



InVitroInVivoCorrelation.jl: A Modular Julia Package for Level A IVIVC

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THE PIPELINE

One scriptable, DataFrames-native call runs the full workflow:

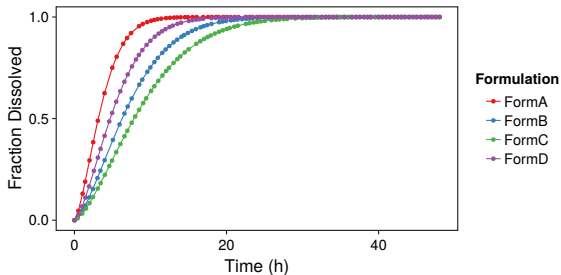
```
result = run_ivivc(  
    pk_df, diss_df;  
    fast_formulation = "IV",  
    validation_formulation = "FormB",  
)
```

ADDITIONAL FEATURES

- ▶ User-defined correlation models (`AbstractCorrelationModel`)
- ▶ Parametric dissolution: Hill, Weibull, double Weibull, Makoid–Banakar
- ▶ Oral IR reference with absorption stripping (`strip_ka`)
- ▶ Parallel study designs: one population UIR (`parallel_study`)
- ▶ Multi-dose support with per-subject dose normalisation
- ▶ FDA f_1/f_2 dissolution similarity metrics

STEP 1: DISSOLUTION DATA

In vitro dissolution profiles for each formulation are interpolated onto a common time grid.



STEP 2: UIR FITTING

A poly-exponential unit impulse response is fitted from the IV reference:

$$h(t) = \sum_{m=1}^M A_m e^{-\alpha_m t}$$

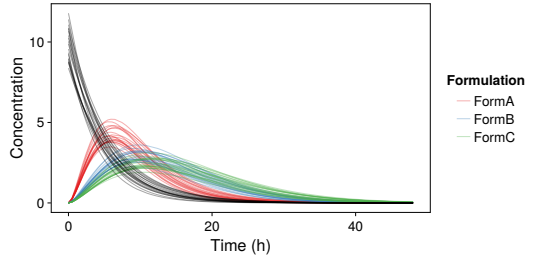
The number of terms M is selected automatically via AICc.

STEP 3: DECONVOLUTION

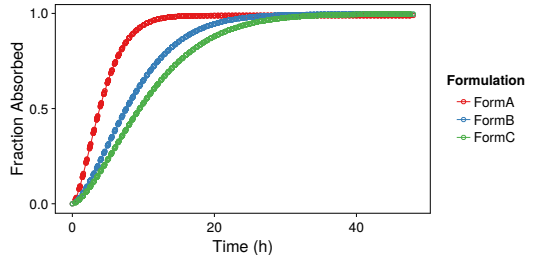
Oral concentration profiles are related to the absorption rate $I(t)$ via convolution with the UIR:

$$C(t) = \int_0^t I(\tau) h(t - \tau) d\tau$$

Deconvolution solves for $I(t)$ using non-negative least squares, yielding the cumulative fraction absorbed.



↓ deconvolution



STEP 4: IVIVC CORRELATION

The Level A model regresses cumulative absorption on cumulative dissolution via an affine time-scaling and linear mapping:

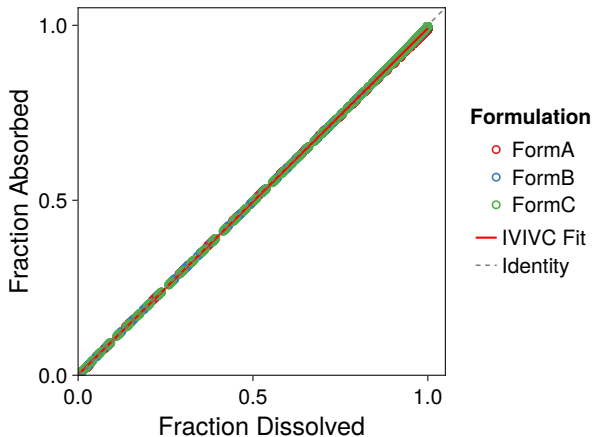
$$F_{\text{abs}}(t) = s_a \cdot F_{\text{diss}}(s_t \cdot t + b_t) + b_a$$

MOTIVATION

- ▶ A validated Level A IVIVC is a point-to-point link between in vitro dissolution and in vivo absorption [2]
- ▶ It sets clinically relevant dissolution specifications [1]
- ▶ It supports regulatory biowaivers, e.g. for post-approval changes [1]

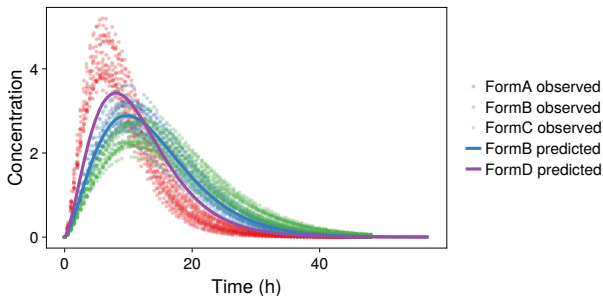
[1] FDA. Guidance for Industry: Extended Release Oral Dosage Forms: Development, Evaluation, and Application of In Vitro/In Vivo Correlations. *U.S. FDA*, 1997.

[2] Cardot JM, Beyssac E, Alric M. In vitro–in vivo correlation: importance of dissolution in IVIVC. *Dissolution Technologies*. 2007;14(1):15–19.



STEP 5: PREDICTION & VALIDATION

For validation and new formulations, predicted absorption is convolved with each subject's fitted UIR and the resulting concentrations are averaged. Dots: observed data (A, B, C). Solid lines: predicted concentrations for Formulation B (held out) and Formulation D (external, no observed PK).



PREDICTION ACCURACY

Prediction errors satisfy FDA guidance acceptance criteria [1].

Formulation	Role	%PE AUC	%PE $C_{\max}$
B	Validation	0.6	0.1
D	External	0.9	0.5

FDA external predictability criterion: %PE $\leq 10\%$ [1, p. 10]

Simulated data: one-compartment IV elimination with inter-subject variability, Weibull absorption, formulation-specific dissolution rates, jittered sparse sampling; no measurement noise.



CONTACT

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