

INTRODUCTION

Ischemia-related spreading depolarizations (SDs) are part of the pathophysiology of cerebrovascular diseases and predict worse outcome. SDs may exacerbate ischemic injury via related atypical hemodynamic responses, but their consequences on tissue pH changes are not yet understood. The regulation of pH changes of neurons is crucial in both physiological and ischemic conditions, because acid loading makes them susceptible for injury. Therefore we set out to compare intracellular pH changes associated with SDs propagating across the intact and the ischemic cortex of rats, visualized by live optical brain imaging.

Aims: We set out to compare intracellular pH changes associated with SDs propagating across the intact and the ischemic cortex of rats, visualized by live optical brain imaging.

METHODS

- Animals: Adult, male Sprague-Dawley rats (n=13)
- Anesthesia: isoflurane (1.5-2.2% in N₂O:O₂/2:1)
- Monitoring mean arterial pressure and arterial blood gases (left femoral artery catheter)
- Transient global forebrain ischemia induction: bilateral occlusion of the common carotid arteries ("two-vessel occlusion", 2VO)
- SD elicitation: topical 1M KCl
- Experimental protocol: Figure 1.
- Experimental design: Figure 2.

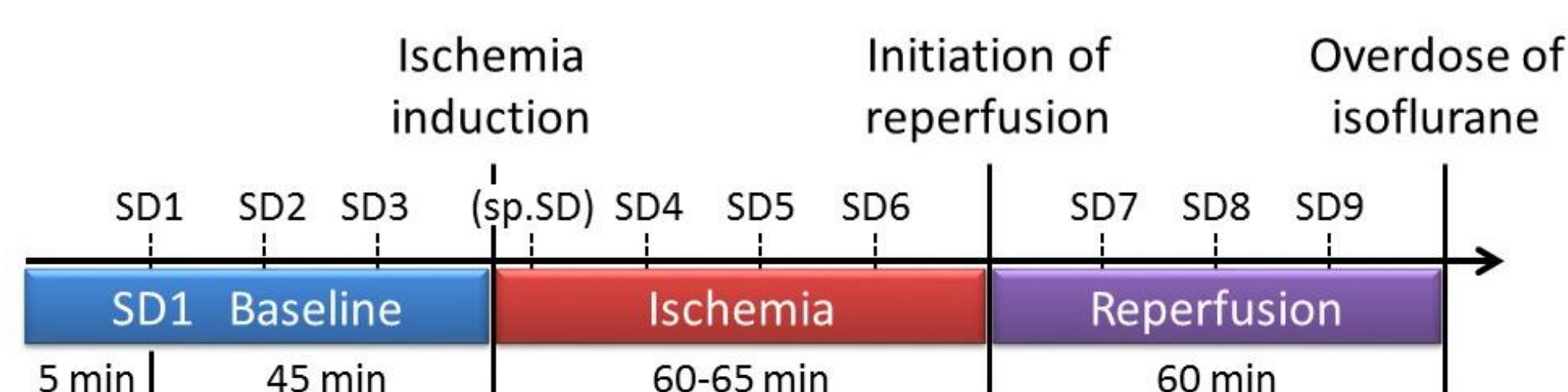


Figure 1. Schematic illustration of the experimental protocol.

METHODS

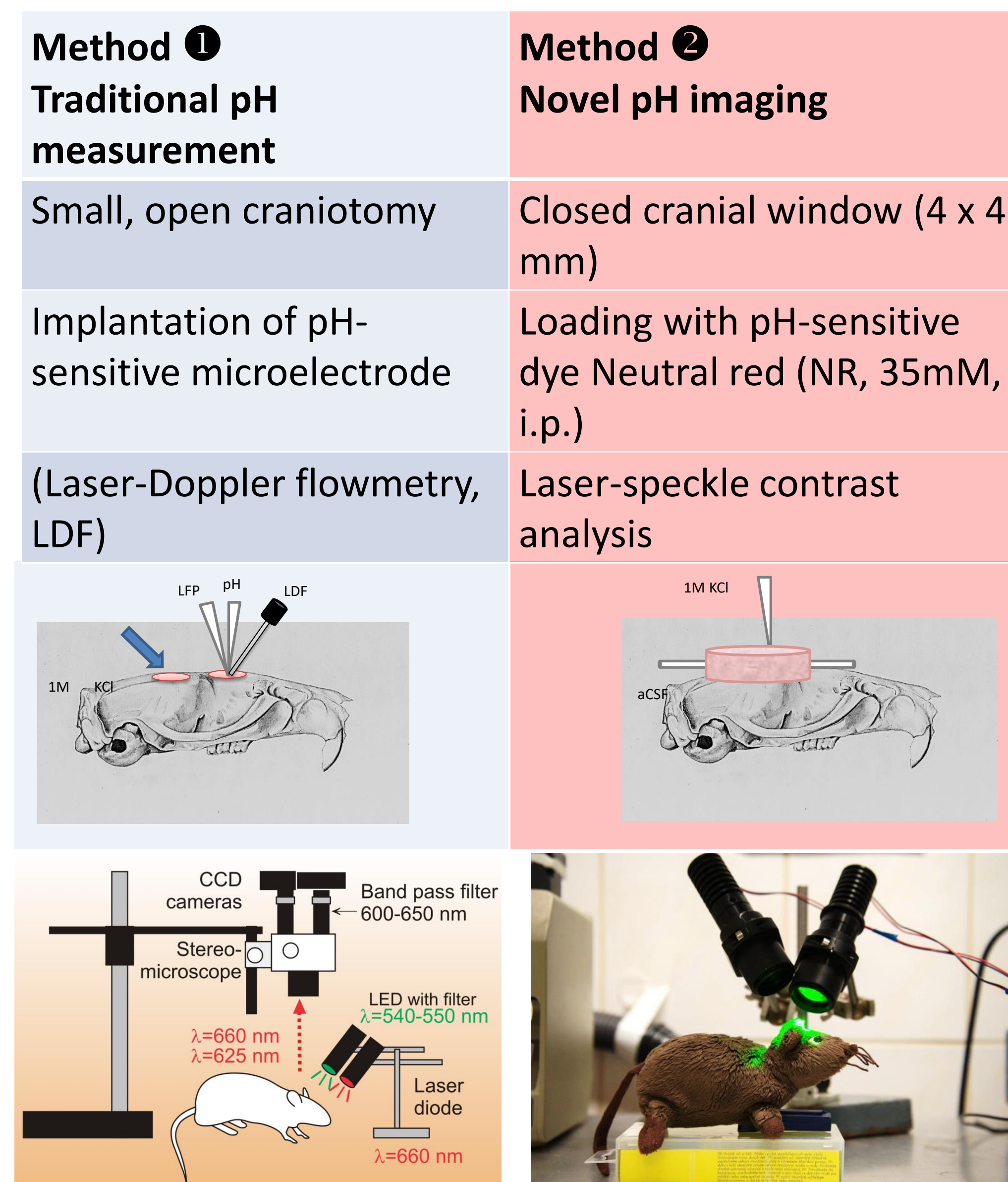


Figure 2. Parallel experimental methods applied.

RESULTS

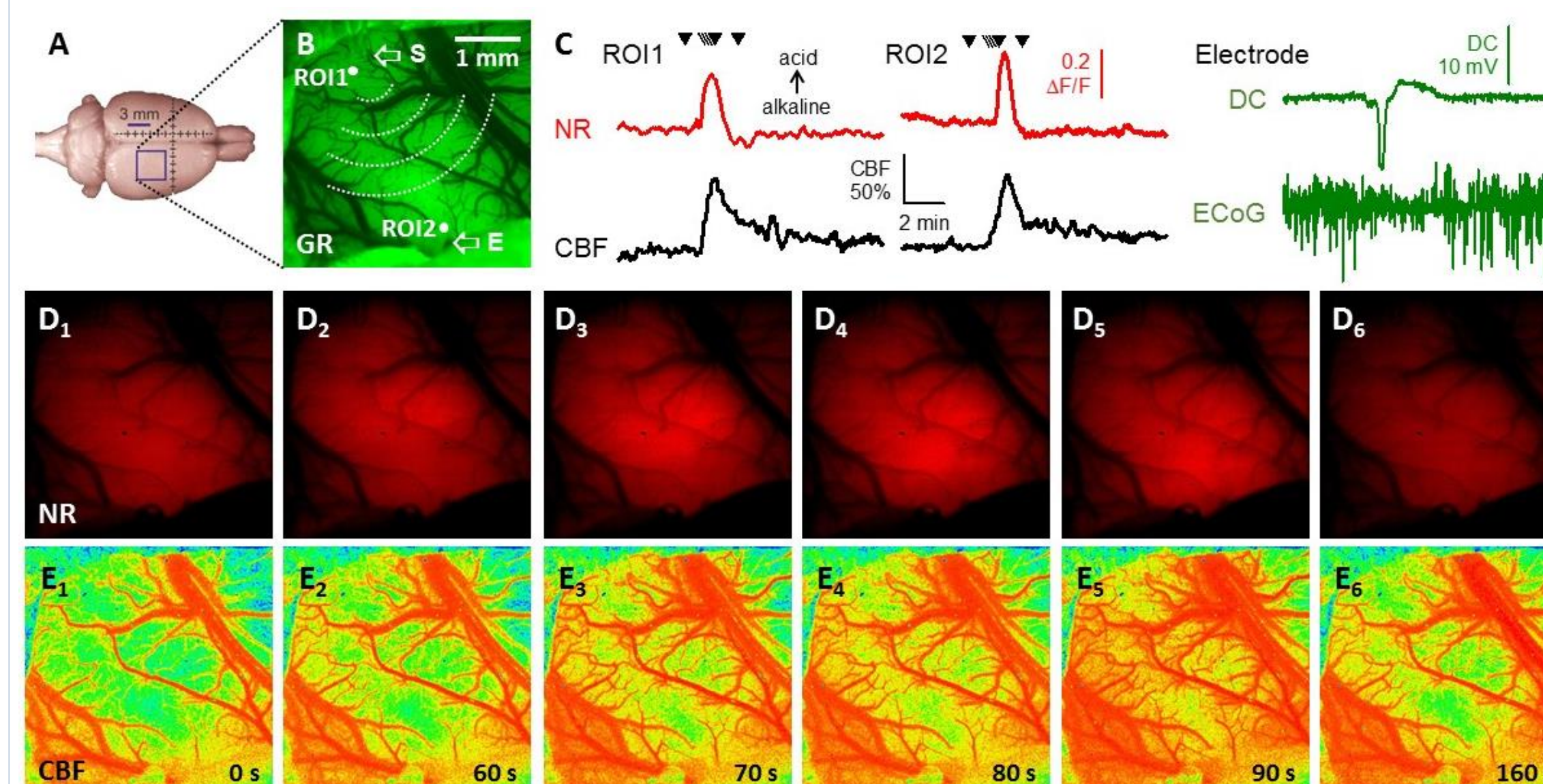


Figure 3. Representative image sequences and graphs illustrate synchronous changes in Neutral red (NR) fluorescence, cerebral blood flow (CBF), direct current (DC) potential and the electrocorticogram (ECoG) with the propagation of a spreading depolarization (SD) wave in the intact cerebral cortex of a young rat.

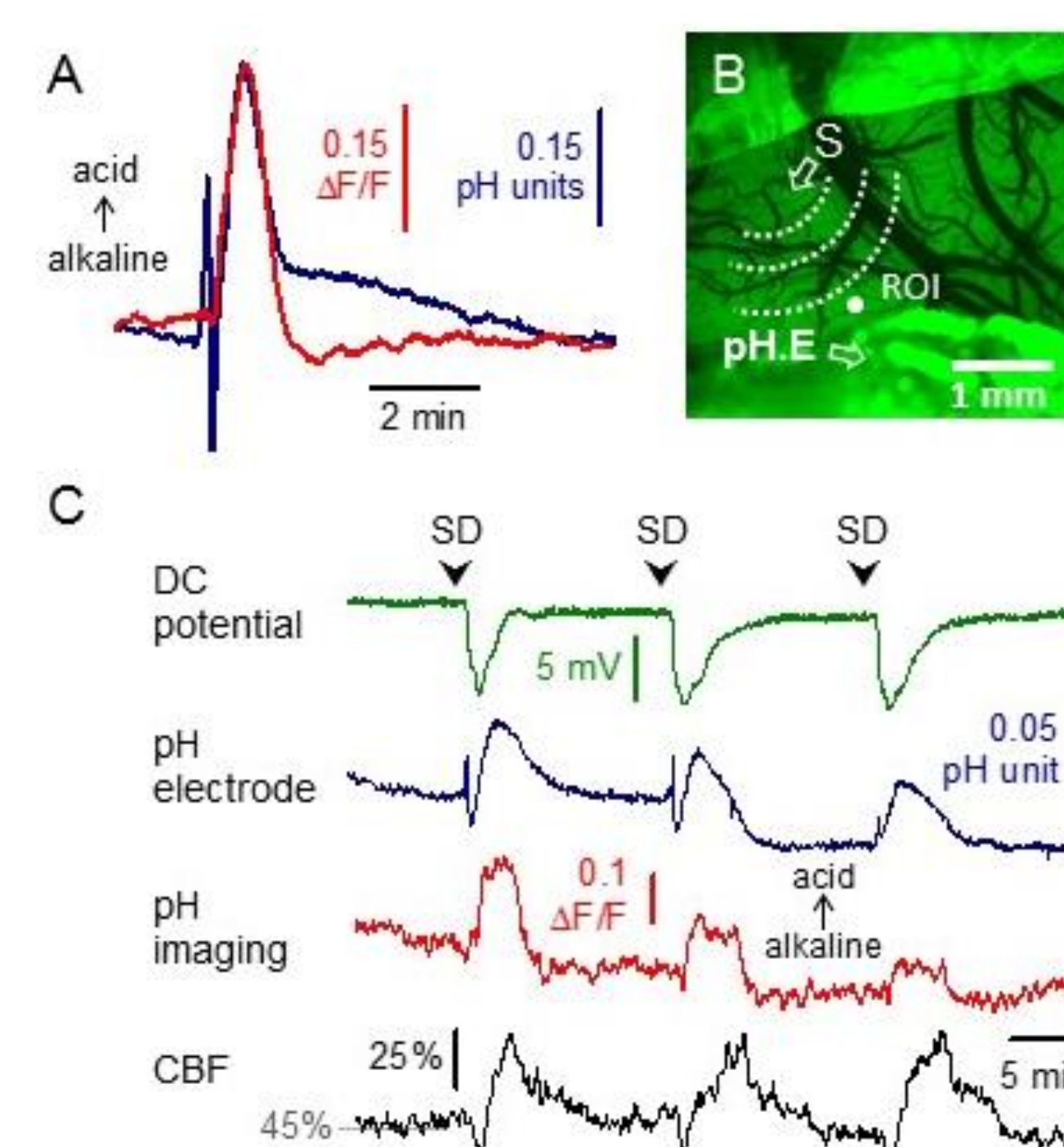


Figure 4. Changes in Neutral red (NR) fluorescence indicate tissue pH variations as validated by pH-sensitive microelectrodes.

NR imaging is reliable
To detect tissue pH variations.

RESULTS

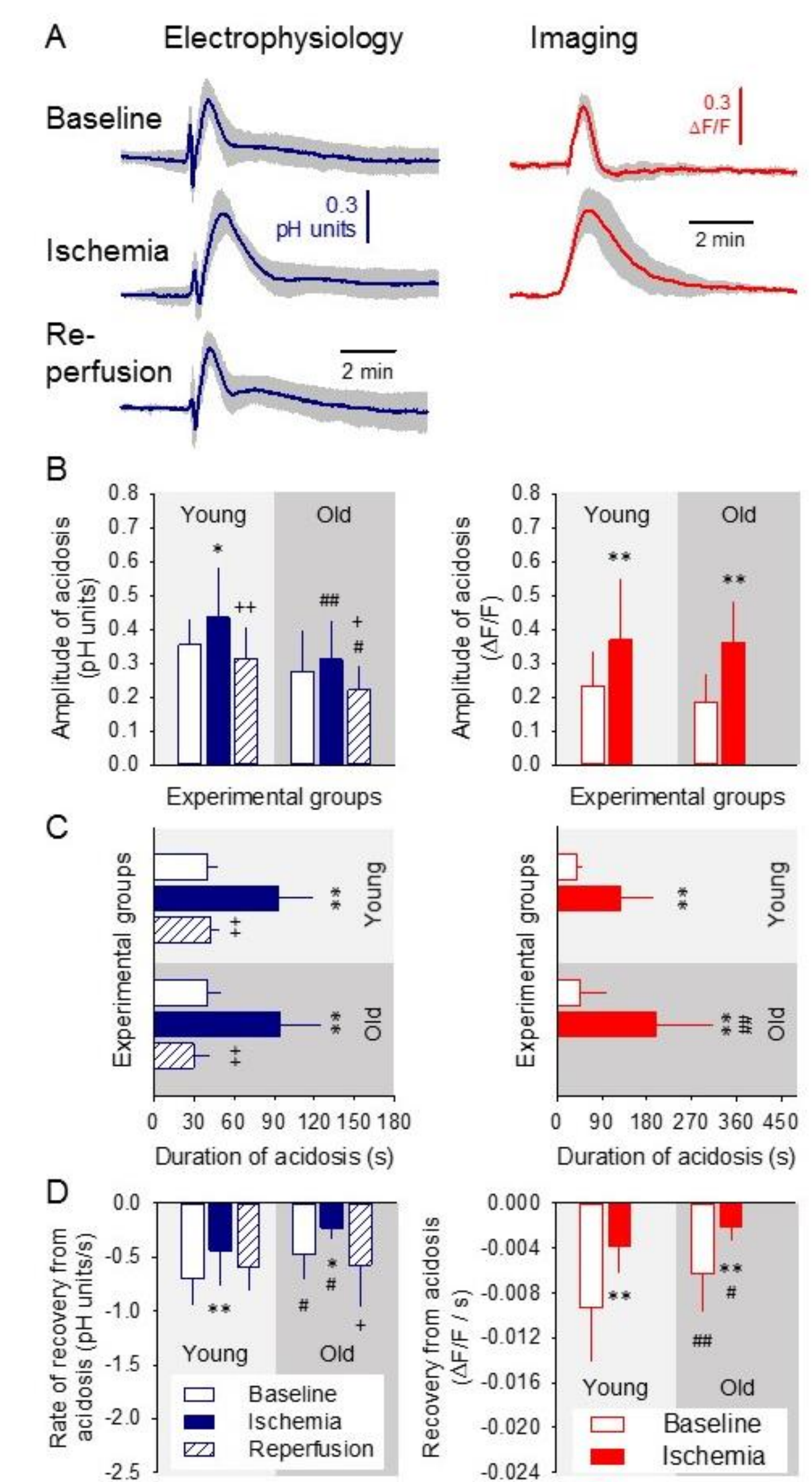
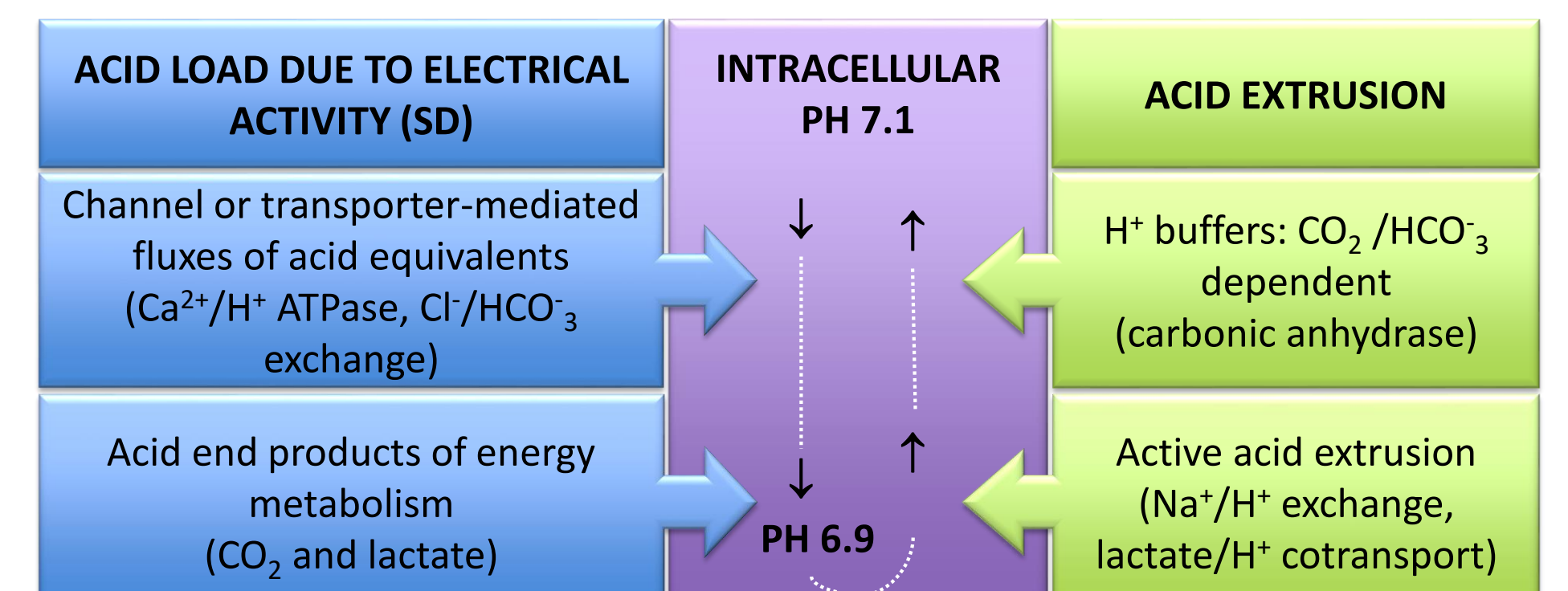


Figure 5. Tissue acidosis with spreading depolarization (SD) is augmented during ischemia, and becomes attenuated in the aged brain. In each panel, data obtained with pH-sensitive microelectrodes is shown on the left, and data derived from Neutral red fluorescence imaging is shown on the right.

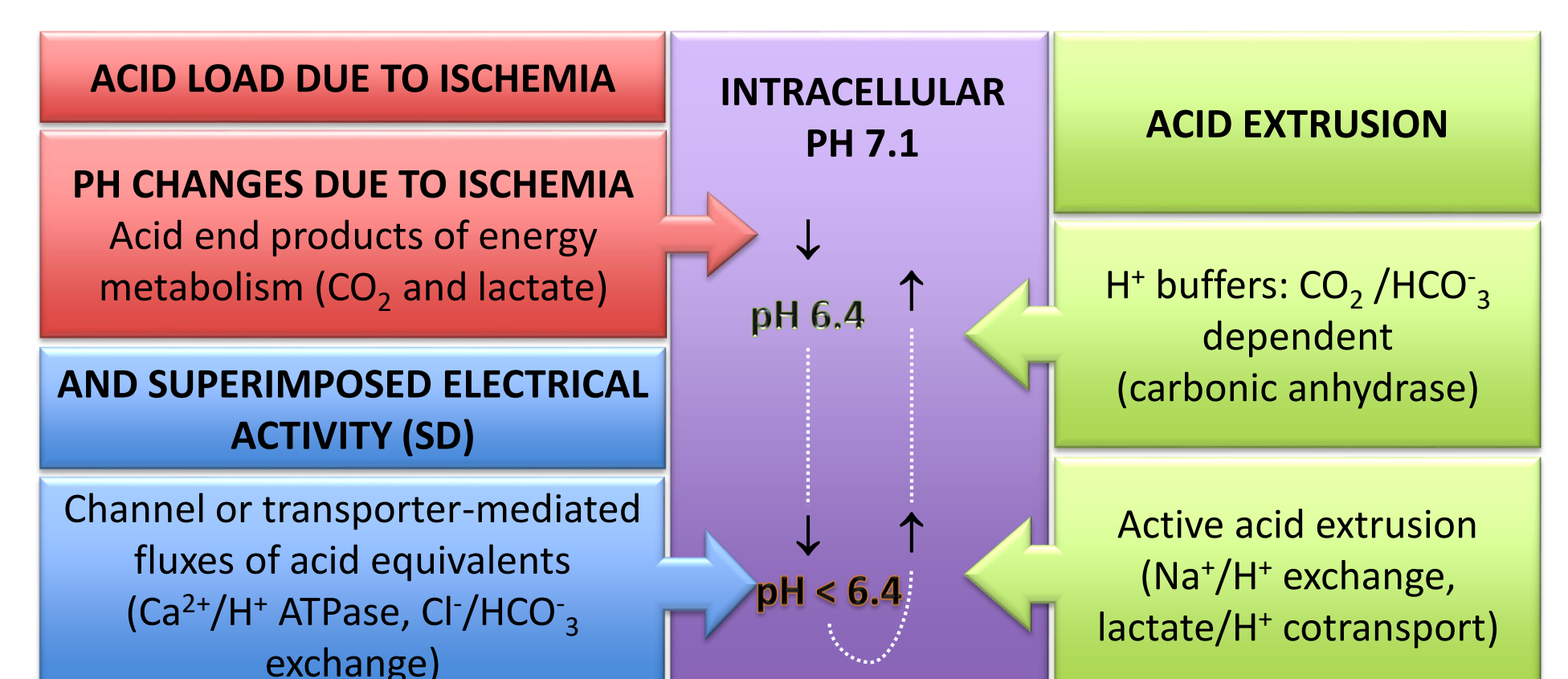
CONCLUSIONS

SD OCCURRENCE IN INTACT CORTEX:



- SD is associated with moderate acidosis
- Acidosis suppresses neuronal excitability and synaptic transmission
- ⇒ The SD-related acidosis may be protective by inhibiting the occurrence of subsequent SDs

SD OCCURRENCE IN ISCHEMIC CORTEX:



- Acidosis due to SD and ischemia is additive (higher amplitude of acidosis)
- Acid extruders work against higher acid load (longer duration of acidosis)
- Exaggerated acid load makes the neurons susceptible for injury
- ⇒ SDs during ischemia have high injurious potential