

# Posterior distribution merges ALL information

The diagram shows the posterior distribution equation with labels for each term:

- posterior**:  $p(\theta, \mu, \Sigma^2, \sigma^2 \mid y, \phi, E, t)$
- fixed parameters**:  $\phi$
- likelihood**:  $p(y \mid \theta, \sigma^2, \phi, E, t)$
- prior**:  $p(\theta \mid \mu, \Sigma^2)$
- hyperparameters**:  $p(\mu)p(\Sigma^2)$
- measurement error**:  $p(\sigma^2)$
- exposure regimen**:  $E$
- dosing time**:  $t$

$$p(\theta, \mu, \Sigma^2, \sigma^2 \mid y, \phi, E, t) \propto p(y \mid \theta, \sigma^2, \phi, E, t) p(\theta \mid \mu, \Sigma^2) p(\mu) p(\Sigma^2) p(\sigma^2)$$

- Modelling assumptions have to make sense
  - Note 1: physiological parameters can be naturally truncated
  - Note 2: certain random quantities are positive and skewed right - log-normal distribution
  - Note 3: parameters are high-dimensional vectors

# PBPK model unknowns vs. amount of data

- May not be possible to uniquely identify the parameter values  $\theta$
- Drop out non-sensitive parameters based on matrix of sensitivity functions

$$\frac{\partial y_i}{\partial \theta_j} \cdot \frac{\Delta \theta_j}{\Delta y_i}$$

- Which parameters  $\Theta_j$  cause large/small changes to output  $y_i$  when changed?
  - Fix parameters that are non-sensitive
    - Part of “Preliminary model calibration”