

# IS THE INTERACTION OF INHALATION ANESTHETICS ADDITIVE?

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**Introduction:** We proposed the parallel/serial neural network model for drug interaction, called MUMPS (Multi-Unit and Multi-Path System).<sup>1-3</sup> The mathematical characters of the MUMPS model indicated that the synergy was most common interaction, the additive interaction can occur only when the relative potencies of two drugs on each conduction unit in the whole neural network are equal, and the antagonistic interaction was rare. Eger *et al*<sup>4</sup> showed that the interactions among the inhalation anesthetics were additive, if the 10% difference from ideal line was allowed. They showed that the interaction of cyclopropane-benzene was additive (total MAC 0.979), although the potency of benzene to inhibit NMDA was stronger than cyclopropane. This finding is contradiction to our prediction as mentioned above. This study examines the effect of the high affinity site on the MUMPS model.

**Method:** We tested the interaction of two anesthetics on the MUMPS network ( $m=200$  and  $n=20$ ). The first anesthetic has the same potency on entire network, and the second has two different potencies; the high affinity binding sites has 100 times higher than the other.

**Results:** Figure showed the effect of the number of conduction unit ( $n_H$ ) and pathway ( $m_H$ ) where the relative potency of the second anesthetic is high. Total MAC is the sum of relative concentrations ( $V^{first} + V^{second}$ ) when the 50% probability of maximal effect and  $V^{first} = V^{second}$ . The grey plate in Figure 3 of Appendix indicate the total MAC = 0.9. Above this plate, the interaction is recognized as additive according to the definition of Eger *et al*.<sup>4</sup> When  $m_H$  is less than about 120 or  $n_H$  is less than about 1, the total MAC is more 0.9 and the interaction was recognized as additive.

**Conclusion:** This finding indicated that the interaction was recognized as additive, when the number of the high potency unit was limited, even though two different potencies (binding sites) of the second anesthetic exist on the neural network. The 10% difference is acceptable on clinical practice, but may not be acceptable for the theoretical approach.

## References:

1. Mechanisms of Anesthesia Conference (MAC) 2010, Toronto, June 15-18 in 2010.
2. J Anesth 2004; 18: 94-9.
3. Anesthesiology 2006; 105: A1200.
4. Anesth Analg 2008; 107: 479-85

