

Organization U.S. Environmental Protection Agency (EPA)

Reference Code EPA-NSSC-0009-28

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Description The EPA National Student Services Contract has an immediate opening for a part time (20 hours per week) Virtual Tissues Laboratory and position with the Office of Research and Development at the EPA facility in Research Triangle Park, NC.

The Office of Research and Development at the EPA supports high-quality research to improve the scientific basis for decisions on national environmental issues and help EPA achieve its environmental goals. Research is conducted in a broad range of environmental areas by scientists in EPA laboratories and at universities across the country.

What the EPA project is about

The Center for Computational Toxicology and Exposure (CCTE) provides the science needed to support Agency decisions by performing rapid chemical screening and evaluation that allows thousands of chemicals to be evaluated for potential risk in a very short amount of time. EPA's Toxicity Forecaster (ToxCast) uses high-throughput screening (HTS) methods and computational toxicology approaches to rank and prioritize chemicals. Within CCTE, the Biomolecular and Computational Toxicology Division (BCTD) focuses on expanding and refining the development and use of new approach methods (NAMs) for assessing toxicity of large numbers of chemicals with less reliance on animal testing.

What experience and skills will you gain?

As a team member, you will assist in the building and testing of a cell agent-based model of the developing neurovascular unit (NVU) that recapitulates the dynamics of diverse cell types of neurogenic (neuroprogenitors), angiogenic (endothelial cells, pericytes), and hematopoietic (microglia) lineages as they come together forming the blood-brain barrier (BBB). Utilizing a system-state map of BBB ancestry [Saili et al. (2019), Birth Defects Res] and ToxCast data [Zurlinden et al. (2020), Reprod Toxicol], the student shall assist with: (i) visualization of toxicity signatures for angiogenic and neurogenic lineages using Toxicological Prioritization Index as an analytical framework (ToxPi); (ii) building a computational model prototype of the developing neurovascular unit (cNVU) that translates ToxPi signatures into predicted effects on vascularization and differentiation of the embryonic neural tube; (iii) analysis to flag key events underlying adverse BBB phenotypes; and (iv) implementation of the cNVU model for in silico prediction of developmental toxicity for selected chemicals of interest. Results can contribute unique information toward NAM-based evaluations of chemical hazards to fetal brain development.

How you will apply your skills

🅼 ORAU Pathfinder



Whether you are just starting your career or already at a senior level, ORAU offers internships, fellowships, research opportunities, and contract positions that can provide you with invaluable experience. Download the ORAU Pathfinder mobile app and find the right opportunity to propel you along your career path!





Responsibilities in support for defining ToxPi signatures will include:

- Mine chemical-bioactivity data from EPA's CompTox Chemicals Dashboard;
- Link relevant bioactivity concentration profiles, metadata and literature review to an NVU network editor built in CellDesigner;
- Visualize and rank potential disrupters of NVU formation using the ToxPi analytical framework.

Responsibilities in assisting in the building of a computational cNVU prototype will include:

- Build an input-output parameterization table for cellular dynamics based on information captured in the ToxPi signature model;
- Update and expand an agent-based model prototype for endothelial, neurogenic, and microglial cells using an open-access multicellular simulation environment; and
- Implement automated quantitative data outflows to tabulate cell dynamic parameter indices for simulations trials using ImageJ processing in Java.

Responsibilities in performing sensitivity analysis on the cNVU prototype will include:

- Parallel processing of cNVU simulation models to evaluate emergent phenotypes enabled, but not specified, in the model software code (n=8 simulations per test);
- Quantitative analysis of emergent phenotypes in the cNVU simulations following electronic (*in silico*) perturbation of specified biochemical parameter(s); and
- Statistical evaluation of model output emergent features as a function of altered input parameters across a range of singular or combinatorial perturbations.

Responsibilities in supporting the implementation of defined chemical case studies will include:

- Selection of 4-6 chemicals for case studies testing the cNVU prototype based on ToxPi signatures and *in vitro* data availability for validation of model output;
- cNVU model parametrization to perform synthetic concentrationresponse evaluation of angiogenic and neurogenic phenotypes for case studies based on ToxCast bioactivity data; and
- Statistical evaluation to determine the predicted point of departure of emergent phenotypes versus untreated (normal) simulation pools.

Communication support responsibilities will include:



- Participating as a member of a multi-disciplinary research team
- Documenting all research efforts
- Presenting work in lab meetings and at scientific conferences as appropriate or required.

The responsibilities listed above can be learned by the student while performing the job.

Required Knowledge, Skills, Work Experience, and Education

- Demonstrated education and/or experience from high-school STEM (science, technology, engineering or math) curricula;
- Basic experience programming in Python, R or other scripting languages; and
- Strong written, oral and electronic communication skills to present their work to EPA scientists in the Virtual Tissue Models research area and the Computational Toxicology and Bioinformatics Branch (CTBB) of the CTTE/BCTD.

Location: This job will be located EPA's facility in Research Triangle Park, NC.

Salary: Selected applicant will become a temporary employee of ORAU and will receive an hourly wage of \$16.89 for hours worked.

Hours: Part-time (20 hours per week).

Travel: No travel is required.

Expected start date: The position is part time and expected to begin May 2021. The selected applicant will become a temporary employee of ORAU working as a contractor to EPA. The initial project is through May 14, 2022, with up to 3 additional option periods.

For more information, contact EPAjobs@orau.org. Do not contact EPA directly.

EPA ORD employees, their spouses, and children are not eligible to participate in this program.

- Qualifications Be at least 18 years of age and
 - Be enrolled as a full-time undergraduate student with at least one year of college and seeking a BS or BA degree in the field of mathematics, computational biology, developmental biology, toxicology, neuroscience or a related field **and**
 - Be a citizen of the United States of America or a Legal Permanent Resident.
 - Eligibility Citizenship: LPR or U.S. Citizen



Requirements • **Degree:** Currently pursuing a Bachelor's Degree.

- Discipline(s):
 - Life Health and Medical Sciences (46)
 - Mathematics and Statistics (<u>10</u>)
- Affirmation I certify that I am at least 18 years of age; be enrolled as a full-time undergraduate student with at least one year of college and seeking a BS or BA degree in the field of mathematics, computational biology, developmental biology, toxicology, neuroscience or a related field from an accredited university or college within the last 24 months; a citizen or a Legal Permanent Resident of the United States of America; and not a current employee of EPA ORD or the spouse or child of an EPA ORD employee.

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