

NONMEM to NLME: PD – Count data

Agenda

- Model Description
- Exploratory Data Analysis
- Input Data
- Model in NM-TRAN and PML Code
- Demo
- Summary
- Q&A

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NONMEM to NLME: count data

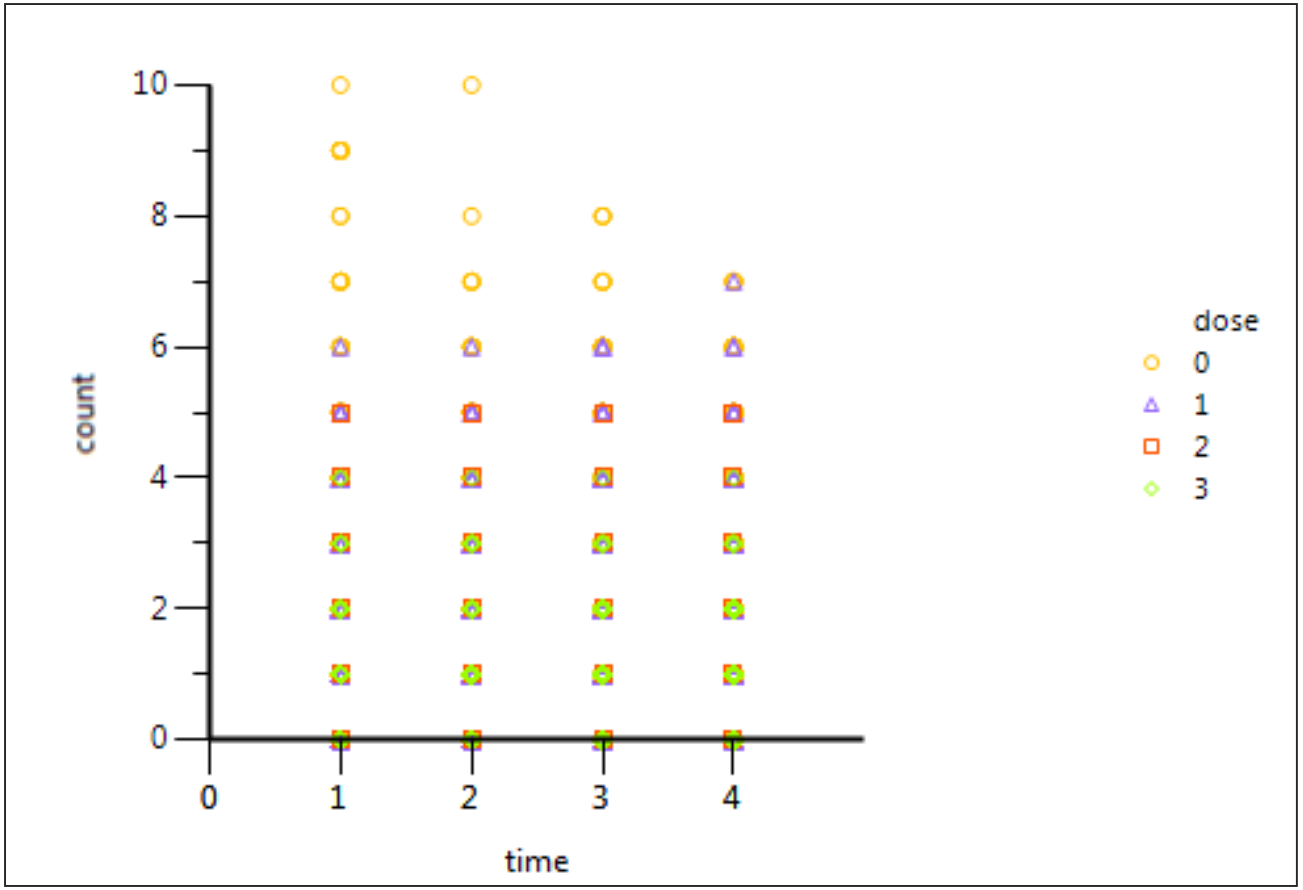
- Model Description
  - Structural Model
    - Count model: Poisson distribution
    - No error model
  - Structural Parameters
    - Loglambda
    - Coeff
  - Random Effect
    - Eta on Loglambda, variance: 0.1 (~30% population variability)
  - Engine
    - Laplacian

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PKPD: count data

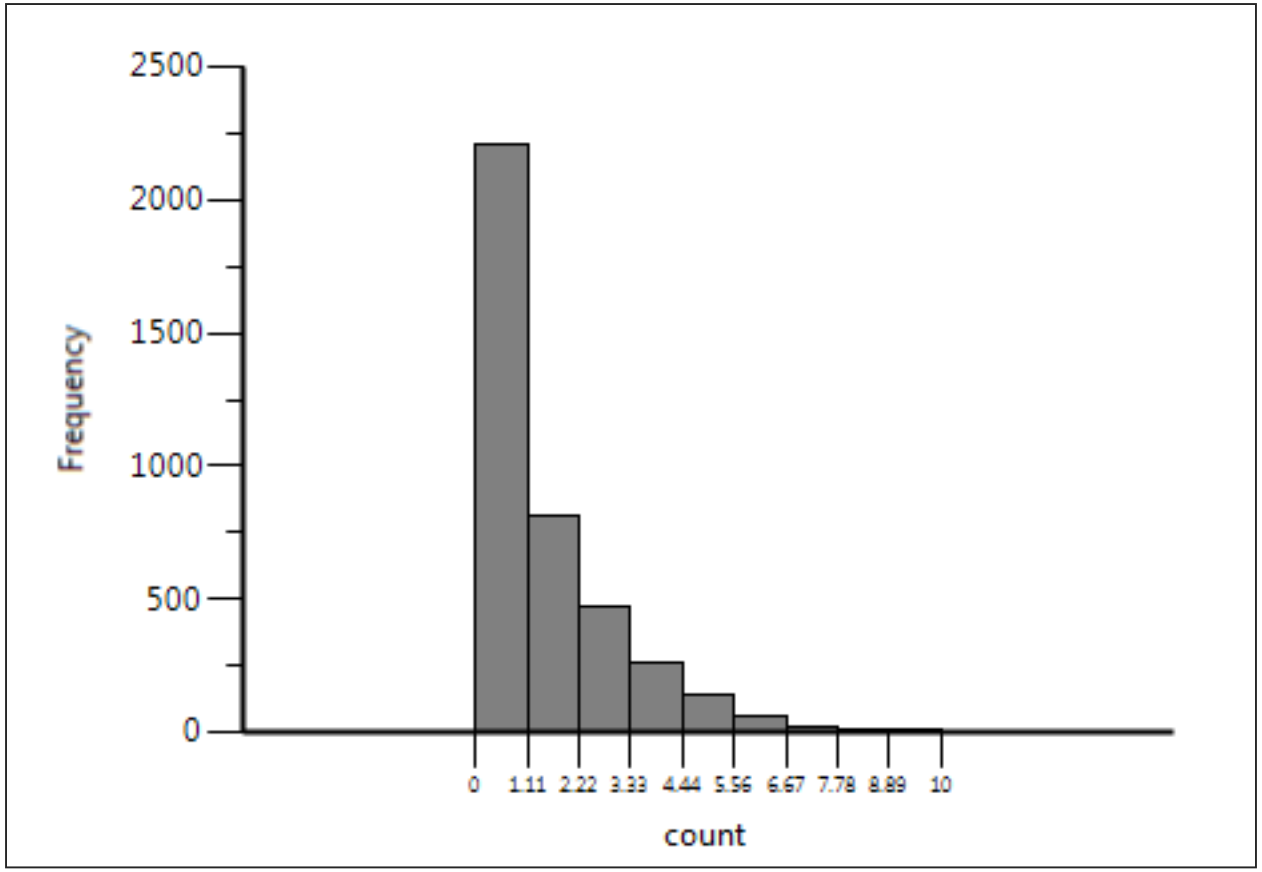
- Counts versus Time:



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PKPD: count data

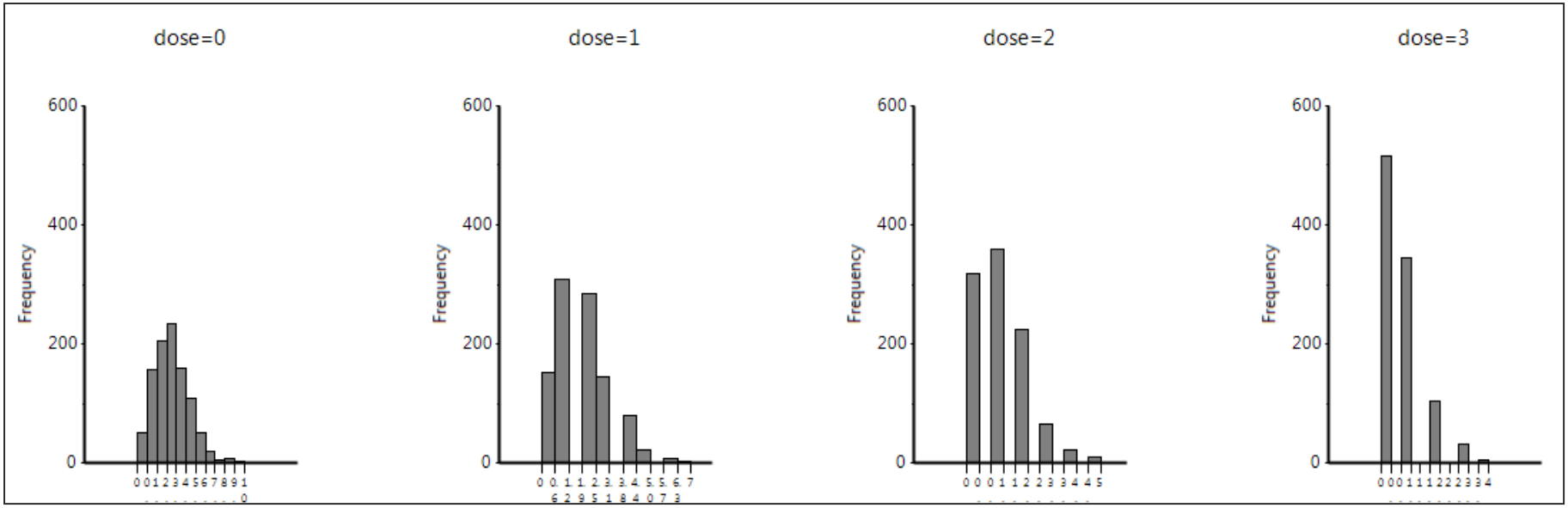
- Count distribution (all):



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PKPD: count data

- Count distribution (by dose):



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count data: Input Data

- NONMEM & NLME

	id	dose	tend	count	tmid
1	1	1	0	.	0
2	1	1	1	1	0.5
3	1	1	2	0	1.5
4	1	1	3	0	2.5
5	1	1	4	2	3.5
6	2	2	0	.	0
7	2	2	1	1	0.5
8	2	2	2	1	1.5
9	2	2	3	1	2.5
10	2	2	4	1	3.5
11	3	3	0	.	0
12	3	3	1	0	0.5
13	3	3	2	0	1.5
14	3	3	3	3	2.5
15	3	3	4	0	3.5
16	4	0	0	.	0
17	4	0	1	5	0.5
18	4	0	2	7	1.5
19	4	0	3	3	2.5
20	4	0	4	3	3.5

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NONMEM to NLME: count data

NONMEM

```
;Input
$PROB Poisson Model
$INPUT id dose tend DV tmid
$DATA data.csv

;Parameters
$PRED
coefdose = Theta(1)
BASE=THETA(2)+ ETA(1)
LAMB=BASE + coefdose*dose
cumhaz=EXP(LAMB)
```

NLME

```
#Input
fcovariate(dose)


#Parameters
stparm(coef = tvcoef)
stparm(loglambda = tvloglambda
+ eta1)
```

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NONMEM to NLME: count data

NONMEM

```
; Estimation Code
LFAC=GAMLN(DV+1.0)
IF(DV.LE.1) LFAC=0
LPOI = -cumhaz+DV*LOG(cumhaz)-LFAC
Y=-2*(LPOI)
```

NLME

```
# count statement
count(DV, exp(loglambda+coef*dose))
```

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NONMEM to NLME: count data

NONMEM

```
; fixed effects
$THETA
 (1)        ;coefdose
 (0,2)      ;tvloglambda

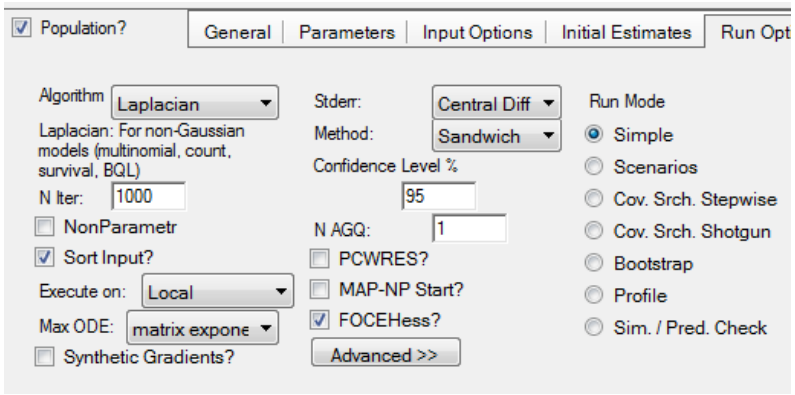
; random effects
$OMEGA
 0.1 FIX    ;eta1

;estimation method
$ESTIM MAXEVAL=9999
METHOD=COND LAPLACE -2LL
PRINT=1 MSFO=msf1
$COV
```

NLME

```
# fixed effects
fixef(tvcoef = c(, 1, ))
fixef(tvloglambda = c(, 2, ))

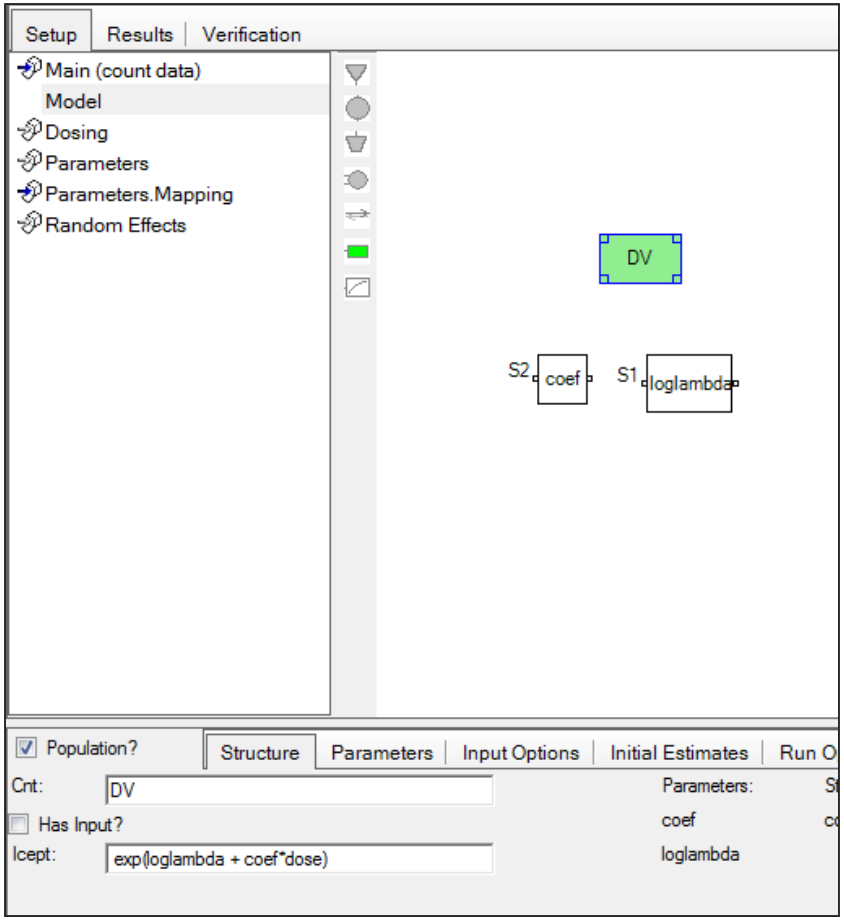
# random effect
ranef(diag(eta1)(freeze) = c(0.1))
```

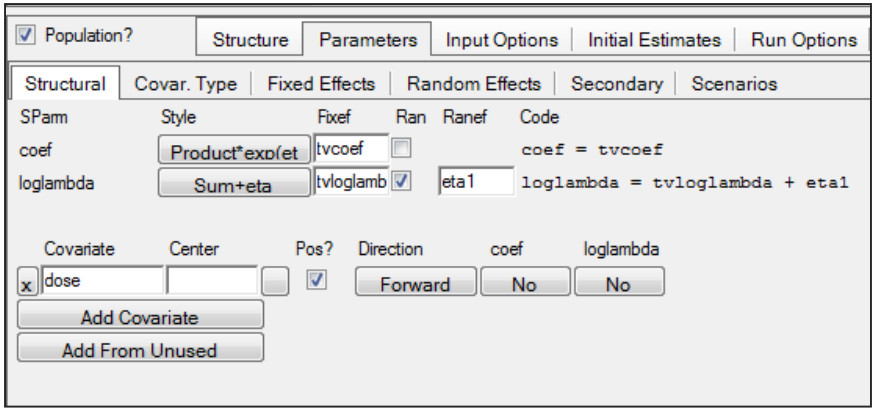


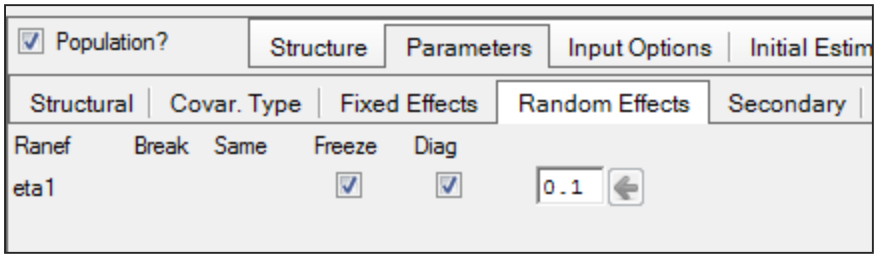
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count data: Graphical Model







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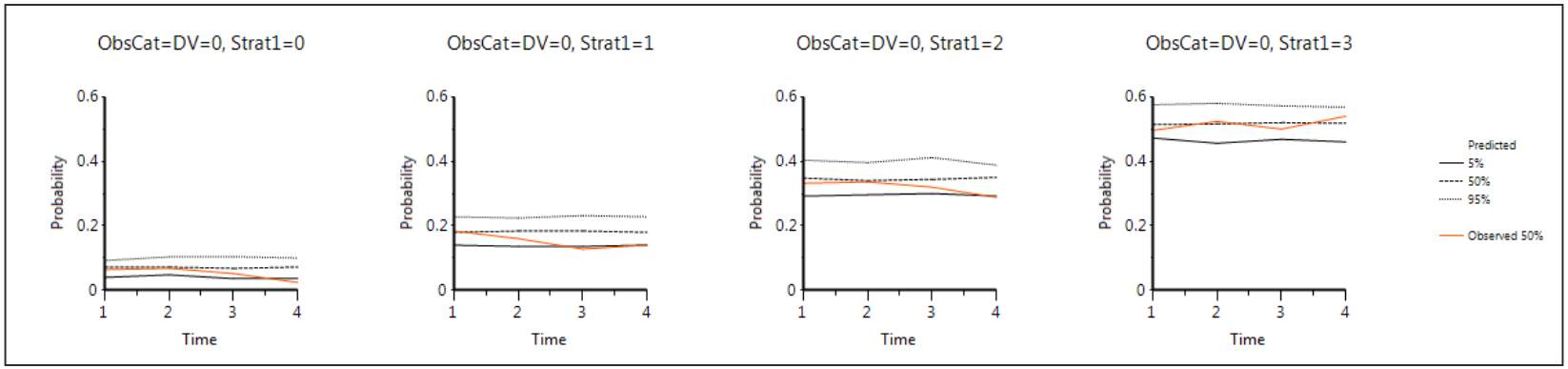
Demo

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count data : Summary

	SW			
	NLME		NONMEM	
Parameter	Estimate	Stderr	Estimate	Stderr
tvcoef	-0.50	0.01	-0.50	0.01
tvloglambda	0.84	0.02	1.06	0.02

VPC:



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Questions?



Certara University

- Link:
  - https://www.certarauniversity.com/lms
- Advanced PKPD courses:



(302-CL) Advanced Categorical and Time-to-Event Population Modeling using Phoenix NLME

$1,495 (Academia $748)

Course Description



This course is designed to explore advanced techniques in pharmacokinetic and pharmacodynamics modelling and simulation using categorical, count and time-to-event data. Detailed discussion of Pharsight Modeling Language (PML) covers how the Phoenix NLME engine functions and in depth lectures on the statistical theory underlying analysis of categorical, count and time-to-event data provide the necessary background to allow for complex model development. Hands-on examples from current literature to provide a complete training experience. Topics include approaches to handling data below the limit of quantitation limit, longitudinal frequency data, repeated measures time-to-event pharmacodynamics responses, drop out models, categorical pharmacodynamics endpoints, and translating models between NONMEM and Phoenix NLME.

The fee is in US dollars and includes training materials, tea, coffee and lunch. All travel, accommodation and evening meal expenses are the responsibility of the attendee. Contact info@certarauniversity.com for academic discount

All attendees are required to provide their own laptop for use during the course. Please bring a computer mouse.

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