Climate Change, Cyanobacteria, and Disease

The link between environmental toxins, climate change, and Amyotrophic Lateral Sclerosis (ALS)

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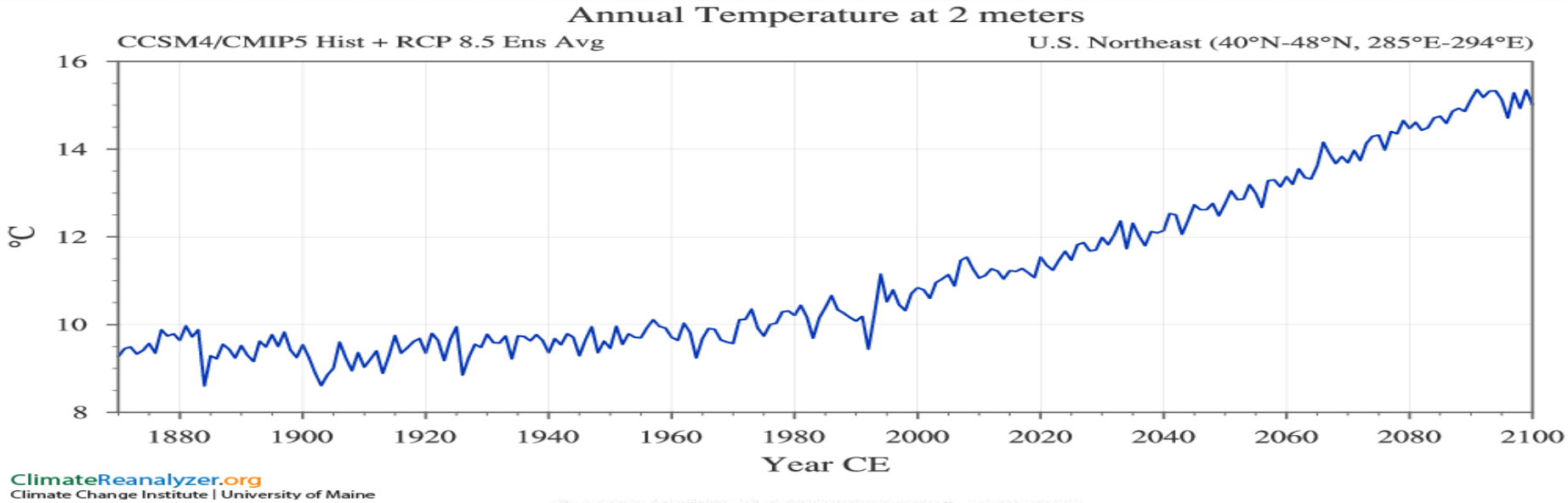
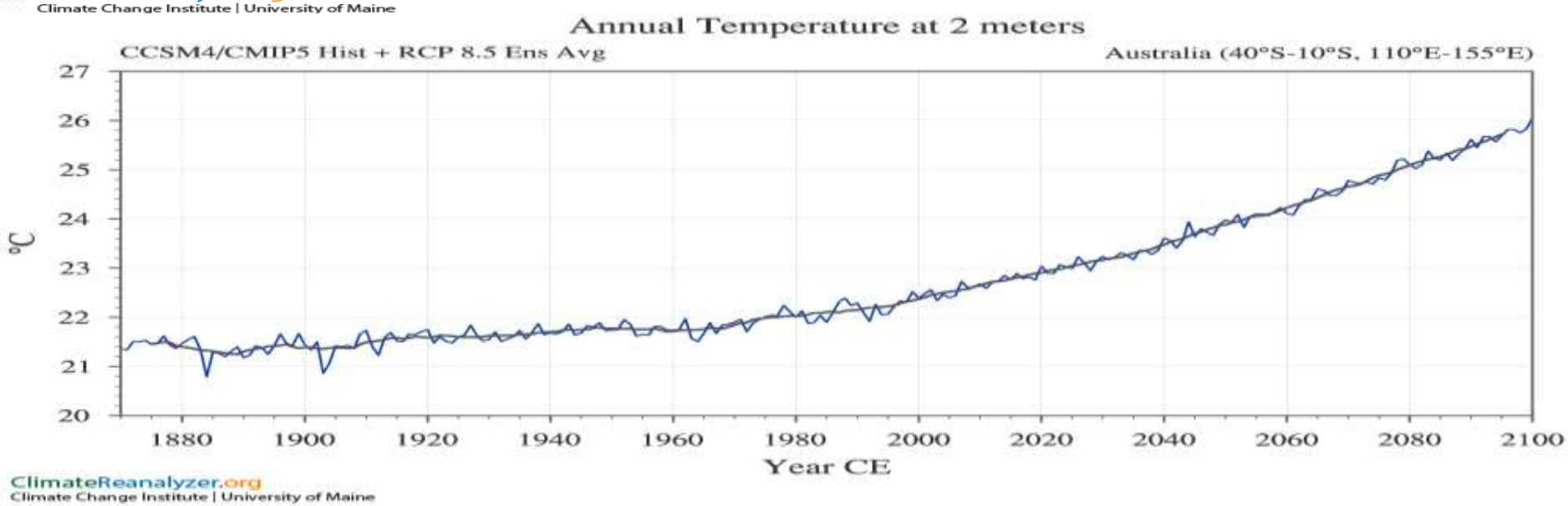
Our planet is warming





Blue-green algae are predicted to increase with global temperatures

- Blue-green algae (**cyanobacteria**) can produce harmful algal blooms (**HABs**)
- Cyanobacteria are temperature sensitive
  - Increase in HABs
  - Harmful species will likely outcompete less toxic species of cyanobacteria

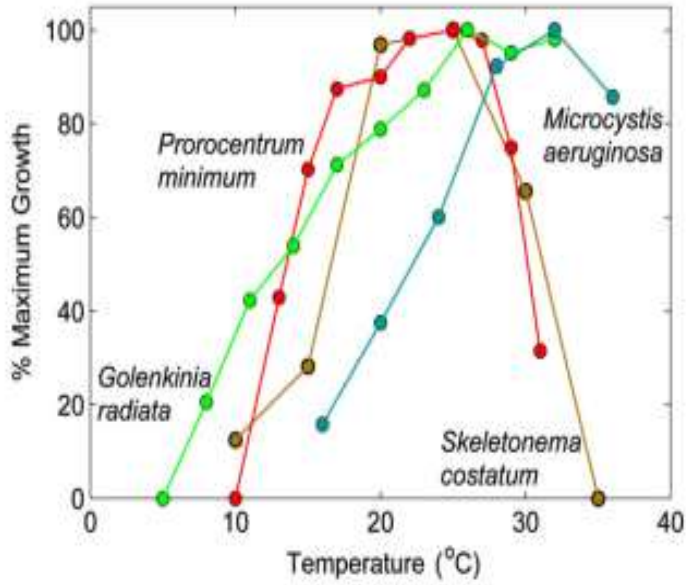
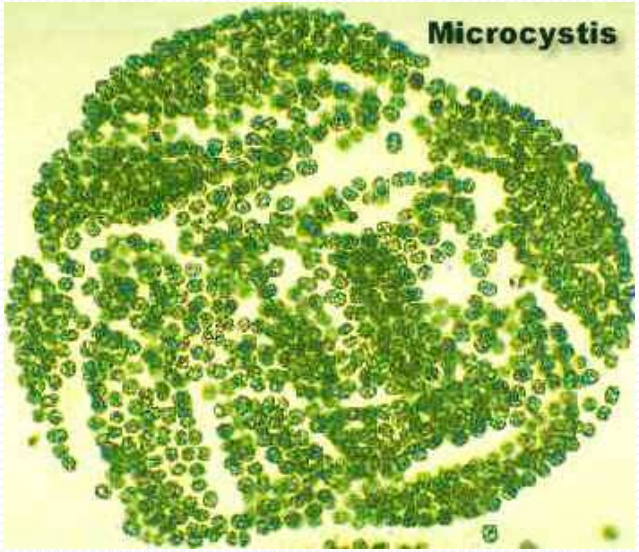


Fig. 4 – Effects of temperature on species-specific growth rates of a representative CyanoHAB species (*Microcystis aeruginosa*) vs. commonly encountered eukaryotic algal bloom species, including the chlorophyte *Golenkinia radiata*, the diatom *Skeletonema costatum*, and the dinoflagellate *Prorocentrum minimum*. Growth rate data are from Reynolds (2006), Grzebyk and Berland (1995), and Yamamoto and Nakahara (2005).

Paerl and Paul, 2012

HABs contain toxins that negatively effect human health

- Increased toxins released with the blooms
- People can come in contact with these toxins through:
  - Drinking
  - Agriculture
  - Recreational Activity
    - Boating
    - Fishing
    - Water Skiing
    - Swimming

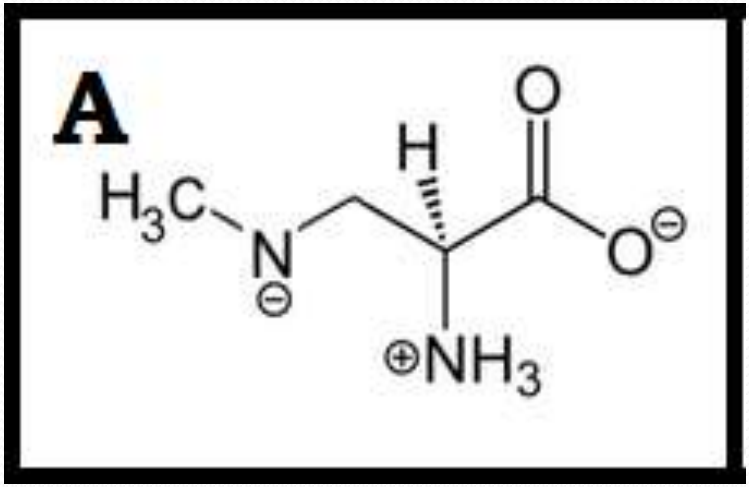


http://www.lmw.vic.gov.au/

BMAA is produced by many harmful cyanobacteria

- **BMAA** is beta-Methylamino-L-alanine
  - a non-proteinogenic amino acid
- **BMAA** is associated with an increased prevalence of neurodegenerative diseases:
  - Alzheimer's disease
  - Parkinson's disease
  - **Amyotrophic lateral sclerosis (ALS)**

BMAA



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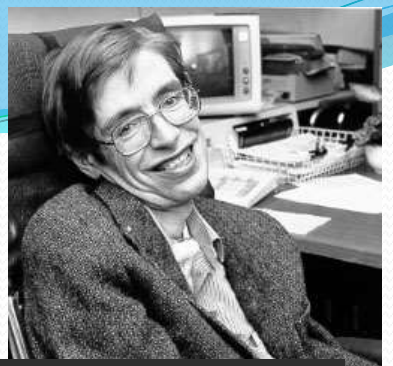
What is Amyotrophic lateral sclerosis (ALS)?



- Fatal disease with no cure
  - Only FDA approved treatment (Riluzole) extends a person's life by a few months (with severe side effects)
  - Usually die 2-4 years after diagnosis

Stephen Hawking (Photo: NSA)

Studying HAB toxins in lakes from several places

- Maine
- Other NE States
- Western Victoria, Australia

Maine's fresh water lakes are experiencing HABs

- Working with the Maine DEP to sample 10 lakes throughout Maine
- Testing HAB surface water for the toxin, **BMAA**
  - Detect the current concentration
  - See if BMAA concentrations increase over several years
    - Connection to climate change?
      - Does temperature increase correlate with increased HABs?

An algae bloom in Sabattus Pond in Maine (from Portland Press Herald)

Several lakes in Victoria, Australia are experiencing HABs

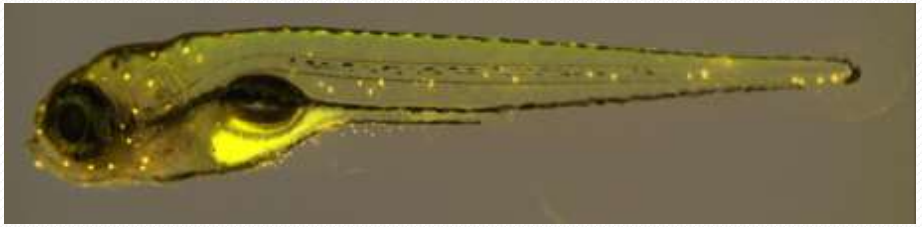
- Lakes in Victoria are experiencing cyanobacterial HABs
  - Lake Bullen Merri, Deep lake, Lake Colac
    - Lakes used for recreational activities
- Is **BMAA** is present in any lakes in Victoria, Australia?
  - At what concentration?
- Any effect of climate change on HABs in these lakes?

Lake Bullen Merri, Victoria. Camperdown Chronicle 2014.

We use zebrafish to study the toxic effects

- Well established model for toxicology research
- Response similarly to mammals after toxic insult
- Spawn in large numbers
- Inexpensive to maintain
- Translucent at a young age

5 day old zebrafish



Adult zebrafish

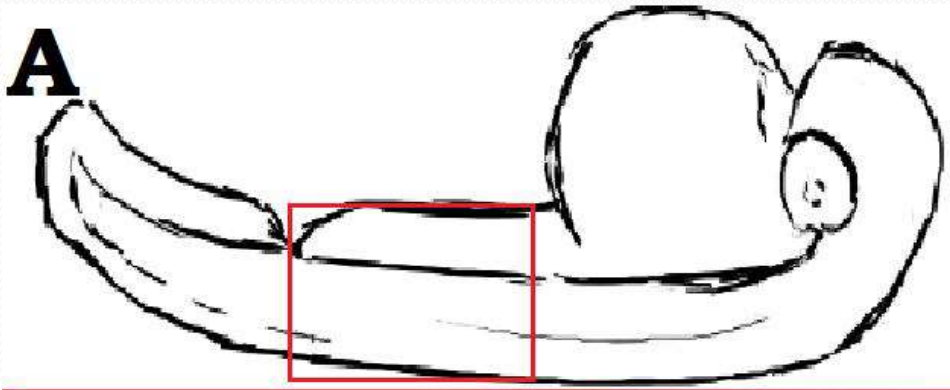
https://www.sanger.ac.uk/ and http://www.zf-health.org/

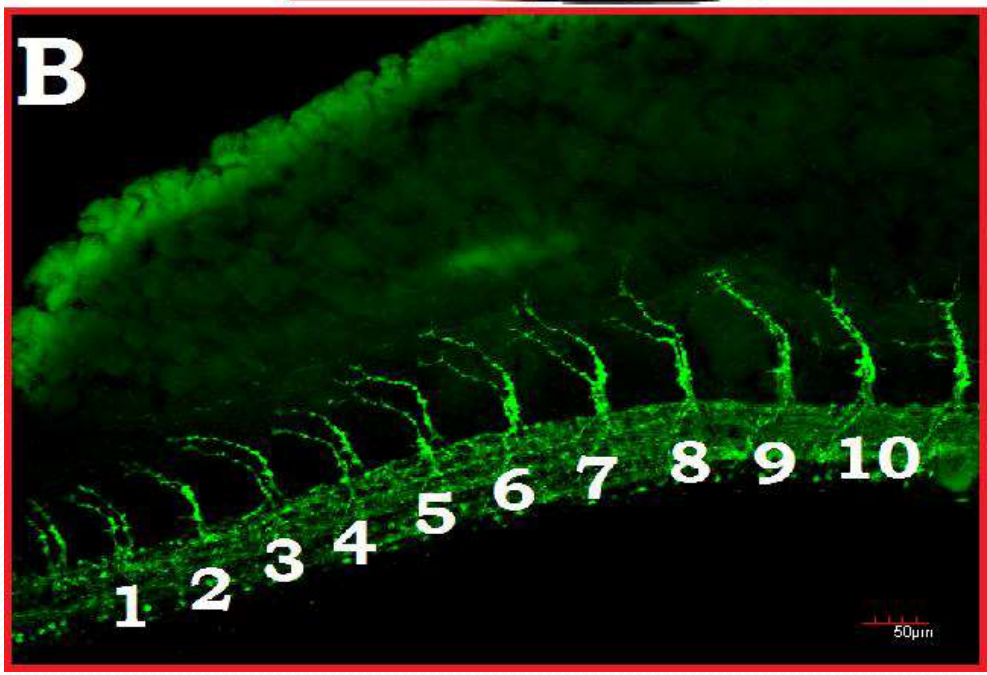
Several techniques are used to examine toxic effects with Zebrafish

1. Examine changes in neuronal **length** at the neuromuscular junction (**NMJ**) at 30 hours of age
2. Quantifying pre and post synaptic **connections** at the **NMJ** at 72 hours of age
3. Examine **neuromuscular fitness** using a behavioral **spin task assay** at 5, 10, and 15 months of age
    1. 15 months is middle to old age in zebrafish

Assess neural length at 30 hours

- Zebrafish are exposed to a toxin from fertilization until they are 5 days old
- Examine neurons at the NMJ
  - Measure the length of the neurons





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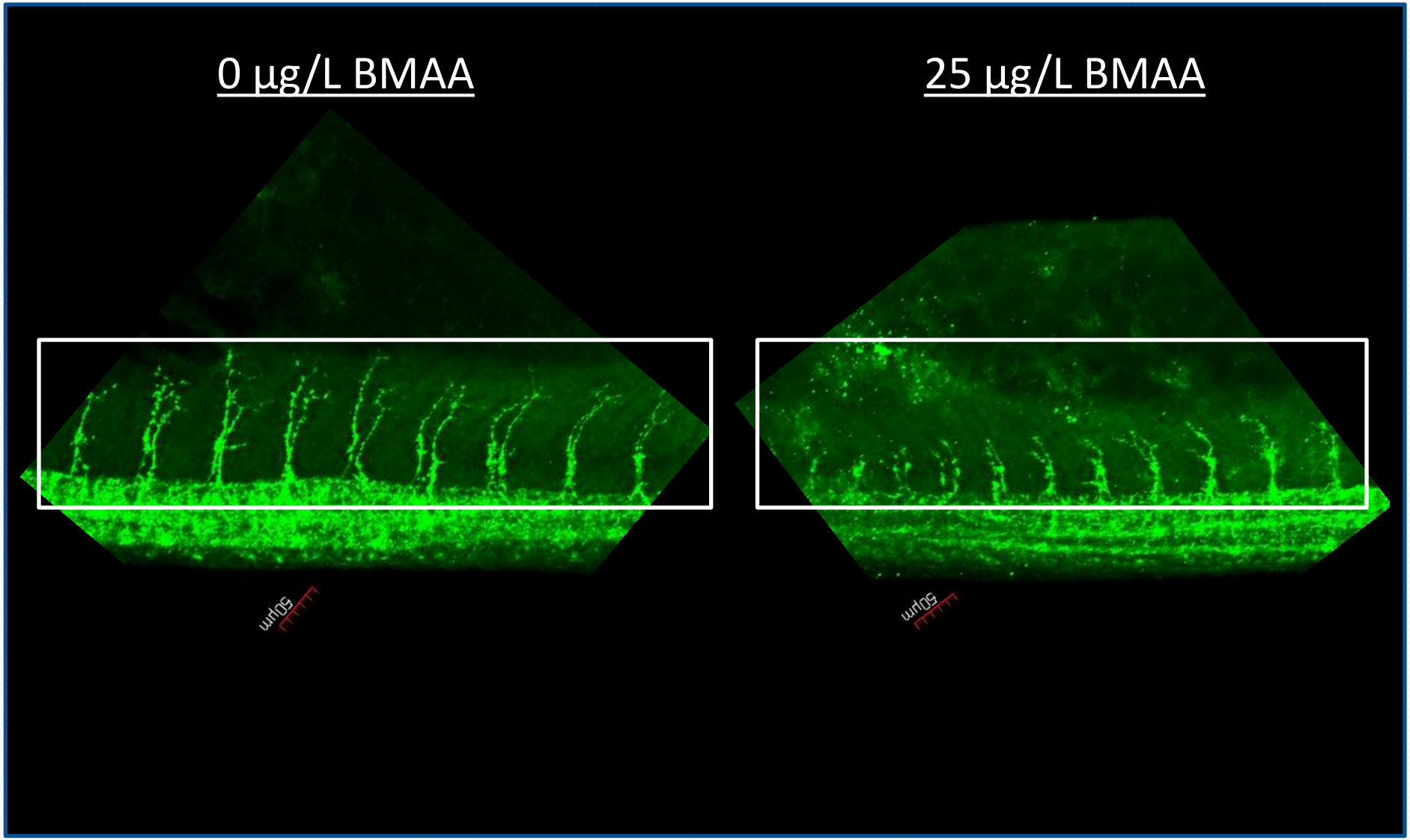
Nerve Length effected by early developmental exposure to BMAA



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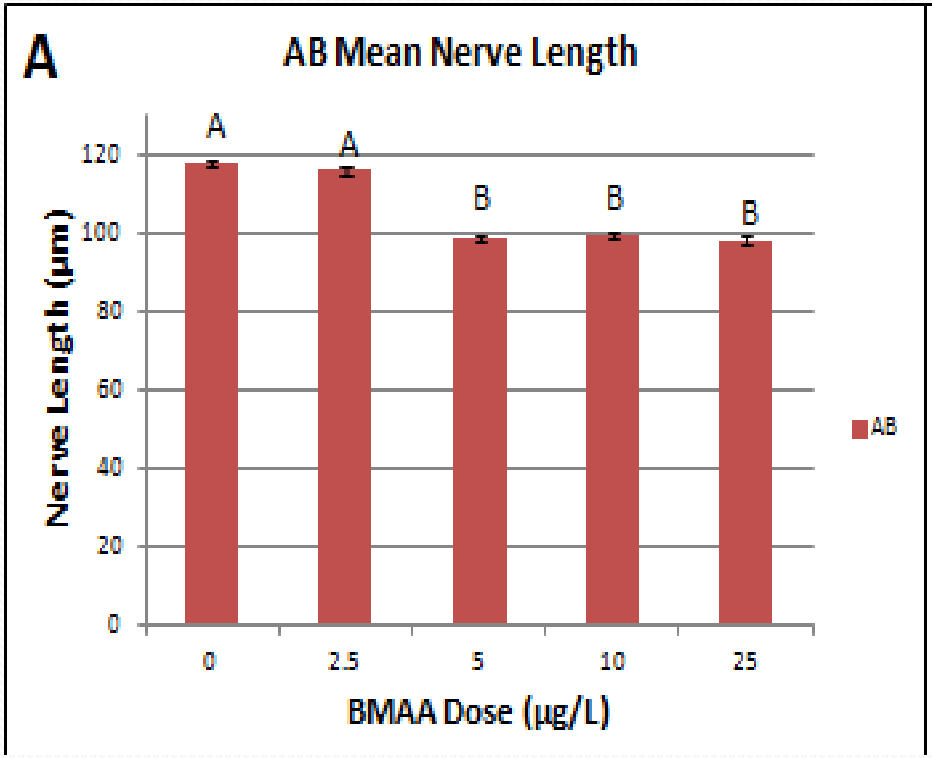
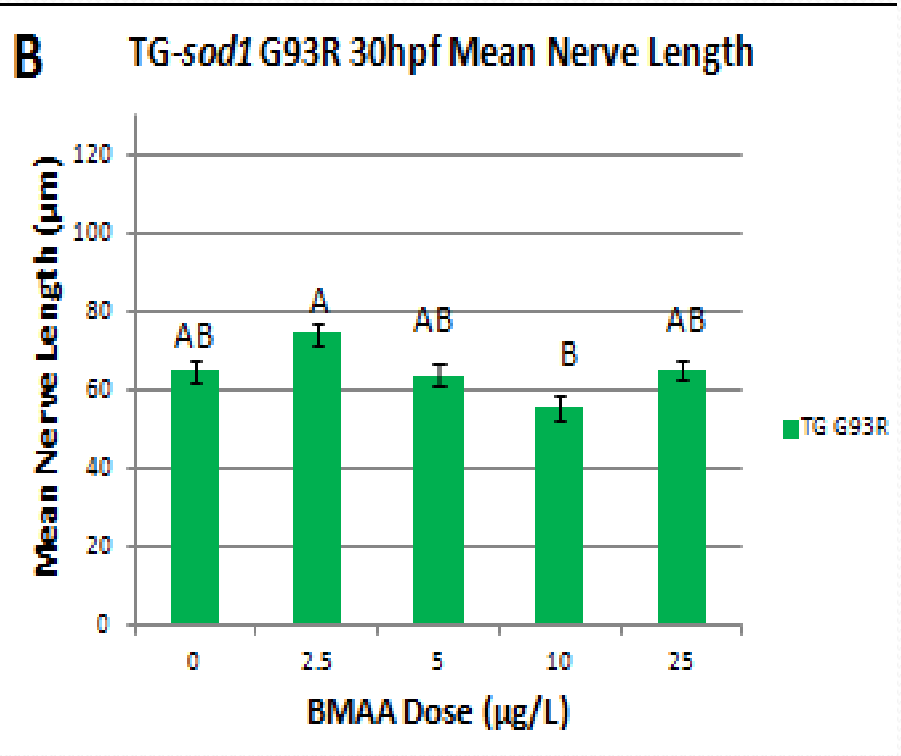
Zebrafish have reduced nerve length at after exposure to BMAA (0-30 hours)





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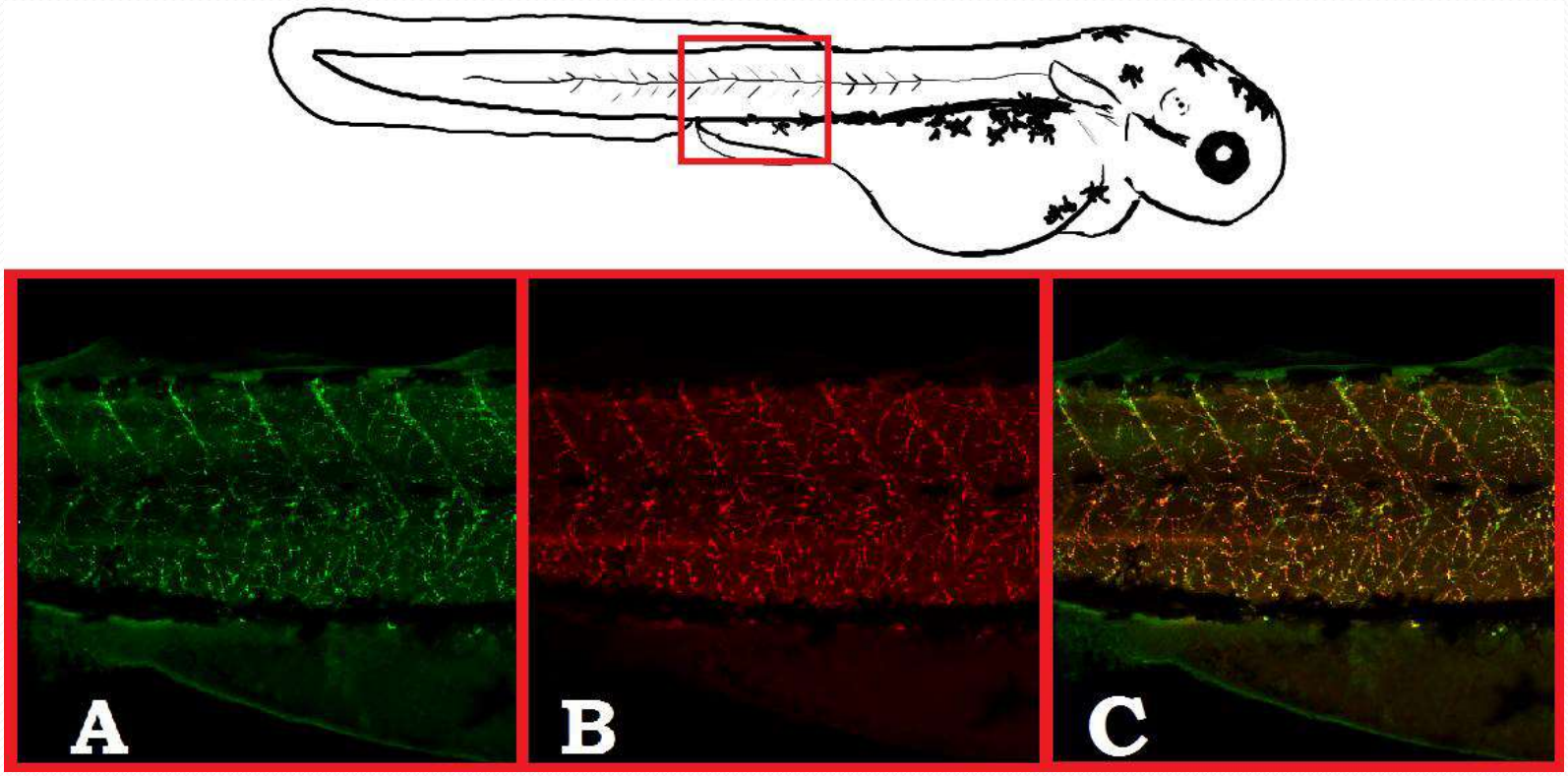
Quantifying pre and post synaptic connections at 72 hours

- Determine if there is an effect of the toxin on how the neurons and muscles are lining up at the NMJ



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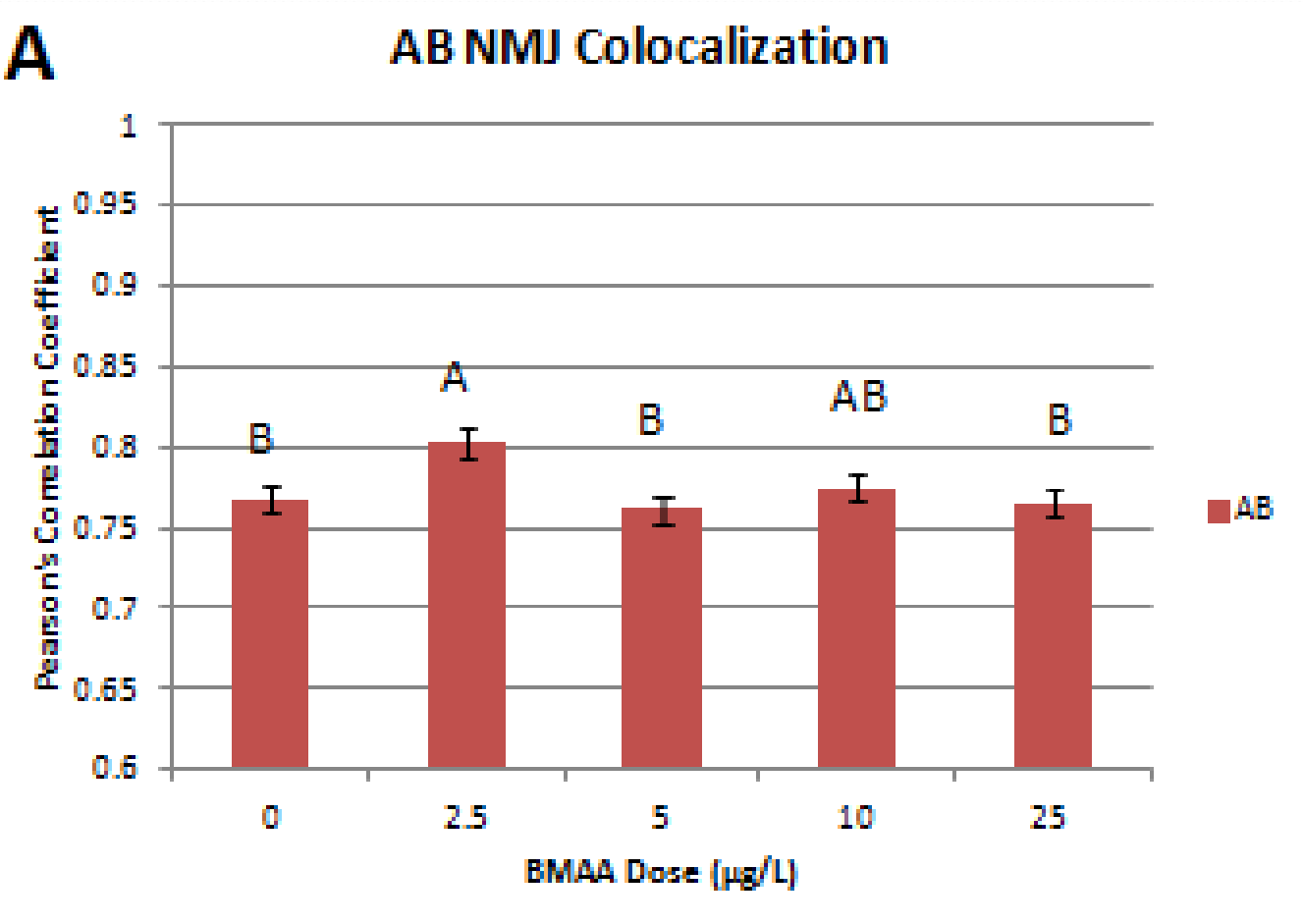
Co-localization altered after exposure to BMAA



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Behavioral test - Spin Task Assay

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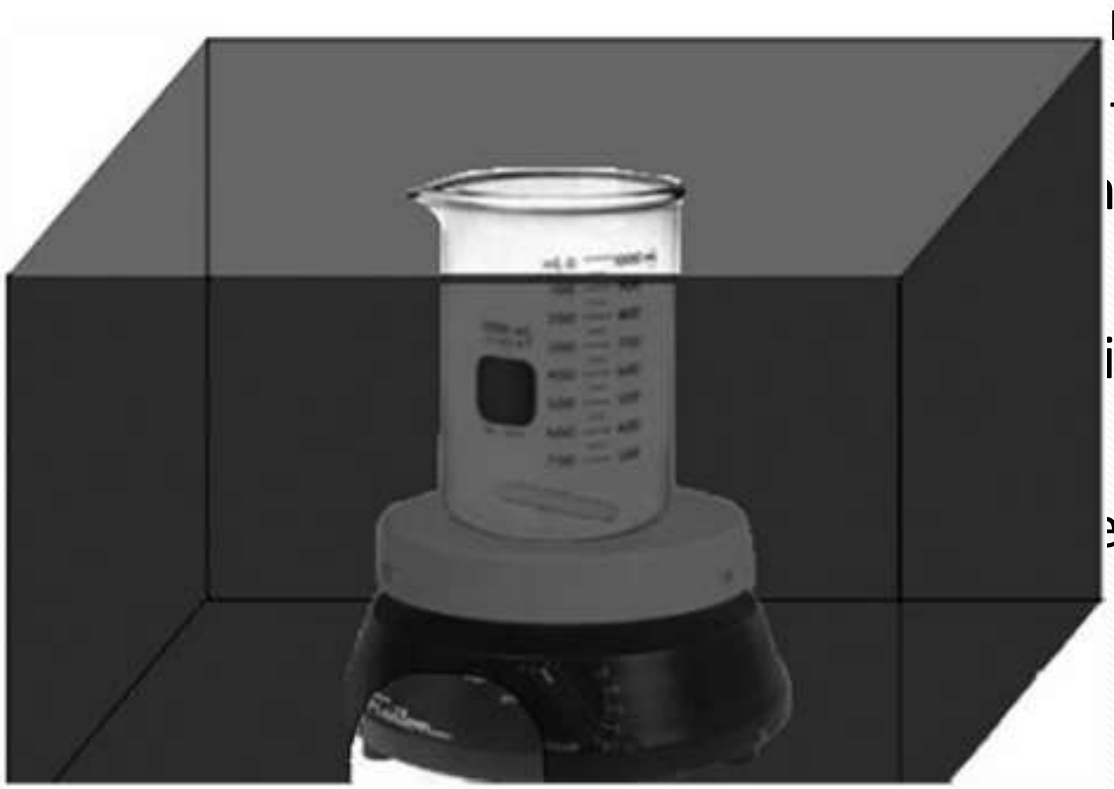
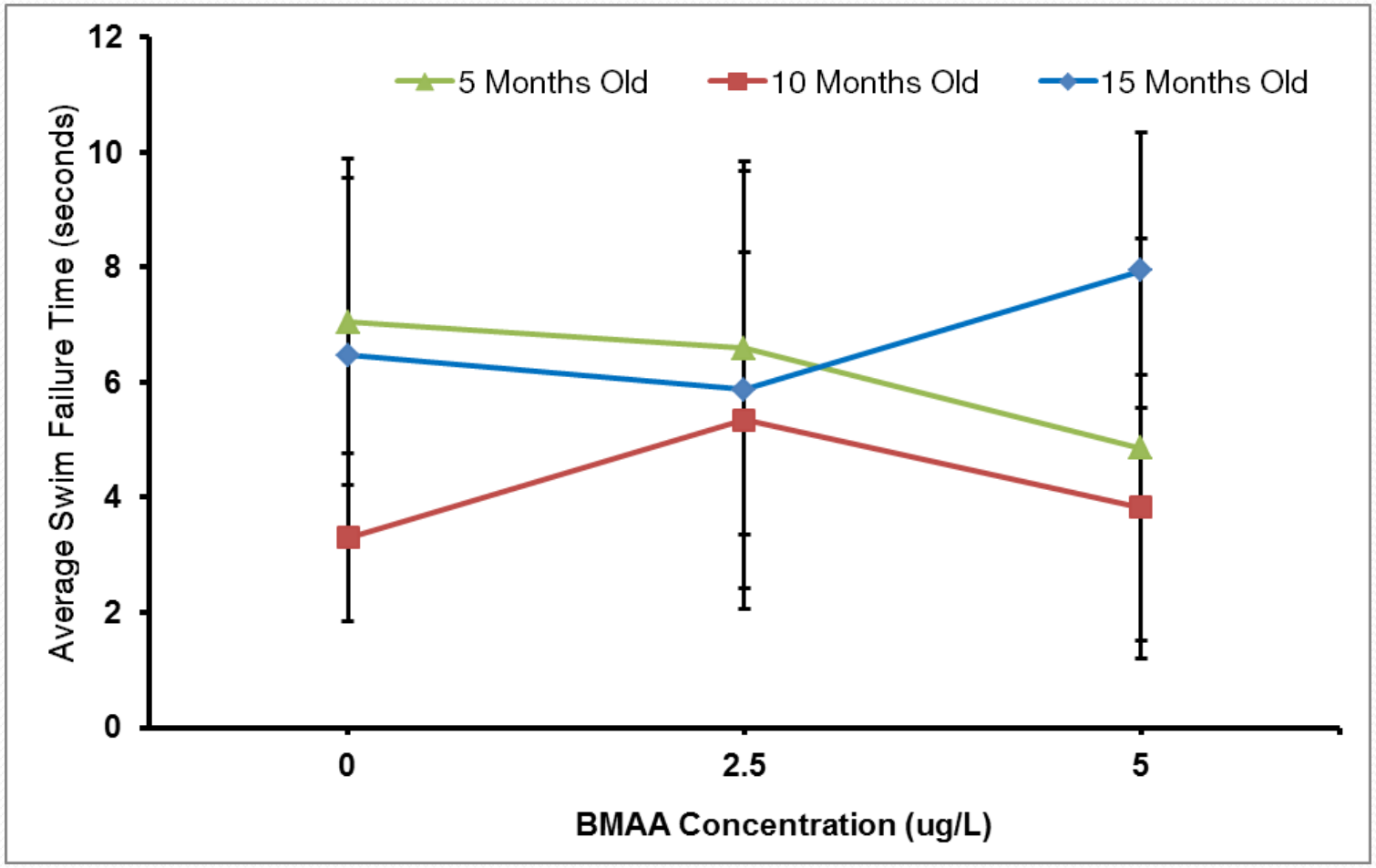


FIG. 1. Design of the apparatus for the Spinning Task. A beaker on top of a stirrer is placed inside walls made of black cardboard.

Blazina et al., 2013

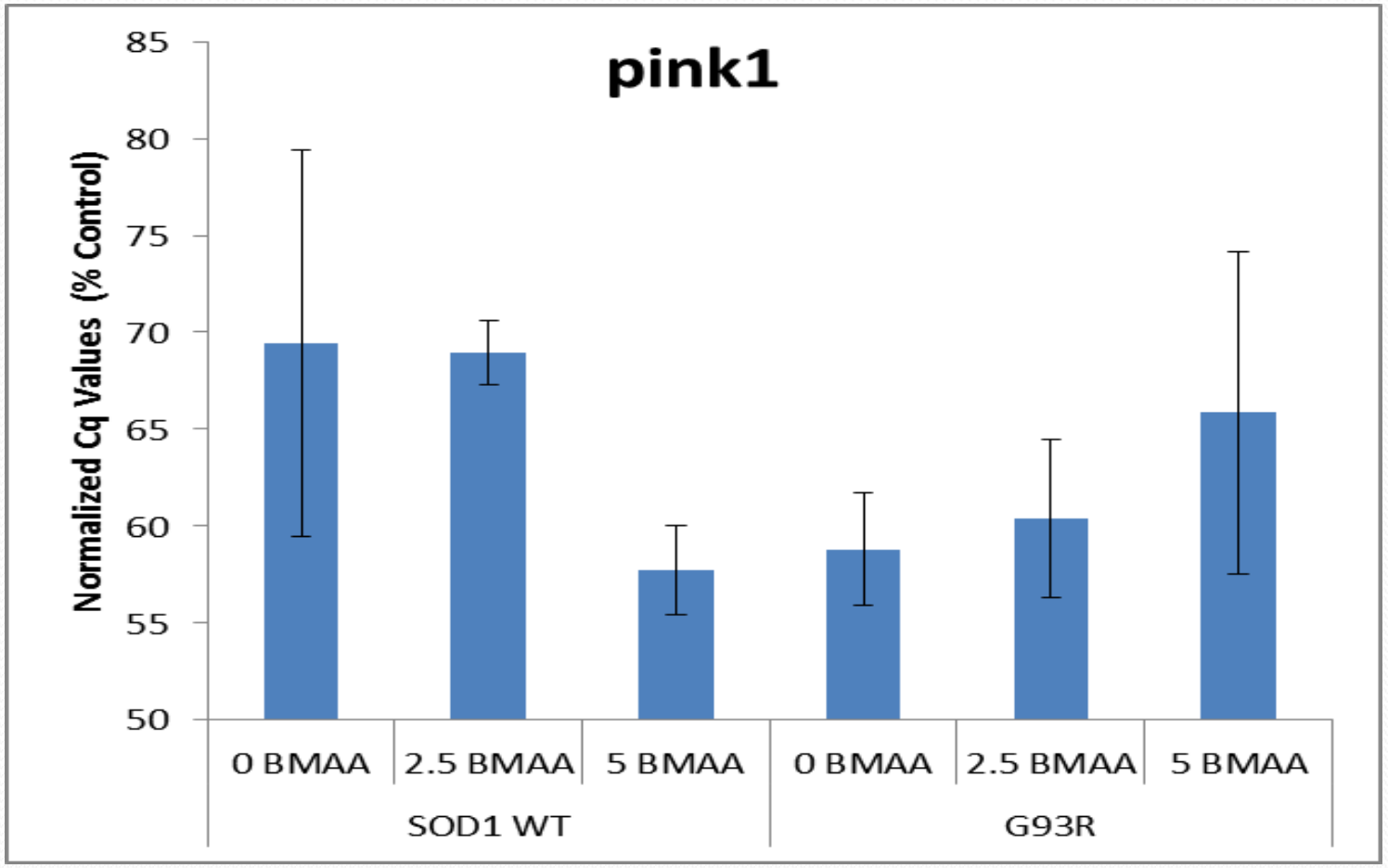
Early developmental exposure to BMAA alters transgenic zebrafish's ability to swim



Does early BMAA exposure alter spinal RNA expression later in life?

- Fish exposed to BMAA from 0 to 5 days old
- Raised to 6 months old
- Fish sacrificed for RNA analysis
  - Spinal tissue removed and analyzed

RNA Expression of Pink1 is altered by early developmental exposure to BMAA



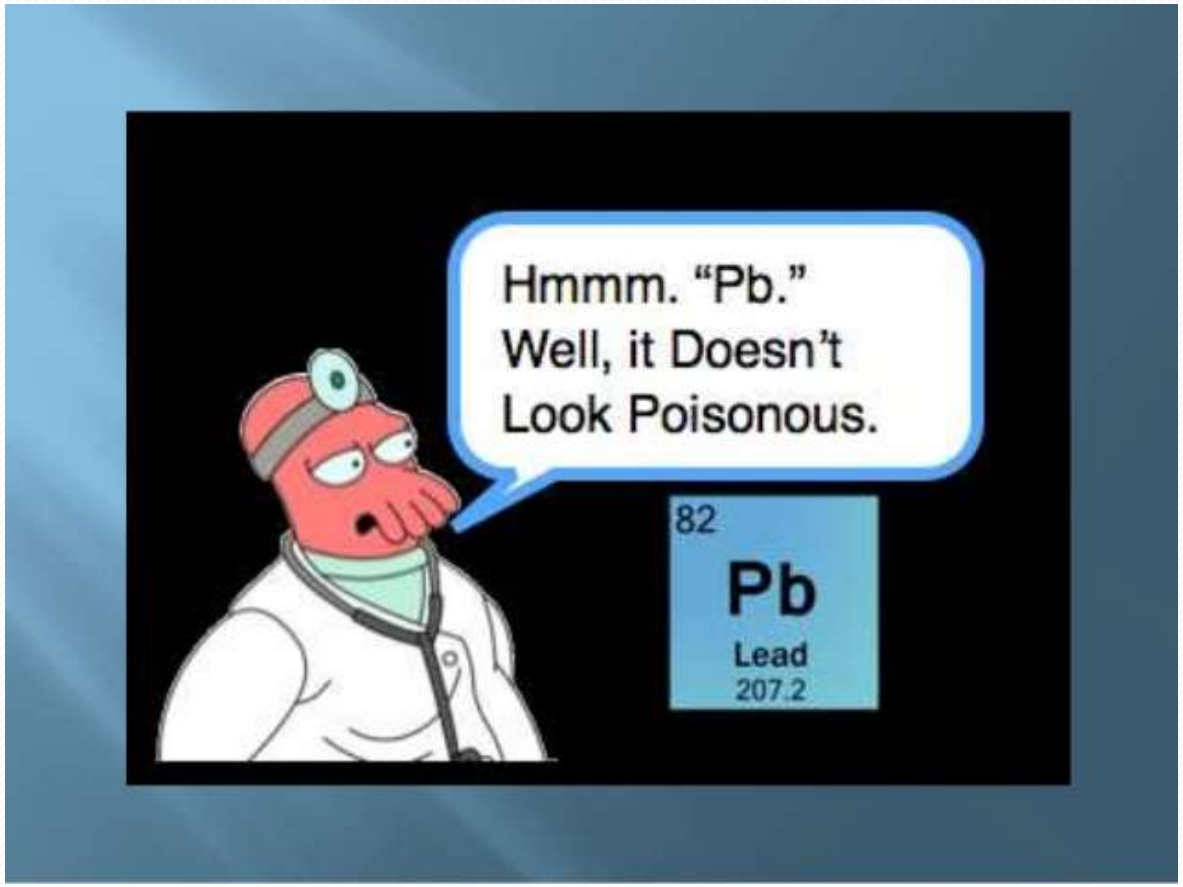
What can we do to protect people from BMAA?

- Determine the molecular mechanism of how BMAA is effecting zebrafish neurological development
  - Does the mechanism translate to humans?

    Develop medications to block BMAA's effects
- Inform policy makers on ways to reduce BMAA exposure
  - Reduced HABs
    - Chemical or biological removable of algae?
  - Filter water
  - Block public access

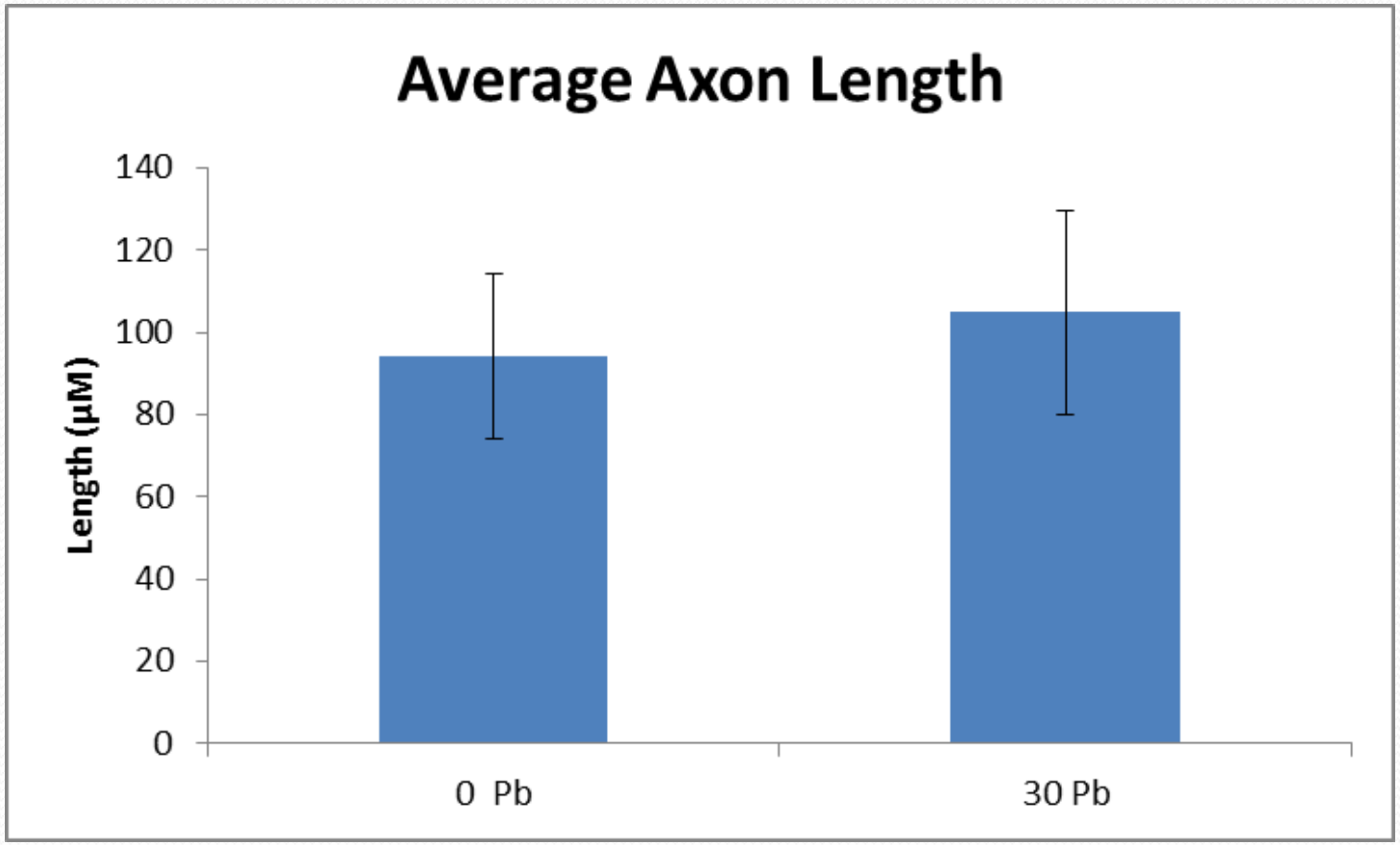
Studying other environmental toxins too

- Lead
- Malathion
  - Pesticide



https://www.slideshare.net/daliaelshafei/lead-poisoning-66994675

Is nerve length at the **NMJ** effected by early **lead (Pb)** exposure?



Summary

- Our planet is warming and HABs are likely to increase in abundance
  - The HAB toxin, BMAA, is particularly concerning
- Early developmental exposure to BMAA has effect on NMJ development
  - Fish swimming ability altered later in life

Future Directions

- What are the current concentrations of BMAA in Maine lakes?
  - How is climate change altering BMAA concentrations?
- Do these specific concentrations effect zebrafish neurological health?
- Does early exposure to other environmental toxins effect zebrafish neuromuscular development?
  - If so, is adult zebrafish swimming behavior effected later in life?

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Questions?

Any behavior effects detected in 5 month old zebrafish?