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A Time-Variant Parameter as a Wiener Process using the effects Modeling Framework

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Abstract: This paper describes Modeling a parameter in such a way, however, requires a priori knowledge of the time course of the parameter. In many cases, the time course of the parameter is unknown or is actually the quantity of interest. What is needed in these cases is a way to fit the parameter as an arbitrarily shaped function. Typical pharmacokinetic models consider parameters such as volume, clearance, and absorption rate to be constant over the duration of the study. More sophisticated models may attempt to parameterize changes to the constants, such as tying clearance to a circadian rhythm or modeling drug absorption with a sigmoid curve.

Introduction:

The Wiener Process is essentially a random walk W(t) with

- Zero initial value, W(0)=0
- Zero expected value, E[W(t)]=0
- Independent increments W(t)-W(s)$\sim$ N(0,t-s), for $0 < s < t$
- Variance proportional to the square root of the time between increments (steps in value).

Given that the Wiener Process, W, is either directly observed over a set $T = \{t_1, t_2, t_3, ...\}$, define

$$W(T_i) = \sum_{t \leq T_i} w_t, \quad w_i \sim N(0, (T_i - T_{i-1})\sigma_w^2)$$

The increments of W are independent and can be transformed to identically distributed normal variables:

$$w_i = (T_i - T_{i-1})^{1/2}\eta_{w_i}, \qquad \eta_{w_i} \sim N(0, \sigma_w^2)$$