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| MEAs (single cells) or LFP<br>electrodes, EEG (population<br>recordings)  | Genetically encoded optical indicators (calcium or voltage)  |
|---|--|
|   |  |
| ~200  | ~500 (in vivo) <sup>19-21</sup>  |
| 100 µm (due to tissue damage,<br>electrode wiring and volume<br>conduction of extracellular currents)   | ~1–5 µm (due to light scattering,<br>photon budget per time and spatial<br>bins) <sup>141</sup>  |
| Action potentials and LFPs  | Calcium indicators: action potential events (routinely achieved in vivo) Voltage indicators: action potentials and subthreshold potentials (not routinely achieved in vivo)  |
| Sub-millisecond range (practically no limit)  | Millisecond range (limited by indicator properties)  |
| Only possible indirectly and post hoc   | Direct through specific genetic targeting of indicator or marker protein   |
| Modest (exact absolute and relative<br>positions of recorded neurons<br>generally unknown)  | Microscopic level (due to light scattering in tissue)  |
| Practically unlimited   | Depth in cortex routinely ~400 μm (up to 700 μm) <sup>99,141</sup> ; deeper with invasive procedures <sup>50</sup>   |
| Challenging, modest success rate <sup>142-144</sup>   | Possible with high success rate <sup>21</sup>  |
|   |  |
| LFP: ~100 μm, frequency dependent<br>(volume conduction)<br>ECG and EEG: modest spatial<br>resolution and ambiguous in<br>localization of signals <sup>24</sup>                     | Microscopic level (due to light scattering in tissue, ~100 μm in wide-field, non-confocal epifluorescence imaging)   |
| Extracellular currents from local<br>and distant sources; mainly synaptic<br>currents but also action currents <sup>24</sup>  | Calcium indicators: population action potential activity Voltage indicators: volume averaged membrane potential (mainly synaptic potentials)   |
| Not possible in tissues in which<br>different cell types are intermingled<br>(although optoelectronic<br>device-based technologies may<br>eventually enable this) <sup>20,145</sup> | Possible through specific genetic targeting  |
|   | electrodes, EEG (population recordings)  ~200  100 µm (due to tissue damage, electrode wiring and volume conduction of extracellular currents)  Action potentials and LFPs  Sub-millisecond range (practically no limit)  Only possible indirectly and post hoc  Modest (exact absolute and relative positions of recorded neurons generally unknown)  Practically unlimited  Challenging, modest success rate <sup>142-144</sup> LFP: ~100 µm, frequency dependent (volume conduction) ECG and EEG: modest spatial resolution and ambiguous in localization of signals <sup>24</sup> Extracellular currents from local and distant sources; mainly synaptic currents but also action currents <sup>24</sup> Not possible in tissues in which different cell types are intermingled (although optoelectronic device-based technologies may |

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