

# Respiratory Controlled Delivery of an Ultrashort Acting Opioid: A Pilot Study in Swine

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## Introduction

- Treating pain in austere conditions is challenging due to reduced access to oxygen, electricity, specialized medical equipment, and trained personnel.
- Inhaled delivery of nebulized remifentanyl can provide immediate, effective and safer pain control for forward operating units without IV access, and/or specialized medical personnel.

## Hypotheses

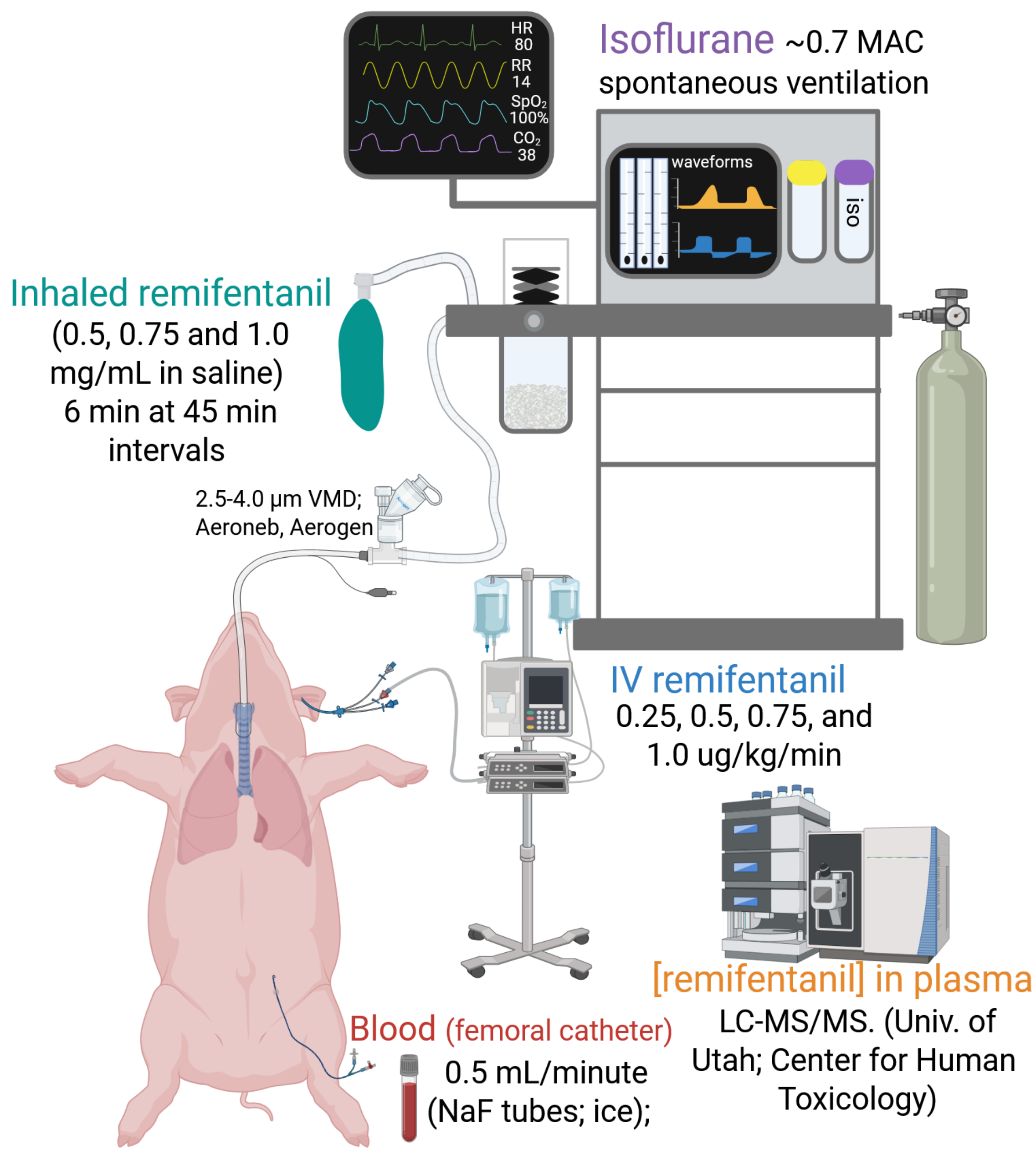
- Inhaled remifentanyl yields analgesic plasma level concentrations comparable to intravenous delivery.
- Respiratory suppression spontaneously reverses due to the rapid elimination of remifentanyl before significant oxygen desaturation can occur.

## Methods/Approach

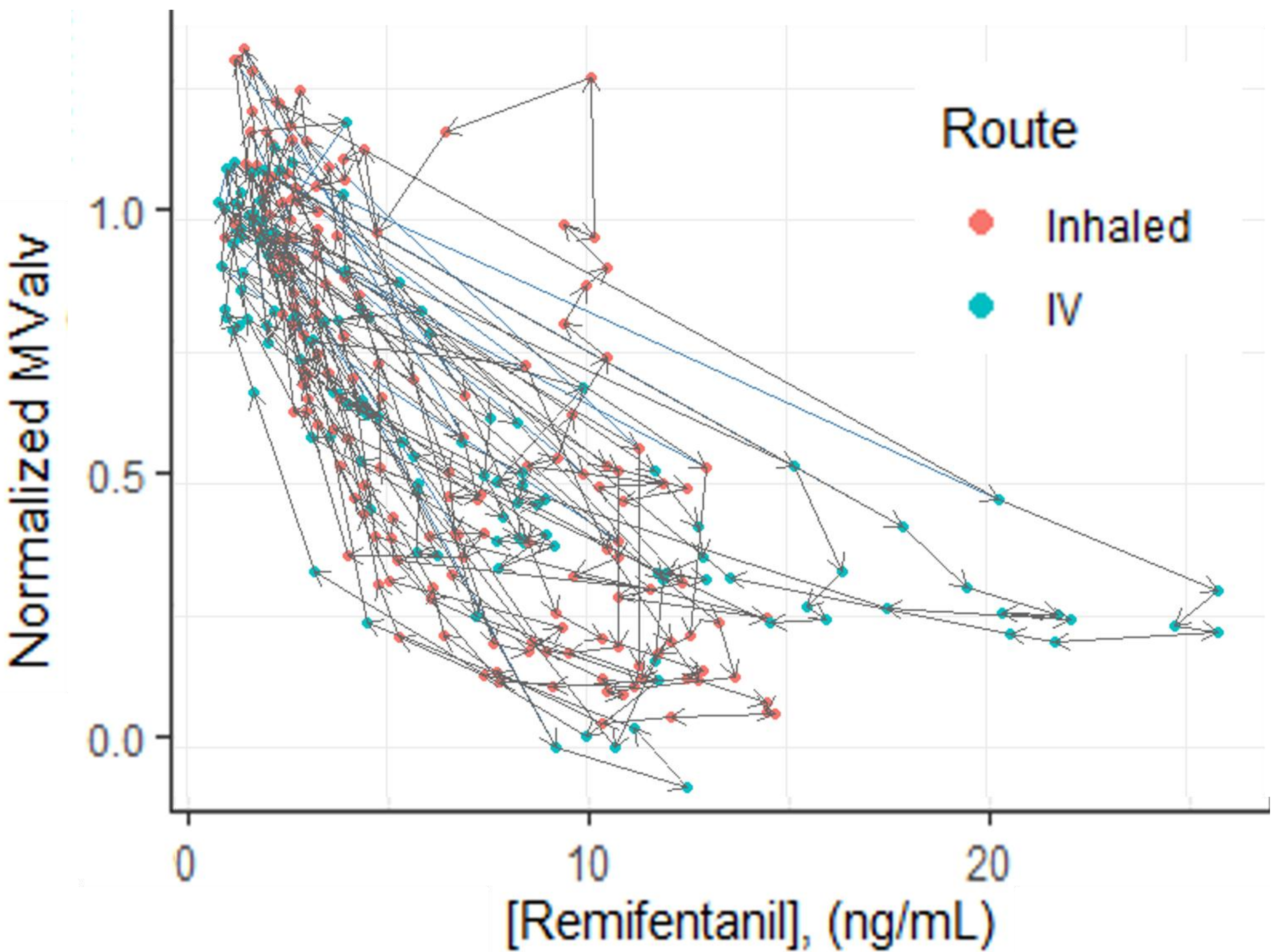
- Isoflurane-anesthetized, spontaneously breathing swine (n=6), were serially dosed with nebulized remifentanyl aerosol via an endotracheal tube (**Phase 1**).
- Pigs were then serially dosed via IV (**Phase 2**).
- Blood was collected at 1.5 min intervals, stored on ice, and processed into plasma.
- Plasma remifentanyl quantification and PK/PD modeling were performed.



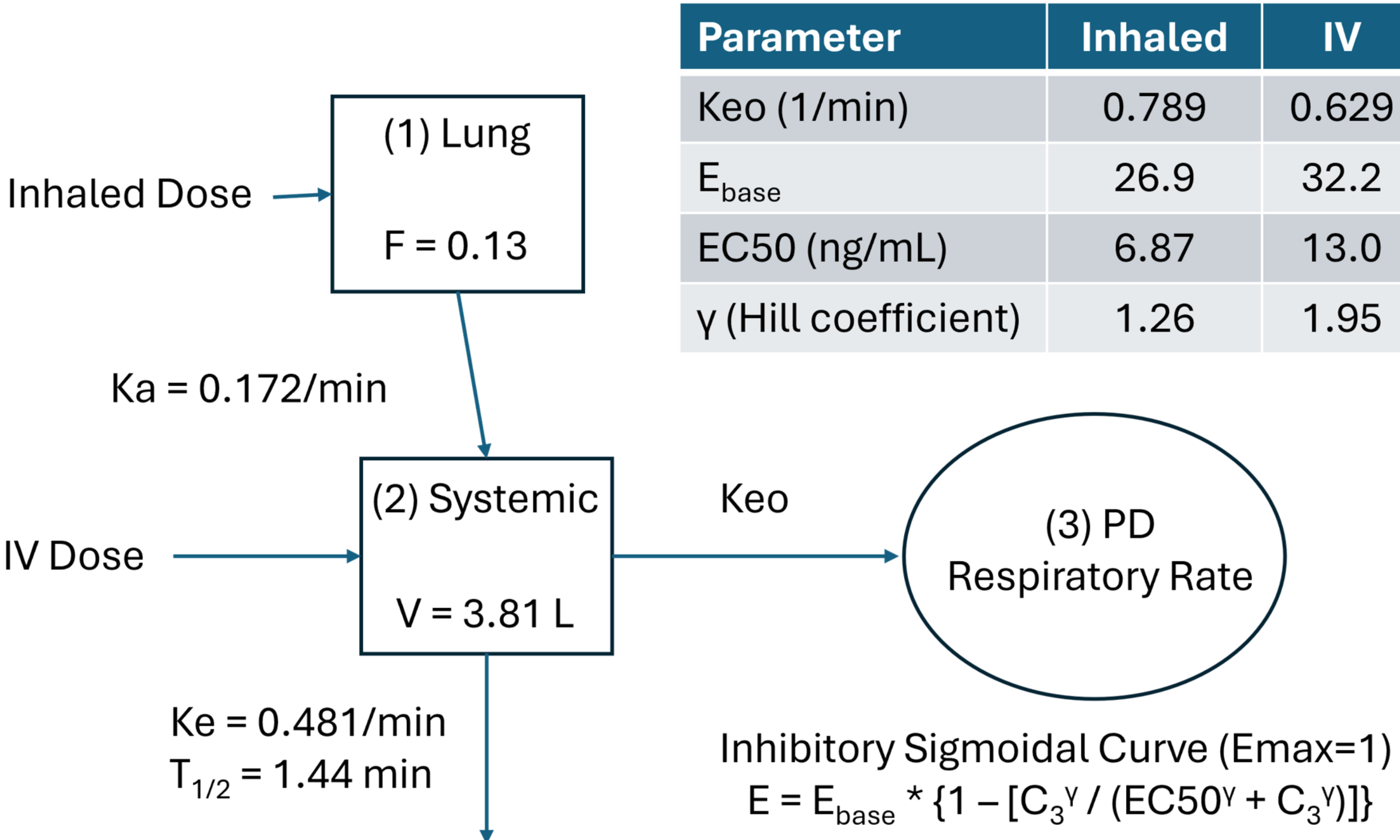
### Remifentanyl Exposure Model



### Hysteresis plots of MValv as a function of remifentanyl dosage



### PK/PD Model and Parameters for Inhaled Remifentanyl



| Parameter            | Inhaled | IV    |
|----------------------|---------|-------|
| Keo (1/min)          | 0.789   | 0.629 |
| E <sub>base</sub>    | 26.9    | 32.2  |
| EC50 (ng/mL)         | 6.87    | 13.0  |
| γ (Hill coefficient) | 1.26    | 1.95  |

## Results

- MValv exhibited similar concentration-dependent changes regardless of administration route.
- Respiratory suppression spontaneously reversed within minutes of dose discontinuation due to rapid drug elimination.
- Inhaled remifentanyl dosing appeared to self-titrate with respiratory suppression, minimizing overdose risk.

## Conclusion

- Inhaled remifentanyl may have safety and application advantages relative to IV dosing.
  - Safer and more efficacious analgesia regimen in forward operating units.
  - Remifentanyl may be able to be dosed by respiratory effort alone.

## Support

- University of Utah Remote Austere Conditions Grant Opportunity.