Harnessing Intermittent Hemodialysis to Study Individual Pharmacokinetics

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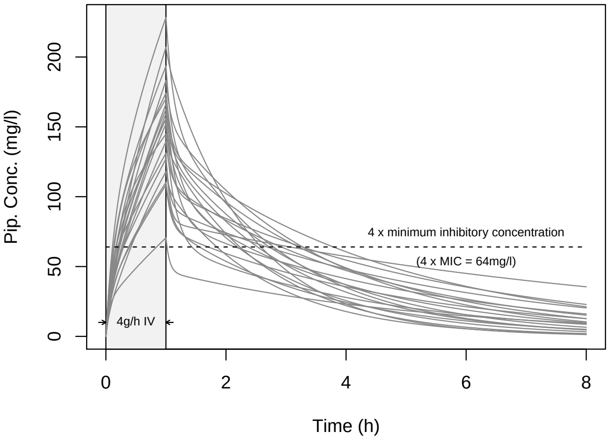
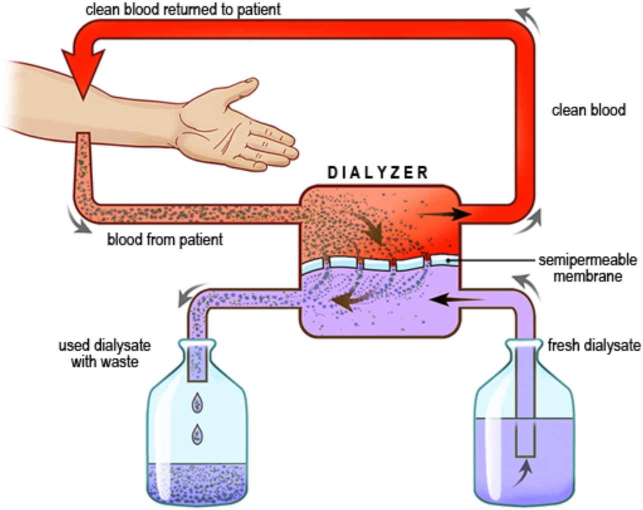
Piperacillin Pharmacokinetics



Hemodialysis



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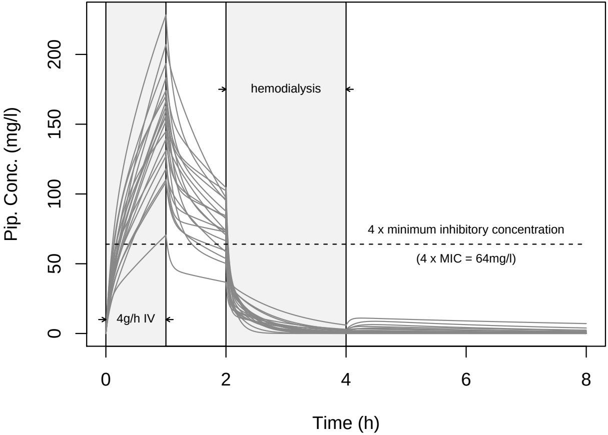
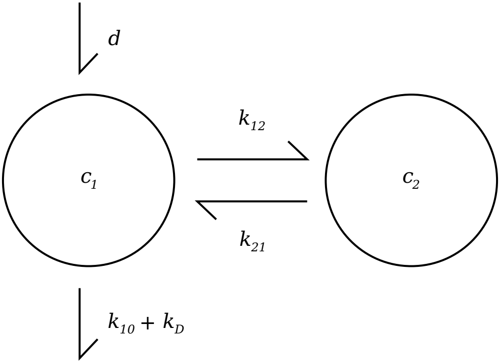
Piperacillin Pharmacokinetics with Hemodialysis



Two-Compartment Model



Two-Compartment Model

$$
\begin{aligned}
\frac{dC_1}{dt} &= d/V_1 \quad -(k_{10}+k_D)C_1 \quad -k_{12}C_1 \quad +k_{21}C_2 \\
\frac{dC_2}{dt} &= \qquad\qquad\qquad\qquad\quad +k_{12}C_1 \quad -k_{21}C_2
\end{aligned}
$$

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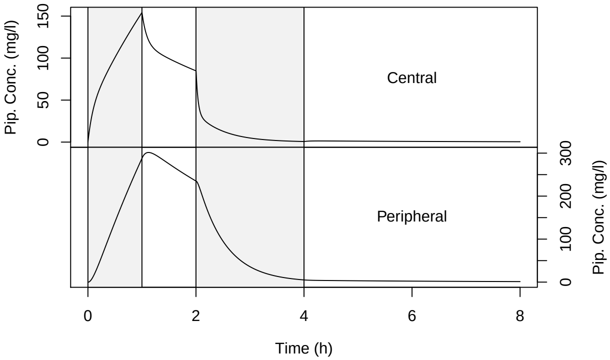
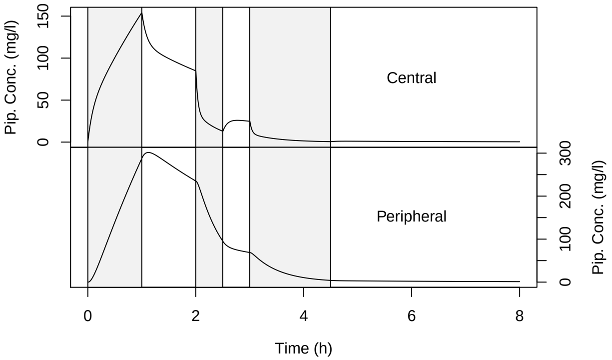
Two-Compartmen Model: Piperacillin with Hemodialysis



Two-Compartmen Model: Piperacillin with Hemodialysis



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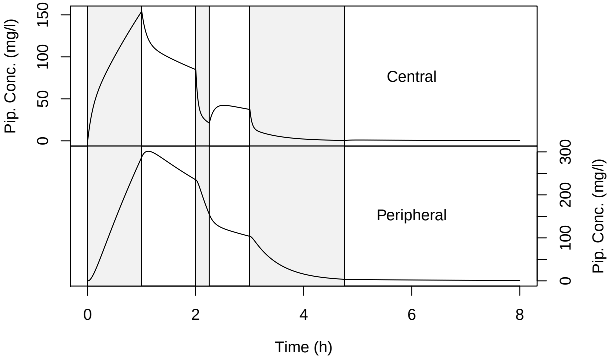
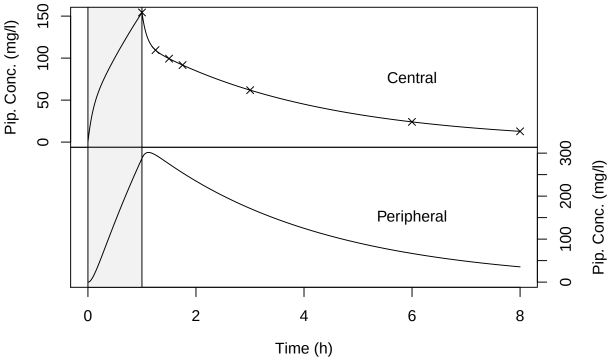
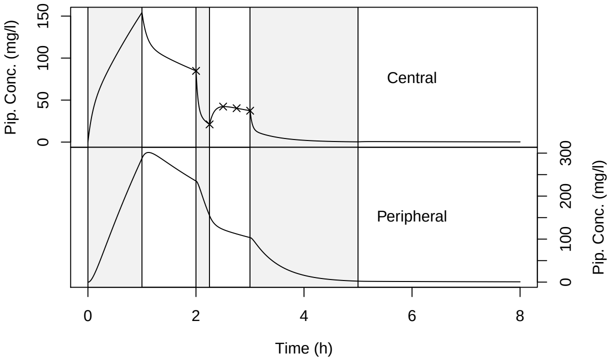
Two-Compartmen Model: Piperacillin with Hemodialysis



Conventional PK Sampling



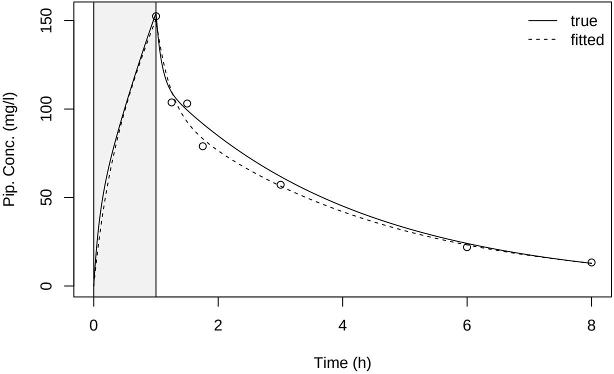
Intradialytic PK Sampling



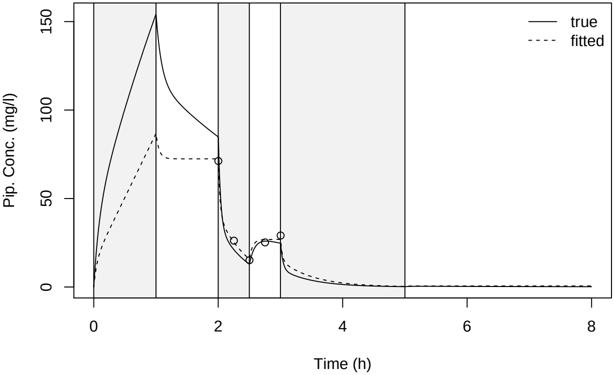
Intradialytic PK Sampling: Potential Advantages

- sample from machine or dialysate (no phlebotomy)
- shorter sampling period
- better PK estimates
  - smaller measurement error
  - dynamic aspect informative about k_{12} and k_{21}

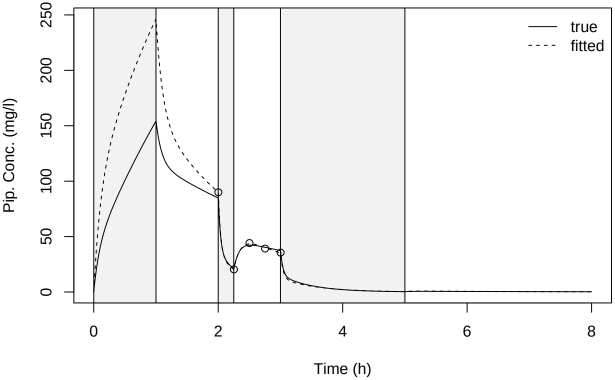
Conventional PK Sampling: Simulation Example



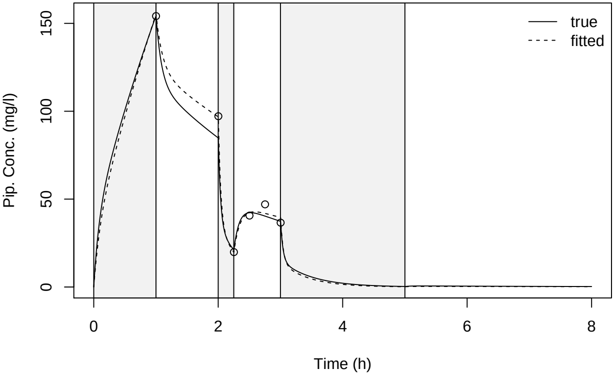
Intradialytic PK Sampling: Simulation Example 1



Intradialytic PK Sampling: Simulation Example 2



Intradialytic PK Sampling: Simulation Example 3



Simulation Results

	k_{10}	V_1	k_{12}	k_{21}	T>4×MIC
Bias: Conventional	0.14	-0.43	0.02	-0.10	0.81
Bias: Intradialytic	-0.03	-0.02	0.03	0.01	-0.01
RMSE: Conventional	2.52	0.98	2.97	0.92	0.18
RMSE: Intradialytic	0.47	0.24	0.20	0.25	0.07

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Conclusions

intradialytic sampling may:

- reduce sampling time
- reduce phlebotomy
- reduce blood usage
- improve PK estimates!

Ongoing Considerations

- interpatient PK variability
- algorithmic optimial design