MEA Acute Update Suggestions

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# Delete active\_electrodes\_number\_up, bursting\_electrodes\_number\_up

We determined that these 2 endpoints (aeids 2961, 2973) are not informative because in ~75% of the wells, all 16 of the electrodes are active and bursting in the baseline recording. Therefore, in the majority of wells, it is not possible for the treatment to cause an increase in the response relative to baseline for these endpoints.

# Methods to update for MEA Acute endpoints

Note: the following updates apply to all MEA Acute endpoints except the LDH and AB endpoints.

## Level 3 normalization

For down endpoints, we would like to use the following methods:

* Bval.apid.nwllslowconc.med
* Pval set to -100
* Resp.pc

For up, we would like to use the following methods:

* Bval.apid.nwllslowconc.med
* Pval set to 99th percentile of all rval’s from test wells
* Resp.pc

I have included suggested functions for the pval’s in the *mea\_acute\_tcpl\_update\_2022-01-26.R* to add to the mc3\_mthds in tcpl.

## Level 5 (cutoff)

For active\_electrodes\_number\_dn, bursting\_electrodes\_number\_dn (aeids 2962, 2974) we would like to set the coff to 30% (the bmad for these endpoints is 0, so we don’t want to use a multiple of bmad).

For the rest of the MEA acute endpoints, we would like to use bmad3 as the cutoff.

# Which endpoints / screening types to release

I’m attaching mea\_acute\_status\_by\_aenm\_2022-01-27.csv which indicates which endpoints can be released (after applying the above updates).

For the single conc, we can release aeids 2033-2036. Note that there is also multi-conc data associated with these endpoints in invitrodb, but I have reprocessed the data from those experiments under the other MEA\_acute endpoints. I believe that the multi-conc data associated with aeids 2033-2036 can be deleted.

For the multi-conc, we are releasing the 30 endpoints associated with the 15 assay components identified as most informative in Kosnik, et al. 2019, plus the 2 cytotoxicity/viability endpoints.