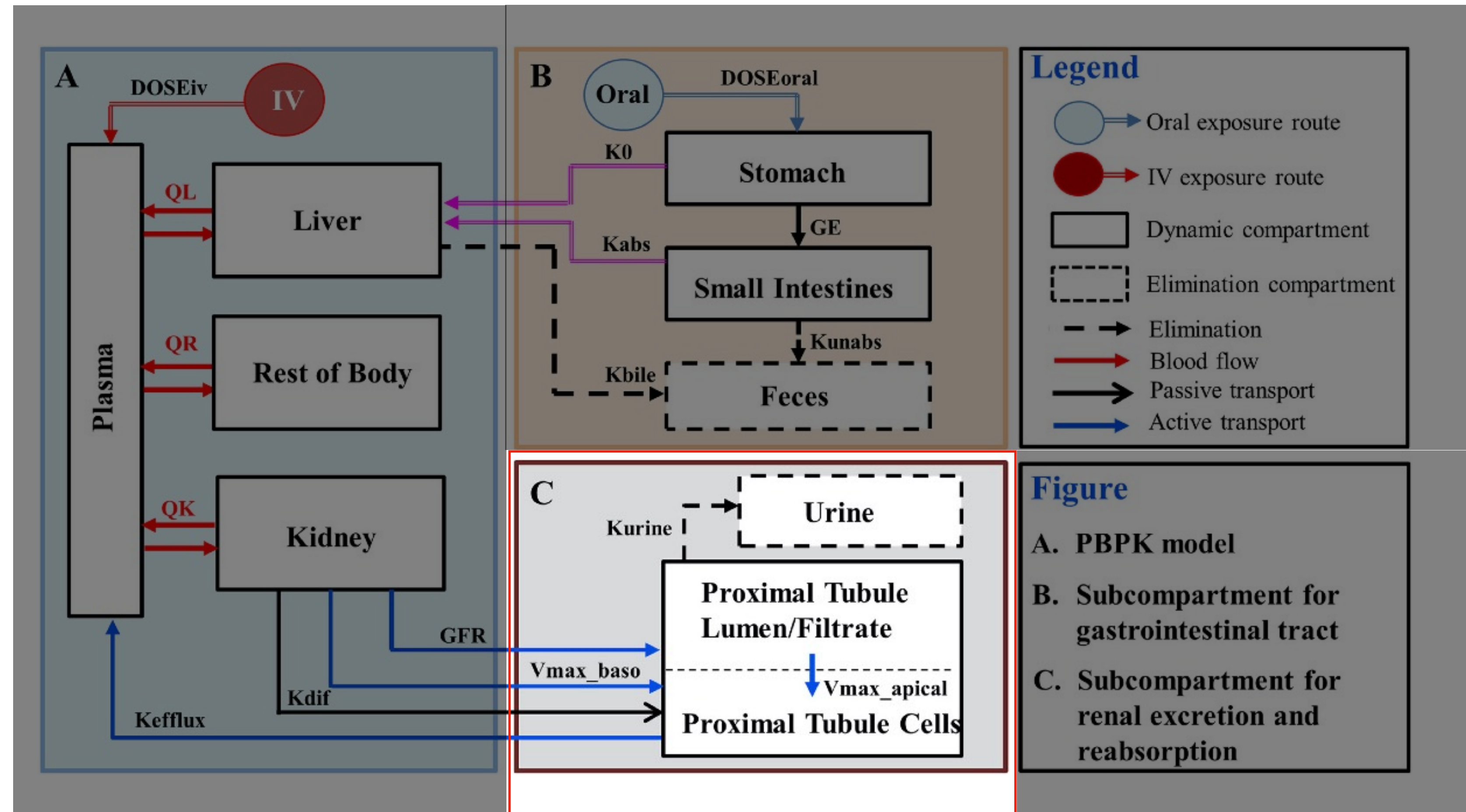


Physiologically based pharmacokinetic model

ODE system

- 3-compartment model for kidney
- proximal tubule lumen/filtrate
- proximal tubule cells
- rest of the kidney



Physiologically based pharmacokinetic model

ODE system : Coefficients

```
HumanPBK.code <- '
$PARAM @annotated
QCC      : 12.500      : L/h/kg^0.75, Cardiac output (Brown 1997, Forsyth 1968)
QLC      : 0.250      : Fraction blood flow to liver (Brown 1997, Fisher 2000)
QKC      : 0.175      : Fraction blood flow to kidney (Brown 1997, Forsyth 1968)
Htc      : 0.44       : Hematocrit for human; ICRP Publication 89 (2003)
BW       : 82.3       : kg, Bodyweight (EPA Factors Handbook, 2011)
VLC      : 0.026      : Fractional liver tissue (Brown 1997)
VKC      : 0.004      : Fractional kidney tissue (Brown 1997)
VPlasC   : 0.0428     : L/kg BW, Fractional plasma (Davies 1993)
VfilC    : 4.0e-4     : L/kg BW, Fraction vol. of filtrate
VPTCC    : 1.35e-4    : L/kg kidney, Vol. of proximal tubule cells (60 million PTC cells/gram kidney, 1 PTC = 2250 um3)
FVBK     : 0.160      : Blood volume fraction of kidney (Brown, 1997)
PL       : 2.67       : Liver/plasma PC; (from human cadaver data, Fabrega, 2014)
PK       : 1.26       : Kidney/plasma PC; (from human cadaver data, Fabrega, 2014)
PRest    : 0.2        : Restofbody/plasma PC; (from mouse tissue data, Loccisano, 2011)
MW       : 500.126    : g/mol, PFOS molecular mass
MKC      : 0.0084     : Fraction mass of kidney (percent of BW); Brown, 1997
Free     : 0.025     : Free fraction of PFOS in plasma (Luccisanno et al., 2011)
Vmax_baso_invitro : 439.20 : pmol/mg protein/min, Vmax of basolateral transporter; averaged in vitro value of rOAT1 and rOAT3 (Nakagawa, 2007)
Km_baso  : 20100      : ug/L, Km of basolateral transpoter, averaged in vitro value of rOAT1 and rOAT3 (Nakagawa, 2007)
Vmax_apical_invitro : 37400 : pmol/mg protein/min, Vmax of apical transporter; averaged invitro value of Oatplal (Weaver, 2010)
Km_apical : 77500     : ug/L, Km of apical transpoter, in vitro value for Oatplal (Weaver, 2010)
RAFbaso  : 1         : Relative activity factor, basolateral transpoters (male) (fit to data); 0.01356 (female)
RAFapi   : 0.0007     : Relative acitivty factor, apical transpoters (fit to data); 0.001356 (female)
protein  : 2.0e-6     : mg protein/proximal tubuel cell, Amount of protein in proximal tubule cells
GFRC     : 24.19      : L/hr/kg kiney, Glomerular filtration rate (male); 41.04 (female) (Corley, 2005)
Kdif     : 0.001      : L/h, Diffusion rate from proximal tubule cells
Kabsc    : 2.120      : 1/(h*BW^0.25), Rate of absorption of chemical from small intestine to liver (fit to data)
KunabsC  : 7.06e-5    : 1/(h*BW^0.25), Rate of unabsorbed dose to appear in feces (fit to data)
GEC      : 3.500      : 1/(h*BW^0.25), Gastric emptying time (Yang, 2013)
K0C      : 1.000      : 1/(h*BW^0.25), Rate of uptake from the stomach into the liver (fit to data)
KeffluxC : 0.100      : 1/(h*BW^0.25), Rate of clearance of PFOS from proximal tubule cells into blood
KbileC   : 0.0001     : 1/(h*BW^0.25), Biliary elimination rate (male); liver to feces storage (fit to data)
KurineC  : 0.063      : 1/(h*BW^0.25), Rate of urine elimination from urine storage (male) (fit to data)
Kvoid    : 0.06974    : (L/hr), Daily urine volume rate (L/hr); Van Haarst, 2004
```