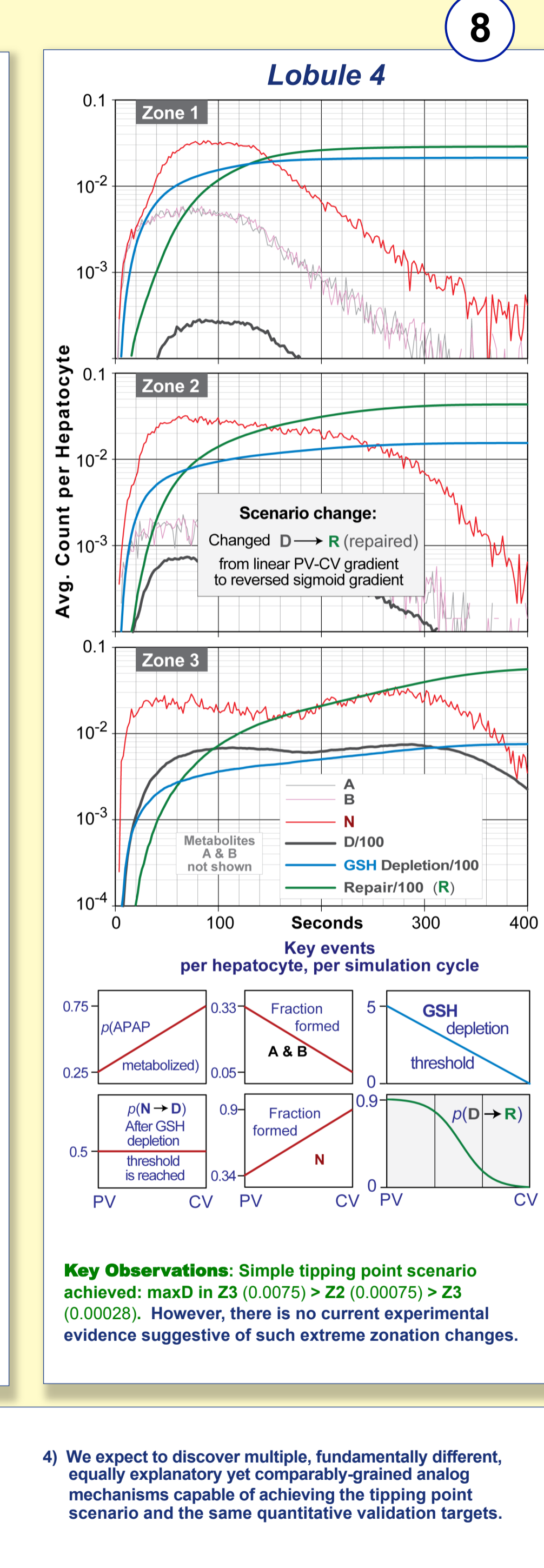
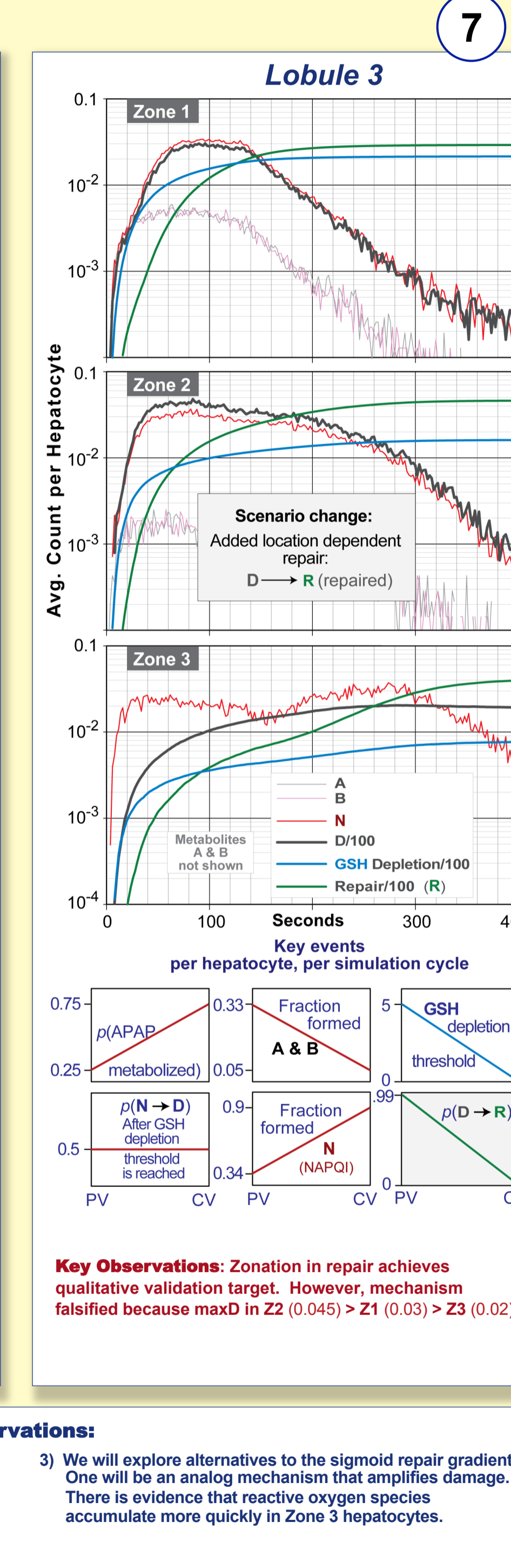
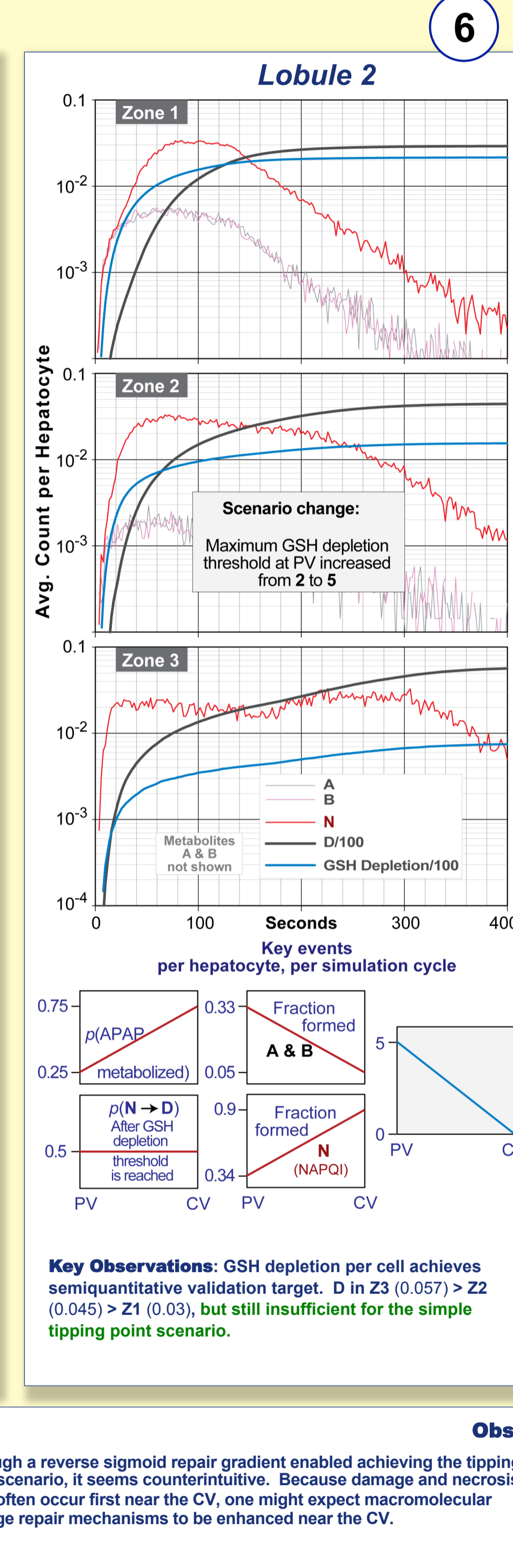
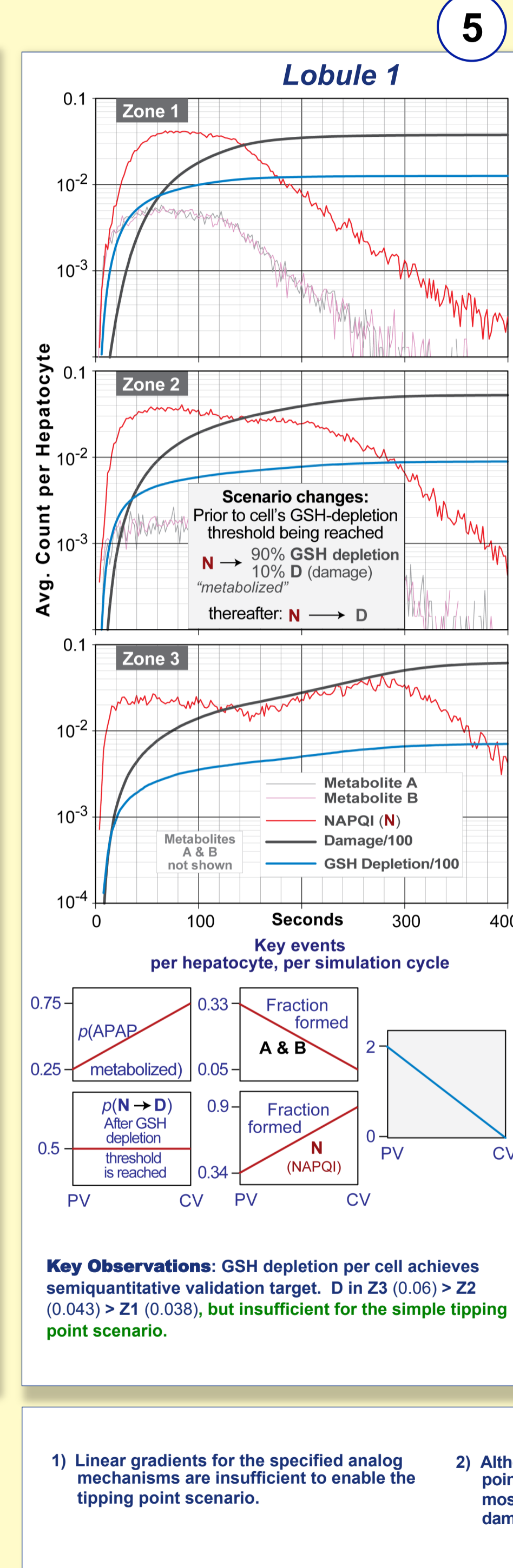
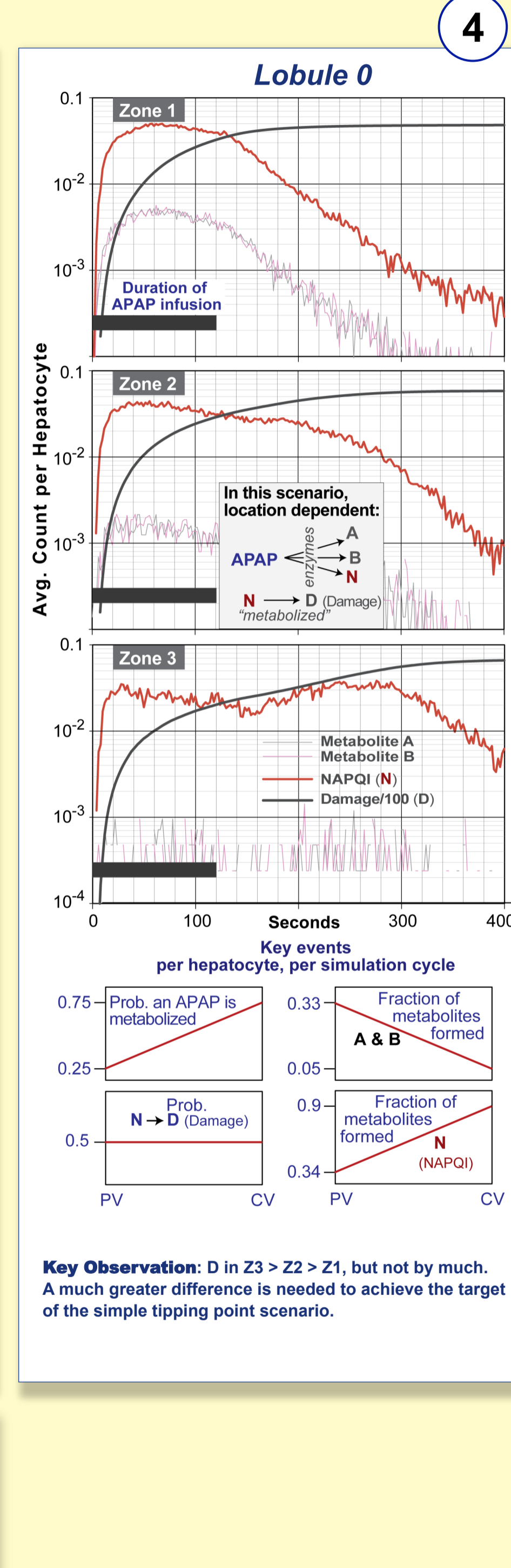
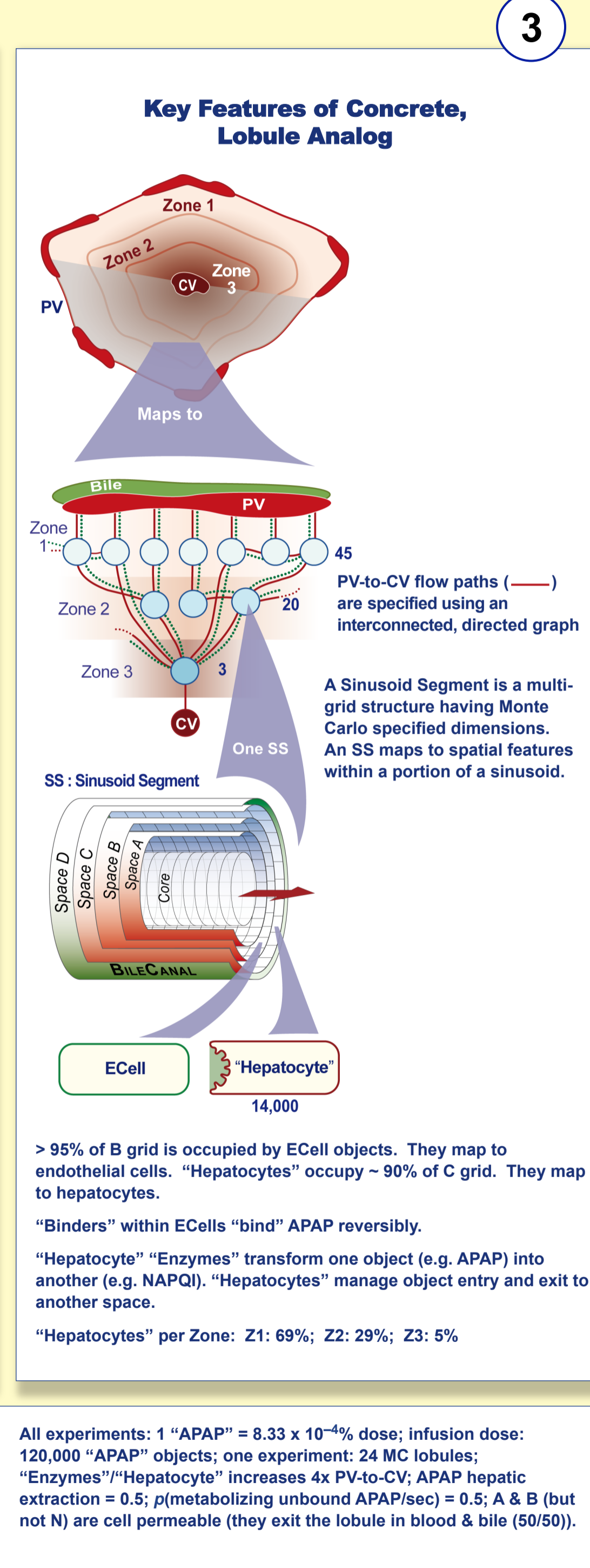
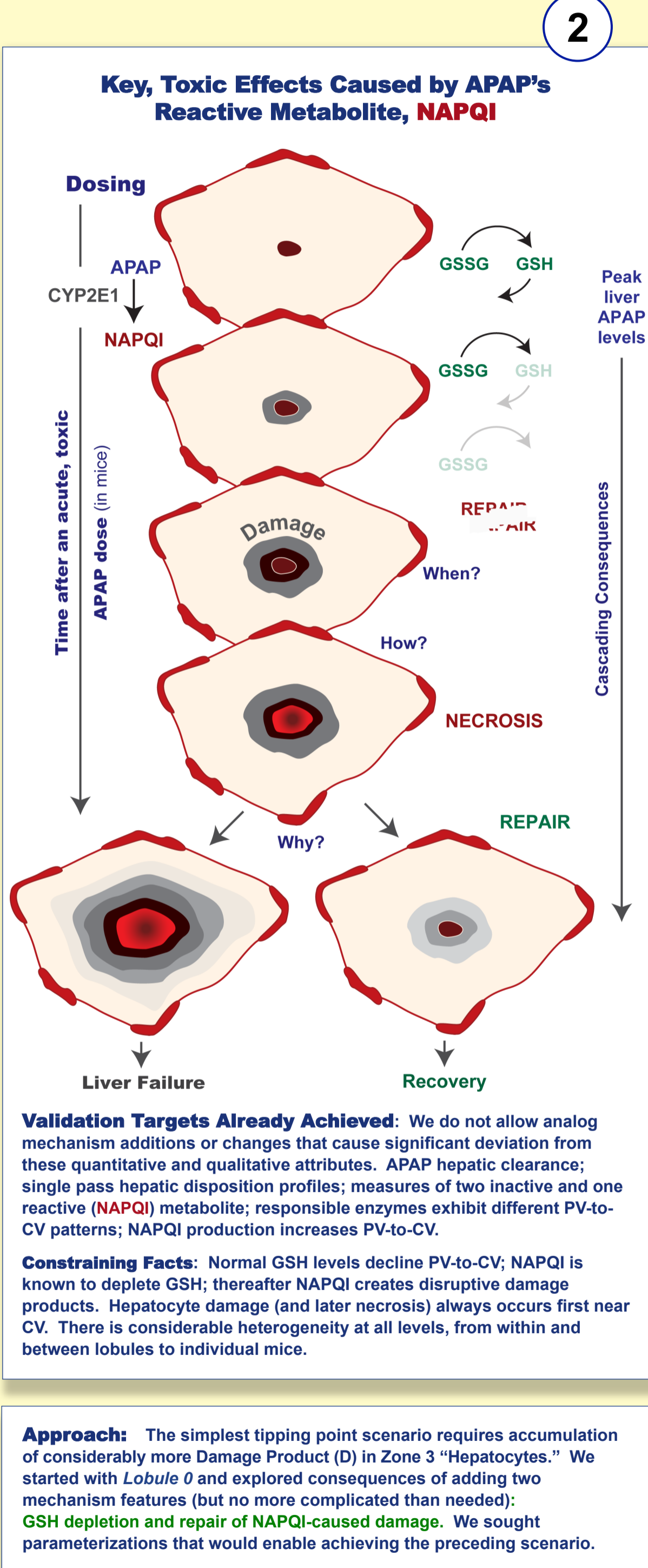
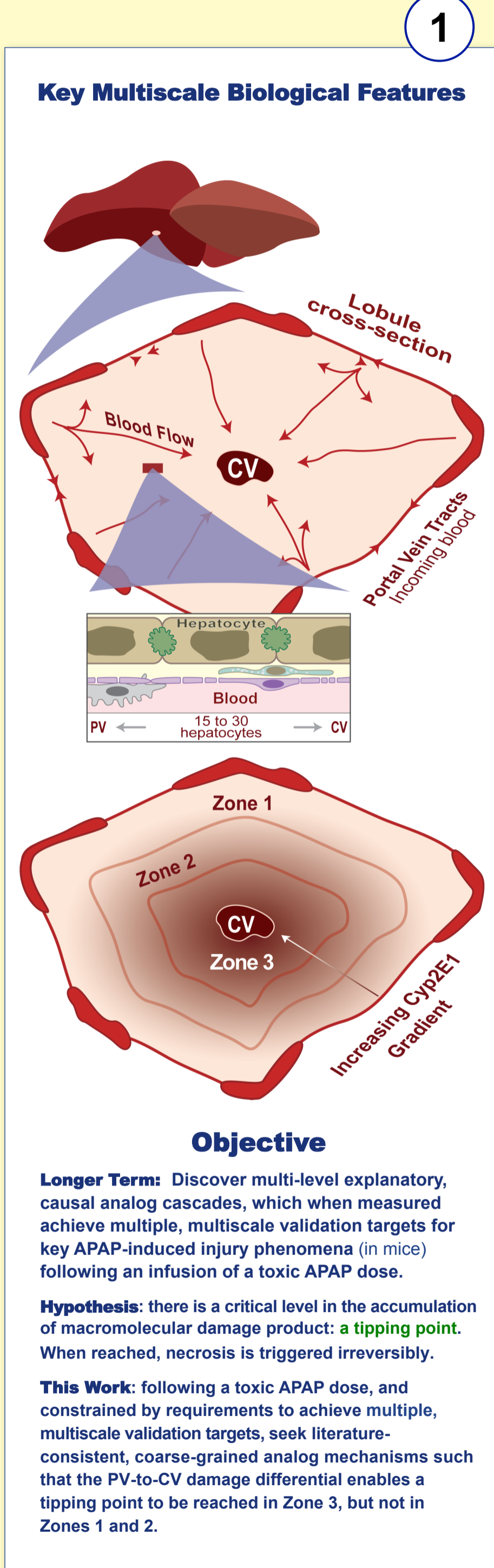


C. Anthony Hunt, Glen E.P. Ropella, and Andrew K. Smith
Bioengineering and Therapeutic Sciences, University of California, San Francisco, CA



- Observations:**
- 1) Linear gradients for the specified analog mechanisms are insufficient to enable the tipping point scenario.
 - 2) Although a reverse sigmoid repair gradient enabled achieving the tipping point scenario, it seems counterintuitive. Because damage and necrosis most often occur first near the CV, one might expect macromolecular damage repair mechanisms to be enhanced near the CV.
 - 3) We will explore alternatives to the sigmoid repair gradient. One will be an analog mechanism that amplifies damage. There is evidence that reactive oxygen species accumulate more quickly in Zone 3 hepatocytes.
 - 4) We expect to discover multiple, fundamentally different, equally explanatory yet comparably-grained analog mechanisms capable of achieving the tipping point scenario and the same quantitative validation targets.