

Description (content, motivation, learning objectives)

Sex and gender have historically been ignored as explanatory variables in [most biomedical research](#). Reasons for this include the concern that inclusion of these variables might escalate experimental costs and complicate data analysis. However in recent decades, several studies, ranging from research on cardiovascular diseases to immunity, showed that these are important explanatory variables. In this workshop we will focus on biological sex and discuss practical approaches for best incorporating it into the design and analysis of biomedical research experiments, with special emphasis on clinical and non-clinical animal experiments.

Topics covered will include:

- Definitions of biological sex in key model organisms, its multidimensional character, and its delineation from “gender” in the case of humans
- Experimental design and analytical approaches to evaluate differences between the sexes
- Experimental designs and analytical approaches to effectively control for the effect of sex on other variables of interest

Examples of concrete questions addressed in the workshop:

- How many male and female mice do we need for a given research project? What are the consequences of including more or fewer?
- Is a binary classification of samples into male and female categories always appropriate? When does it make sense to use other variables - such as hormonal levels or karyotypes - in place of, or in addition to, the biological sex variable?
- How to report the use (and limitation thereof) of sex as a variable in the method section of a paper and in a project proposal? Are there any standards for sex reporting in databases?

We aim at putting participants in a better position to:

- Understand the inherent sex biases embedded in experimental design choices and their impact in subsequent analyses,
- Analyze the produced data appropriately under the lens of the sex dimension and correct sex biases where possible,
- Carefully report the results and raise awareness among data collectors and colleagues about issues related to the inclusion of the sex dimension in biomedical research.

The workshop will include presentations given by invited speakers, facilitated discussions and hands-on exercises.

Relevance to conference attendees and prerequisites

This workshop proposal results from feedback on the workshop [“In all fairness: sex and gender biases in data science and AI, and how to address them”](#) organized by the Diversity Working Group at the SIB Days 2022, where participants expressed an interest to dig deeper and in more practical ways into some discussed topics. The workshop proposal was elaborated for both people involved in data analyses and researchers involved in experimental design (planning of own experiments, embedded bioinformaticians, consulting services to labs). Empowering data analysts and bioinformaticians to better understand experimental design principles (e.g., power analyses, stratification strategies, including categorical labels vs. continuous measures) will help them:

- Detect sex biases in datasets they receive and correct their analyses accordingly;
- Contribute to the design of follow-up experiments in long-term collaborations;
- Contribute effectively to the writing of methods section in papers or answering to reviewers about the inclusion of sex dimension in the work;
- Support their collaborators and PIs with statistical insights on the importance of the sex variable on experimental design aspects.

The prerequisites are:

- a genuine interest in understanding biases in biomedical research and improving research practice
- a basic understanding of research methodologies commonly used in biomedical studies, such as experimental design, data collection, and statistical analysis.

How the proposal aligns with current bioinformatics trends and either builds on or diverges from existing SIB courses

Ignoring sex-specific effects can result in inaccurate conclusions and practices, compromising the scientific integrity of studies. It can not only lead to a lack of reproducibility, but also have ethical and societal consequences, as demonstrated by [sex differences in both safety and efficacy of drugs in the market](#). A better understanding of the sex dimension is thus becoming urgently needed in the scientific community, an incentive reflected by updated policies and selection criteria from funding agencies and peer-reviewed journals.

We could not identify any existing SIB course with similar focus on sex-specific effects or sex-related biases, or specifically focusing on experimental design aspects.

Tentative outline of the tutorial/workshop schedule

10AM-11AM: Introduction to the complexity of biological sex (Talk+demo by Davide Cirillo)

This session will clearly articulate the definitions of sex and gender, emphasizing the fundamental differences between these two concepts. We will then explore the complexity of the biological sex concept, delving into the multifaceted nature of sex determination and its genetic, hormonal, and physiological aspects. Throughout the talk, we will underscore the significance of incorporating biological sex as a crucial variable in research, presenting real-world examples from the literature as a demo to illustrate the [impact of incorporating biological sex in research](#).

11AM-12PM: Biological sex in experimental design (Talk+hands-on by Frédéric Schütz)

We will explore the different types of experimental designs that can be used, while dealing with the constraints of experimental studies on human patients or animal models, how they impact on analysis strategies and ultimately what they can tell on sex-specific effects on a study system. The talk will be followed by a hands-on session that will allow participants to perform tasks on simulated datasets such as power analyses, and see how different choices for analysis can lead to different conclusions.

1PM-1:30PM - Introduction to the practical hands-on session (by Davide Cirillo)

Participants will have the opportunity to apply the concepts learned, using hypothetical or real research scenarios and applying analytical approaches discussed earlier. The goal is to equip participants with practical skills, reinforce theoretical concepts, and apply them concretely. The hands-on activity will be conducted in subgroups to enhance participants' engagement.

1:30PM-3PM - Hands-on session in subgroups

Critical review of concrete case studies selected by the instructors from the literature with the aim of describing the study design, identifying potential issues and suggesting actions that could be taken to improve the study of sex-specific effects. The organizers will prepare material (documented guide, interactive notebook) that will allow each subgroup to dig into real data, e.g., download public datasets and run prepared code to test the effects of different analytical choices on the results.

3PM-4PM Group presentations, wrap-up, outlook

Each subgroup will shortly report their results to the others and reflect on the lessons learned and how this could be integrated into future projects.

Concluding remarks will be provided at the end by the organizers.

Information regarding organizers/instructors

Confirmed instructors (alphabetically): Davide Cirillo and Frédéric Schütz

Organizers (alphabetically): Maïa Berman (SIB Diversity Working group), Davide Cirillo (Life Sciences Department, Barcelona Supercomputing Center), Aitana Neves, Xavier Robin, Julien Roux, Leonore Wigger (SIB DWG)

See attached file for CV of instructors and references to similar initiatives