1. The reason to have splitting interval fitting
2. The change of the physical condition can lead to the change of drug absorption and drug metabolism. Ideally, we expected the drug has a linear kinetics, in which case the absorption coefficient and the elimination coefficient remain the same over the whole. However,
3. In the real life scenario, although the dosing interval can be well documented, the lag time which is the actual onset absorption time of the drug absorption may vary. If not taken care it may lead to an inaccurate model fitting and wrong parameter estimation. However, Based on the concentration-time graph the true onset of a dosage can be determined.
4. For multi dose situation, It is hard to do the whole dosing regimen analysis, which include all the parameter, k, ka, interval tau, the OLS objective function has so many local minimum and is so easy to get trapped in local minimum. By dividing each interval and treating each interval as a single dose scenario.
5. Automated method. In traditional PK modeling software like Winolin, user have to choose the model and set up the initial estimate manually. This automated method will perform the analysis just by given the raw data, no dosing interval needed to assign.
6. The method used
7. Experiment result

Oxycodo\_dosing: tau=8, ka=1.23, k=0.58. We have the multi-dose time-concentration curve.

The splitting algorithm. The fitting optimization method. Variance for the test data was introduced.

The Variance equation follows the y=(1+y)\*sigma

Fig: The DBCD cluster.

Fig: The min point in the graph

Fig: Parameter array and graph