Universität Rostock
Traditio et Innovatio

Elaine
electrically active implants
SFB 1270

Requirements for Documenting Electrical Cell Stimulation Experiments for Replicability and Numerical Modeling

Goal

Find **documentation requirements** for electrical stimulation (ES) experiments to:

1. Ensure **replicability** of ES experiment.
2. Generate input for **computer simulations**.
3. **Understand** the effects of electric fields on cellular mechanisms.

Electrical Cell Stimulation Experiments

- mainly three types of stimulation setups (Fig. 1) used within the experimental setup (Fig. 2)

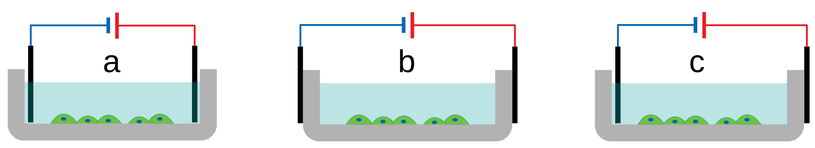

FIGURE 1: Electrical stimulation of biological cells *in vitro*. Differences of direct contact (a), capacitive coupling (b) and semi-capacitive coupling (c).

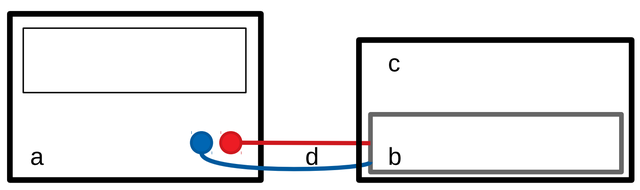

FIGURE 2: Basic set-up of an ES experiment consisting of a function generator with an integrated amplifier (a), a stimulation chamber containing at least one well with the cell culture as well as the electrodes (b), an incubator (c) and electrical wires connecting the electrical power source and the stimulation device (d).

- often custom-built apparatuses in use with various stimulation protocols
- no clear documentation standards exist, often crucial details not described
- **main issues:**
  - electric field strength ($\mathbf{E}$) usually reported, but not measured
  - electrical input variables such as current or voltage not reported

Documentation Guidelines in Biology

- reporting guidelines collected in the *Minimum Information for Biological and Biomedical Investigations (MIBBI)* portal [1]
- suitable: *Minimum Information about a Cellular Assay (MIACA)* guideline (see Table 1)

  $\Rightarrow$ integration of ES step into *MIACA* guideline

TABLE 1: The Cellular Assay Object Model (CA-OM), taken from [2], describes the content and order of theb documentation of cell biological experiments.

Header		Project principles (who, why, what)
		(Bio)Materials (cell line, perturbator(s), instruments, other materials)
Experimental modules	I.	Treatment (cell culture - prior to, during and after perturbation)
	II.	Post treatment (procedures (lysis, staining, ...))
	III.	Data acquisition (instrument settings, procedures)
Data processing		Data analysis (normalization, filtering, statistics / scoring)

Extending the Treatment Part of MIACA

We suggest to extend the treatment part (see Table 1) and document the following stimulus parameters of an ES experiment:

1. Circuit diagram,
2. Current or voltage (peak-to-peak and offset),
3. Waveform (e.g., sine wave, square wave),
4. Frequency,
5. Duty cycle (i.e., on/off-periods),
6. Duration of stimulation,
7. Duration of resting period (non-stimulation),
8. Measured quantities (e.g., voltages or currents, etc.).

Electronic Lab Notebooks (ELNs)

ELNs can be used to store not only the documentation and meta information but also the experimental data itself. They are preferable to conventional lab notebooks in the context of ES documentation because (see Fig. 3):

1. Documentation can readily be shared or published,
2. Documented data can easily be interfaced to simulation tools by using general purpose data formats,
3. ELNs enable users to search for terms and may offer automatic checking of consistencies as well as a means to provide provenance information.

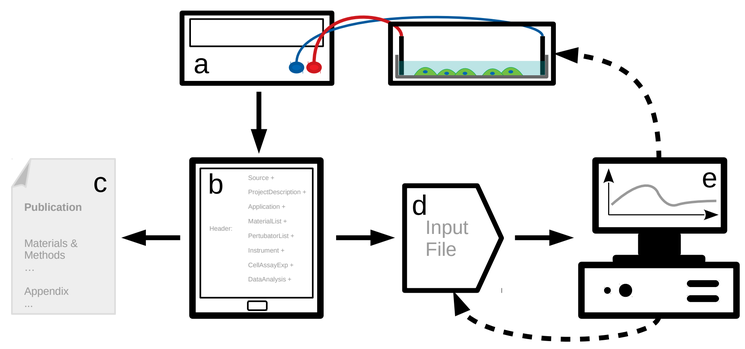

FIGURE 3: Workflow for executing *in vitro* and *in silico* experiments with the support of ELNs. An ES experiment (a) is documented with the help of an ELN template (b). The documentation may be extracted from an ELN and directly put into a publication (c). The documentation may also be filtered for information required to complete an input file (d) that is used for executing a computer simulation (e). The input file may need to be completed with simulation-specific information. The simulation results may then inform researchers about parameters to be tested in wet-lab.

Numerical Simulations

- for sine waves: time-harmonic Maxwell's equations
- often justified: electro-quasistatic approximation, yielding the field equation:

$$\nabla \cdot [\sigma^*(\mathbf{r}, \omega)\ \nabla\Phi(\mathbf{r})] = 0\ , \tag{1}$$

- minimum information to solve (1) by Finite Element methods:
  1. Geometry of the stimulation chamber,
  2. Conductivities and permittivities of all affected materials,
  3. Details about applied stimulus.
- all solution steps summarized in open-source package `EMStimTools` [3]
- exemplary study for direct contact experiment [4] $\Rightarrow$ electric field strength (see Figs. 4, 5)

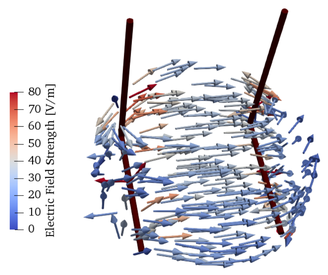

FIGURE 4: Electric field distribution in the well for CAD model of direct contact experiment [4].

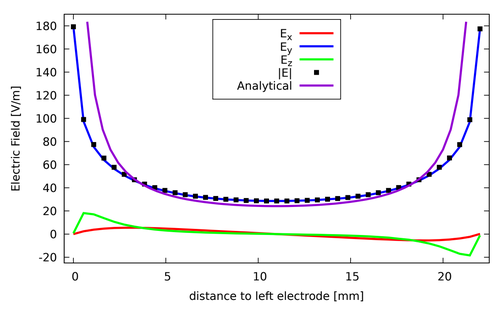

FIGURE 5: Electric field components and strength between the electrodes.

References

[1] C. F. Taylor *et al.*, "Promoting coherent minimum reporting guidelines for biological and biomedical investigations: the MIBBI project," *Nature Biotechnology*, vol. 26, no. 8, pp. 889–896, Aug 2008.

[2] S. Wiemann *et al.*, "MIACA – minimum information about a cellular assay, and the cellular assay object model," http://miaca.sourceforge.net/, accessed: 2019-01-10.

[3] [Online]. Available: https://github.com/j-zimmermann/EMStimTools/releases/tag/v0.1.2.dev0

[4] S. Mobini, L. Leppik, V. Thottakkattumana Parameswaran, and J. H. Barker, "In vitro effect of direct current electrical stimulation on rat mesenchymal stem cells," *PeerJ*, vol. 5, p. e2821, Jan 2017.

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