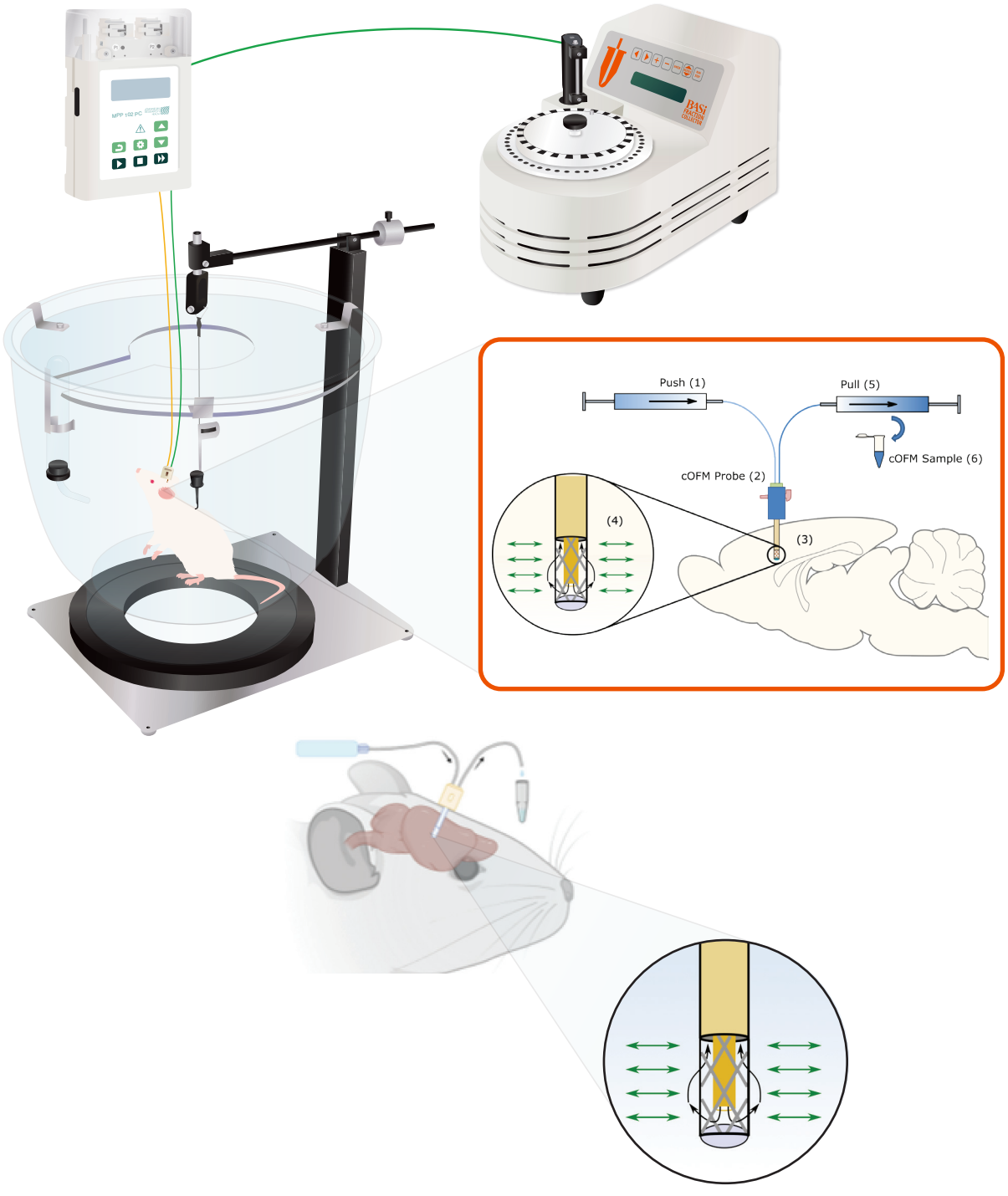
INTEGRATING CEREBRAL OPEN FLOW MICROPERFUSION (cOFM) INTO PK/PD, SAFETY PHARMACOLOGY, AND TOXICOLOGY STUDIES



Cerebral Open Flow Microperfusion (cOFM) is a groundbreaking technique that allows for continuous, real-time sampling of brain interstitial fluid (ISF) with an intact blood-brain barrier (BBB). This approach provides direct insights into drug penetration, distribution, and pharmacodynamics within the brain, and it enables the collection of data that traditional blood sampling or cerebrospinal fluid (CSF) analysis simply cannot capture.

BENEFITS OF cOFM AND BRAIN ISF ANALYSIS

1. ENHANCED UNDERSTANDING OF CNS DRUG PENETRATION:

- **Direct Measurement of Brain Drug Concentrations:** Unlike blood sampling or CSF collection, cOFM samples directly from the brain's interstitial space, offering precise, time-resolved data on free, unbound drug concentrations.
- **Blood-Brain Barrier Dynamics:** cOFM enables real-time monitoring of how drugs cross the BBB, critical for developing CNS-targeted therapies and understanding off-target effects in the brain.

2. IMPROVED PHARMACOKINETIC AND PHARMACODYNAMIC MODELING:

- **Accurate PK/PD Correlation:** Direct ISF sampling reveals drug exposure at the site of action, allowing more robust modeling of drug efficacy and time course.
- **Longitudinal Sampling:** Continuous data capture provides detailed concentration-time profiles without requiring animal sacrifice, reducing inter-animal variability, and aligning with 3Rs principles.

3. SAFETY PHARMACOLOGY AND TOXICOLOGY INSIGHTS:

- **Neurotoxicity Evaluation:** Detect early biomarkers of CNS toxicity by measuring inflammatory mediators (e.g., cytokines, chemokines) and metabolic byproducts in the ISF.
- **Off-Target Effects:** Understand how systemically administered drugs might unexpectedly penetrate the brain and cause adverse neurological effects.
- **Circadian Rhythm Considerations:** cOFM allows for continuous sampling during both active and rest phases, capturing how drug metabolism or toxicity may fluctuate throughout the day.

4. INTEGRATION WITH OTHER TECHNIQUES:

- **Combination with Automated Blood Sampling (ABS):** Align brain ISF data with systemic blood concentration profiles to build a comprehensive PK/PD model.
- **Telemetry Pairing:** Correlate ISF drug levels with real-time physiological data (e.g., EEG, heart rate, body temperature) to uncover links between drug exposure and functional changes.

Cerebral Open Flow Microperfusion revolutionizes how we understand drug behavior in the brain. By directly sampling brain interstitial fluid, cOFM offers unmatched insights into drug distribution, efficacy, and neurotoxicity. Incorporating this technology enables higher-quality data, reduced animal use, and more efficient drug development timelines.

Visit https://www.basinc.com/open-flow-microperfusion-resources for a list of published references and other materials about the use of OFM for drug development.