. First, it proposes a comprehensive stochastic modelling approach to assess the risk due to microplastic intake in polar cod, a species of utmost importance to the Arctic food chain. This risk is assessed in terms of cytotoxicity. Second, it investigates the carcinogenic risk in human beings, particularly the indigenous people of the Arctic, due to microplastic intake. The models are then tested across a wide range of ecological conditions using the data from the available literature.

The research conducted will provide insights into the risk associated with microplastics to the Arctic ecosystem. It will facilitate the policymakers to formulate better Arctic risk management policies and strategies. It will also assist in developing programs to cope with the imminent microplastic risk. The thesis will serve as a vital tool in safeguarding the interests of the indigenous people of the Arctic by devising measures aimed at establishing and strengthening the right to healthcare. The study will provide an impetus for Arctic environmental protection and conservation.

4.3 Recommendations for Future Work

The following suggestions are provided for the further development of the work described in this thesis. The work presented in the thesis can be extended to various other species of the Arctic food chain. The study mainly focuses on the major biotransformation pathway, which is catalyzed by CYP1A enzymes. However, to improve the accuracy of the results, it is suggested that the model should include other biomarkers that are sensitive to oxidation and conjugation phases of the biotransformation process, thus alluding to different biotransformation pathways. Additionally, it is important to consider the effect of inhibited or activated cellular activities on biomarker activities, which can otherwise render inaccurate results. Furthermore, the study did not account for age and sex of the organism, which have an indubitable bearing on the feeding behaviour of organisms while evaluating toxicity risk.

Therefore, future studies can focus on exploring the other biotransformation pathways and corresponding biomarkers in different species, including polar cod and human beings. The impact of sex and gender on ecotoxicity risk due to microplastic intake should be investigated. Capturing details in the model, such as extensive information on the hunting behaviour of various species in the food chain, translocation of species and divergence in food preferences, can produce better results.