Package 'httkexamples'

December 10, 2025

Version 0.0.1

Date 2025-12-03

Title High-Throughput Toxicokinetics Examples

Description High throughput toxicokinetics (``HTTK") is the combination of 1) chemical-specific in vitro measurements or in silico predictions and 2) generic mathematical models, to predict absorption, distribution, metabolism, and excretion by the body. HTTK methods have been described by Pearce et al. (2017) (<doi:10.18637/jss.v079.i04>) and Breen et al. (2021) (<doi:10.1080/17425255.2021.1935867>). Here we provide examples (vignettes) applying HTTK to solve various problems in bioinformatics, toxicology, and exposure science. In accordance with Davidson-Fritz et al. (2025) (<doi:10.1371/journal.pone.0321321>), whenever a new HTTK model is developed, the code to generate the figures evaluating that model is added as a new vignettte.

Depends R (>= 2.10)

Imports httk, rmarkdown, knitr, Rdpack

RdMacros Rdpack

Suggests dplyr, tidyverse, xlsx, Metrics, ggplot2, ggforce, ggpubr, ggrepel, viridis, ggpubr, grid, ggh4x, readr, ggforce, tidyr, stringr, pracma, cgwtools, openxlsx, ggstar, latex2exp, smatr, reshape, gdata,censReg,gmodels,gplots,scales,colorspace,gridExtra, rvcheck

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LazyData true

LazyDataCompression xz

Encoding UTF-8

VignetteBuilder knitr

RoxygenNote 7.3.3

URL https://chemicalinsights.ul.org/

NeedsCompilation no

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Repository CRAN

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Contents

`abraham2024`	*Abraham et al. 2024 Abraham et al. (2024) (*R*hrefhttps://doi.org/10.1016/j.envint.2024.109047doi:10.1016/j.envint.2024.109047) determined the half-lives of 15 per- and polyfluoroalkyl substances in a single male volunteer.*

Description

Abraham et al. 2024 Abraham et al. (2024) (doi:10.1016/j.envint.2024.109047) determined the half-lives of 15 per- and polyfluoroalkyl substances in a single male volunteer.

Usage

```
abraham2024
```

Format

data.frame

Source

Wambaugh et al., Applying High Throughput Toxicokinetics (HTTK) to Per- and Polyfluoro Alkyl Substances (PFAS), submitted

References

Abraham K, Mertens H, Richter L, Mielke H, Schwerdtle T, Monien BH (2024). "Kinetics of 15 per-and polyfluoroalkyl substances (PFAS) after single oral application as a mixture–A pilot investigation in a male volunteer." *Environment International*, **193**, 109047.

armitage_input	*Parameters for in vitro distribution analysis in Honda et al. (2019) Honda et al. (2019) (Rhrefhttps://doi.org/10.1371/journal.pone.0217564doi:10.1371/journal.pone.0217564) used the Armitage et al. (2014) (Rhrefhttps://doi.org/10.1021/es501955gdoi:10.1021/es501955g) mass-balance model to predict the impact of in vitro partitioning on free chemical concentrations.*

Description

Parameters for in vitro distribution analysis in Honda et al. (2019) Honda et al. (2019) (doi:10.1371/journal.pone.0217564) used the Armitage et al. (2014) (doi:10.1021/es501955g) mass-balance model to predict the impact of in vitro partitioning on free chemical concentrations.

Usage

```
armitage_input
```

Format

data.frame

Source

Honda GS, Pearce RG, Pham LL, Setzer RW, Wetmore BA, Sipes NS, Gilbert J, Franz B, Thomas RS, Wambaugh JF (2019). "Using the concordance of in vitro and in vivo data to evaluate extrapolation assumptions." *PloS one*, **14**(5), e0217564. doi:10.1371/journal.pone.0217564.

References

Armitage JM, Wania F, Arnot JA (2014). "Application of mass balance models and the chemical activity concept to facilitate the use of in vitro toxicity data for risk assessment." *Environmental science & technology*, **48**(16), 9770–9779. doi:10.1021/es501955g. Honda GS, Pearce RG, Pham LL, Setzer RW, Wetmore BA, Sipes NS, Gilbert J, Franz B, Thomas RS, Wambaugh JF (2019). "Using the concordance of in vitro and in vivo data to evaluate extrapolation assumptions." *PloS one*, **14**(5), e0217564. doi:10.1371/journal.pone.0217564.

`aylward2014` *Aylward et al. 2014*

Description

Aylward et al. (2014) compiled measurements of the ratio of maternal to fetal cord blood chemical concentrations at birth for a range of chemicals with environmental routes of exposure, including bromodiphenyl ethers, fluorinated compounds, organochlorine pesticides, polyaromatic hydrocarbons, tobacco smoke components, and vitamins.

Aylward et al. (2014) compiled measurements of the ratio of maternal to fetal cord blood chemical concentrations at birth for a range of chemicals with environmental routes of exposure, including bromodiphenyl ethers, fluorinated compounds, organochlorine pesticides, polyaromatic hydrocarbons, tobacco smoke components, and vitamins.

Usage

```
aylward2014
```

```
aylward2014
```

Format

data.frame

data.frame

Source

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

References

Aylward LL, Hays SM, Kirman CR, Marchitti SA, Kenneke JF, English C, Mattison DR, Becker RA (2014). "Relationships of chemical concentrations in maternal and cord blood: a review of available data." *Journal of Toxicology and Environmental Health, Part B*, **17**(3), 175–203. doi:10.1080/10937404.2014.884956.

Aylward LL, Hays SM, Kirman CR, Marchitti SA, Kenneke JF, English C, Mattison DR, Becker RA (2014). "Relationships of chemical concentrations in maternal and cord blood: a review of available data." *Journal of Toxicology and Environmental Health, Part B*, **17**(3), 175–203. doi:10.1080/10937404.2014.884956.

`concentration_data_Linakis2020` *Concentration data involved in Linakis 2020 vignette analysis.*

Description

These rat and human TK concentration vs. time (CvT) data are drawn from the CvTdb (Sayre et el., 2020, doi:10.1038/s4159702004551). Concentrations have all been converted to the units of uM. All data are from inhalation studies.

These rat and human TK concentration vs. time (CvT) data are drawn from the CvTdb (Sayre et el., 2020). Concentrations have all been converted to the units of uM. All data are from inhalation studies.

Usage

```
concentration_data_Linakis2020

concentration_data_Linakis2020
```

Format

A data.frame containing 2142 rows and 16 columns.

A data.frame containing 2142 rows and 16 columns.

Details

Abbreviations used for sampling matrix: BL : blood EEB : end-exhaled breath MEB : mixed exhaled breath VBL : venous blood ABL : arterial blood EB : unspecified exhaled breath sample (assumed to be EEB) PL: plasma +W with work/exercise

Column Name	Description
PREFERRED_NAME	Substance preferred name
DTXSID	Identifier for CompTox Chemical Dashboard
CASRN	Chemical abstracts service registration number
AVERAGE_MASS	Substance molecular weight g/mol
DOSE DOSE_U	Inhalation exposure concentration in parts per million
EXP_LENGTH	Duration of inhalation exposur
TIME	Measurment time
TIME_U	Time units for all times reported
CONC_SPECIES	Species for study
SAMPLING_MATRIX	Matrix analyzed
SOURCE_CVT	Data source identifier within CvTdb
ORIG_CONC_U	Original reported units for concentration
CONCENTRATION	Analyte concentration in uM units

Abbreviations used for sampling matrix: BL : blood EEB : end-exhaled breath MEB : mixed exhaled breath VBL : venous blood ABL : arterial blood EB : unspecified exhaled breath sample (assumed to be EEB) PL: plasma +W with work/exercise

Column Name	Description
PREFERRED_NAME	Substance preferred name
DTXSID	Identifier for CompTox Chemical Dashboard
CASRN	Chemical abstracts service registration number
AVERAGE_MASS	Substance molecular weight g/mol
DOSE DOSE_U	Inhalation exposure concentration in parts per million
EXP_LENGTH	Duration of inhalation exposur
TIME	Measurment time
TIME_U	Time units for all times reported
CONC_SPECIES	Species for study
SAMPLING_MATRIX	Matrix analyzed
SOURCE_CVT	Data source identifier within CvTdb
ORIG_CONC_U	Original reported units for concentration
CONCENTRATION	Analyte concentration in uM units

Author(s)

Matt Linakis

Source

Matt Linakis

Matt Linakis

References

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y. Sayre RR, Wambaugh JF, Grulke CM (2020). "Database of pharmacokinetic time-series data and parameters for 144 environmental chemicals." *Scientific data*, **7**(1), 122. doi:10.1038/s4159702004551.

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y. Sayre RR, Wambaugh JF, Grulke CM (2020). "Database of pharmacokinetic time-series data and parameters for 144 environmental chemicals." *Scientific data*, **7**(1), 122. doi:10.1038/s4159702004551.

dermal.nonvolatilechems

Non-volatile chemicals with ToxCast data Meade et al. (submitted) performed in vitro-in vivo extrapolation for dermal exposures assuming 8 hours of exposure via hands submerged in a liquid with 1 ppm of chemical. These were the chemicals analyzed.

Description

Non-volatile chemicals with ToxCast data Meade et al. (submitted) performed in vitro-in vivo extrapolation for dermal exposures assuming 8 hours of exposure via hands submerged in a liquid with 1 ppm of chemical. These were the chemicals analyzed.

Non-volatile chemicals with ToxCast data Meade et al. (submitted) performed in vitro-in vivo extrapolation for dermal exposures assuming 8 hours of exposure via hands submerged in a liquid with 1 ppm of chemical. These were the chemicals analyzed.

Usage

```
dermal.nonvolatilechems
```

```
dermal.nonvolatilechems
```

Format

data.frame

data.frame

Source

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

References

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

`dermal.toxcast`	*Chemicals with ToxCast data for Meade et al. (submitted) chemicals Meade et al. (submitted) performed in vitro-in vivo extrapolation for dermal exposures assuming 8 hours of exposure via hands submerged in a liquid with 1 ppm of chemical. These are the ToxCast in vitro screening data for those chemicals.*

Description

Chemicals with ToxCast data for Meade et al. (submitted) chemicals Meade et al. (submitted) performed in vitro-in vivo extrapolation for dermal exposures assuming 8 hours of exposure via hands submerged in a liquid with 1 ppm of chemical. These are the ToxCast in vitro screening data for those chemicals.

Usage

```
dermal.toxcast
```

Format

data.frame

Source

https://www.epa.gov/comptox-tools/exploring-toxcast-data

References

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

`dermalCvT2025`	*Toxicokinetic concentration vs. time (CvT) data for Meade et al. (submitted) chemicals Meade et al. (submitted) evaluated a generic PBTK model for dermal exposure using in vivo CvT data curated from the literature. These data will eventually be incorporated in the the CvTdb (Sayre et al., 2020,* Rhrefhttps://doi.org/10.1038/s41597-020-0455-1doi:10.1038/s4159702004551*).*

Description

Toxicokinetic concentration vs. time (CvT) data for Meade et al. (submitted) chemicals Meade et al. (submitted) evaluated a generic PBTK model for dermal exposure using in vivo CvT data curated from the literature. These data will eventually be incorporated in the the CvTdb (Sayre et al., 2020, doi:10.1038/s4159702004551).

Usage

```
dermalCvT2025
```

Format

data.frame

Source

Sayre RR, Wambaugh JF, Grulke CM (2020). "Database of pharmacokinetic time-series data and parameters for 144 environmental chemicals." *Scientific data*, **7**(1), 122. doi:10.1038/s41597020-04551.

References

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted. Sayre RR, Wambaugh JF, Grulke CM (2020). "Database of pharmacokinetic time-series data and parameters for 144 environmental chemicals." *Scientific data*, **7**(1), 122. doi:10.1038/s4159702004551.

Dimitrijevic.IVD *Dimitrijevic et al. (2022)In Vitro Cellular and Nominal Concentration*

Description

Dimitrijevic et al. (2022)In Vitro Cellular and Nominal Concentration

Usage

```
Dimitrijevic.IVD
```

Format

data.table and data.frame

Author(s)

Jon Arnot

References

Dimitrijevic D, Fabian E, Nicol B, Funk-Weyer D, Landsiedel R (2022). "Toward realistic dosimetry in vitro: determining effective concentrations of test substances in cell culture and their prediction by an in silico mass balance model." *Chemical Research in Toxicology*, **35**(11), 1962–1973.

`fetalpcs` *Fetal Partition Coefficients*

Description

Partition coefficients were measured for tissues, including placenta, in vitro by Csanady et al. (2002) for Bisphenol A and Diadzen. Curley et al. (1969) measured the concentration of a variety of pesticides in the cord blood of newborns and in the tissues of infants that were stillborn.

Partition coefficients were measured for tissues, including placenta, in vitro by Csanady et al. (2002) for Bisphenol A and Diadzen. Curley et al. (1969) measured the concentration of a variety of pesticides in the cord blood of newborns and in the tissues of infants that were stillborn.

Usage

```
fetalpcs
```

```
fetalpcs
```

Format

data.frame

data.frame

Details

Three of the chemicals studied by Curley et al. (1969) were modeled by Weijs et al. (2013) using the same partition coefficients for mother and fetus. The values used represented "prior knowledge" summarizing the available literature.

Three of the chemicals studied by Curley et al. (1969) were modeled by Weijs et al. (2013) using the same partition coefficients for mother and fetus. The values used represented "prior knowledge" summarizing the available literature.

Source

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

References

Csanady G, Oberste-Frielinghaus H, Semder B, Baur C, Schneider K, Filser J (2002). "Distribution and unspecific protein binding of the xenoestrogens bisphenol A and daidzein." *Archives of toxicology*, **76**(5-6), 299–305. doi:10.1007/s0020400203395. Curley A, Copeland MF, Kimbrough RD

(1969). "Chlorinated Hydrocarbon Insecticides in Organs of Stillborn and Blood of Newborn Babies." *Archives of Environmental Health: An International Journal*, **19**(5), 628–632. doi:10.1080/00039896.1969.10666901. PMID: 4187028, https://doi.org/10.1080/00039896.1969.10666901. Weijs L, Yang RS, Das K, Covaci A, Blust R (2013). "Application of Bayesian population physiologically based pharmacokinetic (PBPK) modeling and Markov chain Monte Carlo simulations to pesticide kinetics studies in protected marine mammals: DDT, DDE, and DDD in harbor porpoises." *Environmental science & technology*, **47**(9), 4365–4374. doi:10.1021/es400386a.

Csanady G, Oberste-Frielinghaus H, Semder B, Baur C, Schneider K, Filser J (2002). "Distribution and unspecific protein binding of the xenoestrogens bisphenol A and daidzein." *Archives of toxicology*, **76**(5-6), 299–305. doi:10.1007/s0020400203395. Curley A, Copeland MF, Kimbrough RD (1969). "Chlorinated Hydrocarbon Insecticides in Organs of Stillborn and Blood of Newborn Babies." *Archives of Environmental Health: An International Journal*, **19**(5), 628–632. doi:10.1080/00039896.1969.10666901. PMID: 4187028, https://doi.org/10.1080/00039896.1969.10666901. Weijs L, Yang RS, Das K, Covaci A, Blust R (2013). "Application of Bayesian population physiologically based pharmacokinetic (PBPK) modeling and Markov chain Monte Carlo simulations to pesticide kinetics studies in protected marine mammals: DDT, DDE, and DDD in harbor porpoises." *Environmental science & technology*, **47**(9), 4365–4374. doi:10.1021/es400386a.

`Frank2018invivo` *Literature In Vivo Data on Doses Causing Neurological Effects*

Description

Studies were selected from Table 1 in Mundy et al., 2015, as the studies in that publication were cited as examples of compounds with evidence for developmental neurotoxicity. There were sufficient in vitro toxicokinetic data available for this package for only 6 of the 42 chemicals.

Studies were selected from Table 1 in Mundy et al., 2015, as the studies in that publication were cited as examples of compounds with evidence for developmental neurotoxicity. There were sufficient in vitro toxicokinetic data available for this package for only 6 of the 42 chemicals.

Usage

```
Frank2018invivo
```

```
Frank2018invivo
```

Format

A data.frame containing 14 rows and 16 columns.

A data.frame containing 14 rows and 16 columns.

Author(s)

Timothy J. Shafer

References

Frank, Christopher L., et al. "Defining toxicological tipping points in neuronal network development." Toxicology and Applied Pharmacology 354 (2018): 81-93.

Mundy, William R., et al. "Expanding the test set: Chemicals with potential to disrupt mammalian brain development." Neurotoxicology and Teratology 52 (2015): 25-35.

Frank, Christopher L., et al. "Defining toxicological tipping points in neuronal network development." Toxicology and Applied Pharmacology 354 (2018): 81-93.

Mundy, William R., et al. "Expanding the test set: Chemicals with potential to disrupt mammalian brain development." Neurotoxicology and Teratology 52 (2015): 25-35.

---

howgate *Howgate et al. (2006)*

Description

This data set is only used in Vignette 5.

This data set is only used in Vignette 5.

Usage

```
howgate
```

```
howgate
```

Format

A data.table containing 24 rows and 11 columns.

A data.table containing 24 rows and 11 columns.

Author(s)

Caroline Ring

References

Howgate, E. M., et al. "Prediction of in vivo drug clearance from in vitro data. I: impact of inter-individual variability." Xenobiotica 36.6 (2006): 473-497.

Howgate, E. M., et al. "Prediction of in vivo drug clearance from in vitro data. I: impact of inter-individual variability." Xenobiotica 36.6 (2006): 473-497.

huh2011	*Huh et al. 2011 Huh et al. (2011) (Rhrefhttps://doi.org/10.3109/00498254.2011.598582doi:10.3109/00498254.2011.598582) provided interspecies allometric scaling parameters for whole body clearance for a a variety of pharmaceuticals.*

Description

Huh et al. 2011 Huh et al. (2011) (doi:10.3109/00498254.2011.598582) provided interspecies allometric scaling parameters for whole body clearance for a a variety of pharmaceuticals.

Usage

```
huh2011
```

Format

data.frame

Source

Wambaugh et al., Applying High Throughput Toxicokinetics (HTTK) to Per- and Polyfluoro Alkyl Substances (PFAS), submitted

References

Huh Y, Smith DE, Rose Feng M (2011). "Interspecies scaling and prediction of human clearance: comparison of small-and macro-molecule drugs." *Xenobiotica*, **41**(11), 972–987.

johnson	*Johnson et al. (2006)*

Description

This data set is only used in Vignette 5.

This data set is only used in Vignette 5.

Usage

```
johnson
```

```
johnson
```

Format

A data.table containing 60 rows and 11 columns.

A data.table containing 60 rows and 11 columns.

Author(s)

Caroline Ring

References

Johnson, Trevor N., Amin Rostami-Hodjegan, and Geoffrey T. Tucker. "Prediction of the clearance of eleven drugs and associated variability in neonates, infants and children." Clinical pharmacokinetics 45.9 (2006): 931-956.

Johnson, Trevor N., Amin Rostami-Hodjegan, and Geoffrey T. Tucker. "Prediction of the clearance of eleven drugs and associated variability in neonates, infants and children." Clinical pharmacokinetics 45.9 (2006): 931-956.

`meade2025` *Simulation outputs from Meade et al. (submitted) Meade et al. (submitted) performed generic PBTK simulations for dermal exposure under a variety of assumptions. Although the code to recreate these simulations is provided, it is time-intensive. The 2025 outputs from the simulations are stored in this list of data.frames.*

Description

Simulation outputs from Meade et al. (submitted) Meade et al. (submitted) performed generic PBTK simulations for dermal exposure under a variety of assumptions. Although the code to recreate these simulations is provided, it is time-intensive. The 2025 outputs from the simulations are stored in this list of data.frames.

Usage

```
meade2025
```

Format

list

Source

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

References

Meade et al., Incorporating a dermal absorption route into high throughput toxicokinetic modeling, submitted.

`metabolism_data_Linakis2020` *Metabolism data involved in Linakis et al. 2020 (*R*hrefhttps://doi.org/10.1038/s41370-020-0238-ydoi:10.1038/s413700200238y) vignette analysis.*

Description

Metabolism data involved in Linakis et al. 2020 (doi:10.1038/s413700200238y) vignette analysis.

Metabolism data involved in Linakis 2020 vignette analysis.

Usage

```
metabolism_data_Linakis2020
```

```
metabolism_data_Linakis2020
```

Format

A data.frame containing x rows and y columns.

A data.frame containing x rows and y columns.

Author(s)

Matt Linakis

Source

Matt Linakis

Matt Linakis

References

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

Obach2008 *Published Pharmacokinetic Parameters from Obach et al. 2008*

Description

This data set is used in Vignette 4 for steady state concentration.

This data set is used in Vignette 4 for steady state concentration.

Usage

```
Obach2008
```

```
Obach2008
```

Format

A data.frame containing 670 rows and 8 columns.

A data.frame containing 670 rows and 8 columns.

References

Obach, R. Scott, Franco Lombardo, and Nigel J. Waters. "Trend analysis of a database of intravenous pharmacokinetic parameters in humans for 670 drug compounds." Drug Metabolism and Disposition 36.7 (2008): 1385-1405.

Obach, R. Scott, Franco Lombardo, and Nigel J. Waters. "Trend analysis of a database of intravenous pharmacokinetic parameters in humans for 670 drug compounds." Drug Metabolism and Disposition 36.7 (2008): 1385-1405.

onlyp *NHANES Exposure Data*

Description

This data set is only used in Vignette 6.

This data set is only used in Vignette 6.

Usage

```
onlyp
```

```
onlyp
```

Format

A data.table containing 1060 rows and 5 columns.

A data.table containing 1060 rows and 5 columns.

Author(s)

Caroline Ring

References

Wambaugh, John F., et al. "High throughput heuristics for prioritizing human exposure to environmental chemicals." Environmental science & technology 48.21 (2014): 12760-12767.

Wambaugh, John F., et al. "High throughput heuristics for prioritizing human exposure to environmental chemicals." Environmental science & technology 48.21 (2014): 12760-12767.

---

pc.data *Partition Coefficient Data*

Description

Measured rat in vivo partition coefficients and data for predicting them.

Measured rat in vivo partition coefficients and data for predicting them.

Usage

```
pc.data
```

```
pc.data
```

Format

A data.frame.

A data.frame.

Author(s)

Jimena Davis and Robert Pearce

References

Schmitt W (2008). “General approach for the calculation of tissue to plasma partition coefficients.” *Toxicology in vitro*, **22**(2), 457–467. doi:10.1016/j.tiv.2007.09.010.

Schmitt W (2008). “Corrigendum to:’General approach for the calculation of tissue to plasma partition coefficients’[Toxicology in Vitro 22 (2008) 457–467].” *Toxicology in Vitro*, **22**(6), 1666. doi:10.1016/j.tiv.2008.04.020.

Poulin, P. and F.P. Theil, A priori prediction of tissue: plasma partition coefficients of drugs to facilitate the use of physiologically based pharmacokinetic models in drug discovery. Journal of pharmaceutical sciences, 2000. 89(1): p. 16-35.

Rodgers, T. and M. Rowland, Physiologically based pharmacokinetic modelling 2: predicting the tissue distribution of acids, very weak bases, neutrals and zwitterions. Journal of pharmaceutical sciences, 2006. 95(6): p. 1238-1257.

Rodgers, T., D. Leahy, and M. Rowland, Physiologically based pharmacokinetic modeling 1: predicting the tissue distribution of moderate-to-strong bases. Journal of pharmaceutical sciences, 2005. 94(6): p. 1259-1276.

Rodgers, T., D. Leahy, and M. Rowland, Tissue distribution of basic drugs: Accounting for enantiomeric, compound and regional differences amongst beta-blocking drugs in rat. Journal of pharmaceutical sciences, 2005. 94(6): p. 1237-1248.

Gueorguieva, I., et al., Development of a whole body physiologically based model to characterise the pharmacokinetics of benzodiazepines. 1: Estimation of rat tissue-plasma partition ratios. Journal of pharmacokinetics and pharmacodynamics, 2004. 31(4): p. 269-298.

Poulin, P., K. Schoenlein, and F.P. Theil, Prediction of adipose tissue: plasma partition coefficients for structurally unrelated drugs. Journal of pharmaceutical sciences, 2001. 90(4): p. 436-447.

Bjorkman, S., Prediction of the volume of distribution of a drug: which tissue-plasma partition coefficients are needed? Journal of pharmacy and pharmacology, 2002. 54(9): p. 1237-1245.

Yun YE, Edginton AN (2013). "Correlation-based prediction of tissue-to-plasma partition coefficients using readily available input parameters." *Xenobiotica*, **43**(10), 839–852. doi:10.3109/00498254.2013.770182.

Uchimura, T., et al., Prediction of human blood-to-plasma drug concentration ratio. Biopharmaceutics & drug disposition, 2010. 31(5-6): p. 286-297.

Schmitt W (2008). "General approach for the calculation of tissue to plasma partition coefficients." *Toxicology in vitro*, **22**(2), 457–467. doi:10.1016/j.tiv.2007.09.010.

Schmitt W (2008). "Corrigendum to:'General approach for the calculation of tissue to plasma partition coefficients'[Toxicology in Vitro 22 (2008) 457–467]." *Toxicology in Vitro*, **22**(6), 1666. doi:10.1016/j.tiv.2008.04.020.

Poulin, P. and F.P. Theil, A priori prediction of tissue: plasma partition coefficients of drugs to facilitate the use of physiologically based pharmacokinetic models in drug discovery. Journal of pharmaceutical sciences, 2000. 89(1): p. 16-35.

Rodgers, T. and M. Rowland, Physiologically based pharmacokinetic modelling 2: predicting the tissue distribution of acids, very weak bases, neutrals and zwitterions. Journal of pharmaceutical sciences, 2006. 95(6): p. 1238-1257.

Rodgers, T., D. Leahy, and M. Rowland, Physiologically based pharmacokinetic modeling 1: predicting the tissue distribution of moderate-to-strong bases. Journal of pharmaceutical sciences, 2005. 94(6): p. 1259-1276.

Rodgers, T., D. Leahy, and M. Rowland, Tissue distribution of basic drugs: Accounting for enantiomeric, compound and regional differences amongst beta-blocking drugs in rat. Journal of pharmaceutical sciences, 2005. 94(6): p. 1237-1248.

Gueorguieva, I., et al., Development of a whole body physiologically based model to characterise the pharmacokinetics of benzodiazepines. 1: Estimation of rat tissue-plasma partition ratios. Journal of pharmacokinetics and pharmacodynamics, 2004. 31(4): p. 269-298.

Poulin, P., K. Schoenlein, and F.P. Theil, Prediction of adipose tissue: plasma partition coefficients for structurally unrelated drugs. Journal of pharmaceutical sciences, 2001. 90(4): p. 436-447.

Bjorkman, S., Prediction of the volume of distribution of a drug: which tissue-plasma partition coefficients are needed? Journal of pharmacy and pharmacology, 2002. 54(9): p. 1237-1245.

Yun YE, Edginton AN (2013). "Correlation-based prediction of tissue-to-plasma partition coefficients using readily available input parameters." *Xenobiotica*, **43**(10), 839–852. doi:10.3109/00498254.2013.770182.

Uchimura, T., et al., Prediction of human blood-to-plasma drug concentration ratio. Biopharmaceutics & drug disposition, 2010. 31(5-6): p. 286-297.

`pharma` *DRUGS\NORMAN: Pharmaceutical List with EU, Swiss, US Consumption Data*

Description

SWISSPHARMA is a list of pharmaceuticals with consumption data from Switzerland, France, Germany and the USA, used for a suspect screening/exposure modelling approach described in Singer et al 2016, (doi:10.1021/acs.est.5b03332). The original data is available on the NORMAN Suspect List Exchange.

SWISSPHARMA is a list of pharmaceuticals with consumption data from Switzerland, France, Germany and the USA, used for a suspect screening/exposure modelling approach described in Singer et al 2016, DOI: 10.1021/acs.est.5b03332. The original data is available on the NORMAN Suspect List Exchange.

Usage

```
pharma
```

```
pharma
```

Format

An object of class `matrix` (inherits from `array`) with 14 rows and 954 columns.

An object of class `matrix` (inherits from `array`) with 14 rows and 954 columns.

Source

https://comptox.epa.gov/dashboard/chemical_lists/swisspharma

https://comptox.epa.gov/dashboard/chemical_lists/swisspharma

References

Singer HP, Wossner AE, McArdell CS, Fenner K (2016). "Rapid screening for exposure to "non-target" pharmaceuticals from wastewater effluents by combining HRMS-based suspect screening and exposure modeling." *Environmental Science & Technology*, **50**(13), 6698–6707.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

`pksim.pcs` *Partition Coefficients from PK-Sim*

Description

Dallmann et al. (2018) made use of PK-Sim to predict chemical- and tissue- specific partition coefficients. The methods include both the default PK-Sim approach and PK-Sim Standard and Rodgers & Rowland (2006).

Dallmann et al. (2018) made use of PK-Sim to predict chemical- and tissue- specific partition coefficients. The methods include both the default PK-Sim approach and PK-Sim Standard and Rodgers & Rowland (2006).

Usage

```
pksim.pcs
```

```
pksim.pcs
```

Format

data.frame

data.frame

Source

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

References

Dallmann A, Ince I, Coboeken K, Eissing T, Hempel G (2018). "A physiologically based pharmacokinetic model for pregnant women to predict the pharmacokinetics of drugs metabolized via several enzymatic pathways." *Clinical pharmacokinetics*, **57**(6), 749–768. doi:10.1007/s40262017-05945.

Dallmann A, Ince I, Coboeken K, Eissing T, Hempel G (2018). "A physiologically based pharmacokinetic model for pregnant women to predict the pharmacokinetics of drugs metabolized via several enzymatic pathways." *Clinical pharmacokinetics*, **57**(6), 749–768. doi:10.1007/s40262017-05945.

`pregnonpregaucs` *AUCs for Pregnant and Non-Pregnant Women*

Description

Dallmann et al. (2018) includes compiled literature descriptions of toxicokinetic summary statistics, including time-integrated plasma concentrations (area under the curve or AUC) for drugs administered to a sample of subjects including both pregnant and non-pregnant women. The circumstances of the dosing varied slightly between drugs and are summarized in the table.

Dallmann et al. (2018) includes compiled literature descriptions of toxicokinetic summary statistics, including time-integrated plasma concentrations (area under the curve or AUC) for drugs administered to a sample of subjects including both pregnant and non-pregnant women. The circumstances of the dosing varied slightly between drugs and are summarized in the table.

Usage

```
pregnonpregaucs
```

```
pregnonpregaucs
```

Format

data.frame

data.frame

Source

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

References

Dallmann A, Ince I, Coboeken K, Eissing T, Hempel G (2018). "A physiologically based pharmacokinetic model for pregnant women to predict the pharmacokinetics of drugs metabolized via several enzymatic pathways." *Clinical pharmacokinetics*, **57**(6), 749–768. doi:10.1007/s40262017-05945.

Dallmann A, Ince I, Coboeken K, Eissing T, Hempel G (2018). "A physiologically based pharmacokinetic model for pregnant women to predict the pharmacokinetics of drugs metabolized via several enzymatic pathways." *Clinical pharmacokinetics*, **57**(6), 749–768. doi:10.1007/s40262017-05945.

`Scherer2025.IVD` *Literature Measurements of In Vitro Cellular and Nominal Concentration*

Description

Literature Measurements of In Vitro Cellular and Nominal Concentration

Usage

```
Scherer2025.IVD
```

Format

data.table and data.frame

Author(s)

Meredith Scherer

`supptab1_Linakis2020` *Supplementary output from Linakis 2020 vignette analysis.*

Description

Supplementary output from Linakis 2020 vignette analysis.

Supplementary output from Linakis 2020 vignette analysis.

Usage

```
supptab1_Linakis2020
```

```
supptab1_Linakis2020
```

Format

A data.frame containing x rows and y columns.

A data.frame containing x rows and y columns.

Author(s)

Matt Linakis

Source

Matt Linakis

Matt Linakis

References

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

---

supptab2_Linakis2020 *More supplementary output from Linakis 2020 vignette analysis.*

Description

More supplementary output from Linakis 2020 vignette analysis.

More supplementary output from Linakis 2020 vignette analysis.

Usage

```
supptab2_Linakis2020
```

```
supptab2_Linakis2020
```

Format

A data.frame containing x rows and y columns.

A data.frame containing x rows and y columns.

Author(s)

Matt Linakis

Source

Matt Linakis

Matt Linakis

References

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

Linakis MW, Sayre RR, Pearce RG, Sfeir MA, Sipes NS, Pangburn HA, Gearhart JM, Wambaugh JF (2020). "Development and evaluation of a high-throughput inhalation model for organic chemicals." *Journal of exposure science & environmental epidemiology*, **30**(5), 866–877. doi:10.1038/s41370-0200238y.

`thyroid.ac50s` *ToxCast thyroid-related bioactivity data*

Description

Truong et al. 2025 uses ToxCast data for 4 thyroid-related assay endpoints concerning inhibition of deiodinases ("DIO1", "DIO2", "DIO3", and "IYD") and identified 120 priority chemicals with activity for at least one deiodinase. These 120 chemicals were curated after assessment for target selectivity and assay interference.

Usage

```
thyroid.ac50s
```

Format

data.table and data.frame

Details

The AC50s (in uM) for each of the 120 chemicals were retrieved from ToxCast invitrodb v3.5 and are used in the "Full Human Gestational IVIVE" vignette.

References

Truong KT, Wambaugh JF, Kapraun DF, Davidson-Fritz SE, Eytcheson S, Judson RS, Paul Friedman K (2025). "Interpretation of thyroid-relevant bioactivity data for comparison to in vivo exposures: A prioritization approach for putative chemical inhibitors of in vitro deiodinase activity." *Toxicology*. doi:10.1016/j.tox.2025.154157.

truong25.seem3 *SEEM3 Example Data for Truong et al. 2025*

Description

We can grab SEEM daily intake rate predictions already in RData format from https://github.com/HumanExposure/SEEM3RF
Download the file chem.preds-2018-11-28.RData

Usage

```
truong25.seem3
```

Format

data.table and data.frame

Details

We do not have the space to distribute all the SEEM predictions within this R package, but we can give you our "Full Human Gestational IVIVE" example chemicals.

References

Truong KT, Wambaugh JF, Kapraun DF, Davidson-Fritz SE, Eytcheson S, Judson RS, Paul Friedman K (2025). "Interpretation of thyroid-relevant bioactivity data for comparison to in vivo exposures: A prioritization approach for putative chemical inhibitors of in vitro deiodinase activity." *Toxicology*. doi:10.1016/j.tox.2025.154157.

Ring CL, Arnot JA, Bennett DH, Egeghy PP, Fantke P, Huang L, Isaacs KK, Jolliet O, Phillips KA, Price PS, others (2018). "Consensus modeling of median chemical intake for the US population based on predictions of exposure pathways." *Environmental science & technology*, **53**(2), 719–732. doi:10.1021/acs.est.8b04056.

wallis2023 *Wallis et al. 2023 Wallis et al. (2023) (Rhrefhttps://doi.org/10.1021/acs.est.2c08241doi:10.1021/acs.est.2c08241) estimated the human toxicokinetic half-lives for a range of per- and poly-fluorinated alkyl substances (PFAS).*

Description

Wallis et al. 2023 Wallis et al. (2023) (doi:10.1021/acs.est.2c08241) estimated the human toxicokinetic half-lives for a range of per- and poly-fluorinated alkyl substances (PFAS).

Usage

```
wallis2023
```

Format

data.frame

Source

Wambaugh et al., Applying High Throughput Toxicokinetics (HTTK) to Per- and Polyfluoro Alkyl Substances (PFAS), submitted

References

Wallis DJ, Kotlarz N, Knappe DR, Collier DN, Lea CS, Reif D, McCord J, Strynar M, DeWitt JC, Hoppin JA (2023). "Estimation of the half-lives of recently detected per-and polyfluorinated alkyl ethers in an exposed community." *Environmental science & technology*, **57**(41), 15348–15355.

`wambaugh2019` *in vitro Toxicokinetic Data from Wambaugh et al. (2019)*

Description

These data are the new HTTK in vitro data for chemicals reported in Wambaugh et al. (2019) (doi:10.1093/toxsci/kfz205). They are the processed values used to make the figures in that manuscript. These data summarize the results of Bayesian analysis of the in vitro toxicokinetic experiments conducted by Cyprotex to characterize fraction unbound in the presence of pooled human plasma protein and the intrinsic hepatic clearance of the chemical by pooled human hepatocytes.

These data are the new HTTK in vitro data for chemicals reported in Wambaugh et al. (2019) They are the processed values used to make the figures in that manuscript. These data summarize the results of Bayesian analysis of the in vitro toxicokinetic experiments conducted by Cyprotex to characterize fraction unbound in the presence of pooled human plasma protein and the intrnsic hepatic clearance of the chemical by pooled human hepatocytes.

Usage

```
wambaugh2019
```

```
wambaugh2019
```

Format

A data frame with 496 rows and 17 variables:

Compound The name of the chemical

CAS The Chemical Abstracts Service Registry Number

Human.Clint Median of Bayesian credible interval for intrinsic hepatic clearance (uL/min/million hepatocytes)]

Human.Clint.pValue Probability that there is no clearance

Human.Funbound.plasma Median of Bayesian credibl interval for fraction of chemical free in the presence of plasma

pKa_Accept pH(s) at which hydrogen acceptor sites (if any) are at equilibrium

pKa_Donor pH(s) at which hydrogne donor sites (if any) are at equilibrium

DSSTox_Substance_Id Identifier for CompTox Chemical Dashboard

SMILES Simplified Molecular-Input Line-Entry System structure description

Human.Clint.Low95 Lower 95th percentile of Bayesian credible interval for intrinsic hepatic clearance (uL/min/million hepatocytes)

Human.Clint.High95 Uppper 95th percentile of Bayesian credible interval for intrinsic hepatic clearance (uL/min/million hepatocytes)

Human.Clint.Point Point estimate of intrinsic hepatic clearance (uL/min/million hepatocytes)

Human.Funbound.plasma.Low95 Lower 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma

Human.Funbound.plasma.High95 Upper 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma

Human.Funbound.plasma.Point Point estimate of the fraction of chemical free in the presence of plasma

MW Molecular weight (Daltons)

logP log base ten of octanol:water partiion coefficient

A data frame with 496 rows and 17 variables:

Compound The name of the chemical

CAS The Chemical Abstracts Service Registry Number

Human.Clint Median of Bayesian credible interval for intrinsic hepatic clearance (uL/min/million hepatocytes)]

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Human.Clint.Point Point estimate of intrinsic hepatic clearance (uL/min/million hepatocytes)

Human.Funbound.plasma.Low95 Lower 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma

Human.Funbound.plasma.High95 Upper 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma

Human.Funbound.plasma.Point Point estimate of the fraction of chemical free in the presence of plasma

MW Molecular weight (Daltons)

logP log base ten of octanol:water partiion coefficient

Author(s)

John Wambaugh

Source

Wambaugh et al. (2019)

Wambaugh et al. (2019)

References

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

`wambaugh2019.nhanes` *NHANES Chemical Intake Rates for chemicals in Wambaugh et al. (2019)*

Description

These data are a subset of the Bayesian inferences reported by Ring et al. (2017) (doi:10.1016/j.envint.2017.06.004) from the U.S. Centers for Disease Control and Prevention (CDC) National Health and Nutrition Examination Survey (NHANES). They reflect the population median intake rate (mg/kg body weight/day), with uncertainty.

These data are a subset of the Bayesian inferrences reported by Ring et al. (2017) from the U.S. Centers for Disease Control and Prevention (CDC) National Health and Nutrition Examination Survey (NHANES). They reflect the populaton median intake rate (mg/kg body weight/day), with uncertainty.

Usage

```
wambaugh2019.nhanes
```

```
wambaugh2019.nhanes
```

Format

A data frame with 20 rows and 4 variables:

lP The median of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

lP.min The lower 95th percentile of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

lP.max The upper 95th percentile of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

CASRN The Chemical Abstracts Service Registry Number

A data frame with 20 rows and 4 variables:

lP The median of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

lP.min The lower 95th percentile of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

lP.max The upper 95th percentile of the Bayesian credible interval for median population intake rate (mg/kg bodyweight/day)

CASRN The Chemical Abstracts Service Registry Number

Author(s)

John Wambaugh

Source

Wambaugh et al. (2019)

Wambaugh et al. (2019)

References

Ring CL, Pearce RG, Setzer RW, Wetmore BA, Wambaugh JF (2017). "Identifying populations sensitive to environmental chemicals by simulating toxicokinetic variability." *Environment International*, **106**, 105–118. doi:10.1016/j.envint.2017.06.004.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

Ring CL, Pearce RG, Setzer RW, Wetmore BA, Wambaugh JF (2017). "Identifying populations sensitive to environmental chemicals by simulating toxicokinetic variability." *Environment International*, **106**, 105–118. doi:10.1016/j.envint.2017.06.004.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

wambaugh2019.raw *Raw Bayesian in vitro Toxicokinetic Data Analysis from Wambaugh et al. (2019)*

Description

These data are the new HTTK in vitro data for chemicals reported in Wambaugh et al. (2019) They are the output of different Bayesian models evaluated to compare using a single protein concentration vs. the new three concentration titration protocol. These data summarize the results of Bayesian analysis of the in vitro toxicokinetic experiments conducted by Cyprotex to characterize fraction unbound in the presence of pooled human plasma protein and the intrnsic hepatic clearance of the chemical by pooled human hepatocytes. This file includes replicates (diferent CompoundName id's but same chemical')

Usage

```
wambaugh2019.raw
```

Format

A data frame with 530 rows and 28 variables:

DTXSID Identifier for CompTox Chemical Dashboard

Name The name of the chemical

CAS The Chemical Abstracts Service Registry Number

CompoundName Sample name provided by EPA to Cyprotex

Fup.point Point estimate of the fraction of chemical free in the presence of plasma

Base.Fup.Med Median of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of 100 physiological plasma protein data only (base model)

Base.Fup.Low Lower 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of 100 physiological plasma protein data only (base model)

Base.Fup.High Upper 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of 100 physiological plasma protein data only (base model)

Affinity.Fup.Med Median of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of protein titration protocol data (affinity model)

Affinity.Fup.Low Lower 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of protein titration protocol data (affinity model)

Affinity.Fup.High Upper 95th percentile of Bayesian credible interval for fraction of chemical free in the presence of plasma for analysis of protein titration protocol data (affinity model)

Affinity.Kd.Med Median of Bayesian credible interval for protein binding affinity from analysis of protein titration protocol data (affinity model)

Affinity.Kd.Low Lower 95th percentile of Bayesian credible interval for protein binding affinity from analysis of protein titration protocol data (affinity model)

Affinity.Kd.High Upper 95th percentile of Bayesian credible interval for protein binding affinity from analysis of protein titration protocol data (affinity model)

Decreases.Prob Probability that the chemical concentration decreased systematiclally during hepatic clearance assay.

Saturates.Prob Probability that the rate of chemical concentration decrease varied between the 1 and 10 uM hepatic clearance experiments.

Slope.1uM.Median Estimated slope for chemcial concentration decrease in the 1 uM hepatic clearance assay.

Slope.10uM.Median Estimated slope for chemcial concentration decrease in the 10 uM hepatic clearance assay.

CLint.1uM.Median Median of Bayesian credible interval for intrinsic hepatic clearance at 1 uM initital chemical concentration (uL/min/million hepatocytes)]

CLint.1uM.Low95th Lower 95th percentile of Bayesian credible interval for intrinsic hepatic clearance at 1 uM initital chemical concentration (uL/min/million hepatocytes)

CLint.1uM.High95th Uppper 95th percentile of Bayesian credible interval for intrinsic hepatic clearance at 1 uM initital chemical concentration(uL/min/million hepatocytes)

CLint.10uM.Median Median of Bayesian credible interval for intrinsic hepatic clearance at 10 uM initital chemical concentration (uL/min/million hepatocytes)]

CLint.10uM.Low95th Lower 95th percentile of Bayesian credible interval for intrinsic hepatic clearance at 10 uM initital chemical concentration (uL/min/million hepatocytes)

CLint.10uM.High95th Uppper 95th percentile of Bayesian credible interval for intrinsic hepatic clearance at 10 uM initital chemical concentration(uL/min/million hepatocytes)

CLint.1uM.Point Point estimate of intrinsic hepatic clearance (uL/min/million hepatocytes) for 1 uM initial chemical concentration

CLint.10uM.Point Point estimate of intrinsic hepatic clearance (uL/min/million hepatocytes) for 10 uM initial chemical concentration

Fit Classification of clearance observed

SMILES Simplified Molecular-Input Line-Entry System structure description

Author(s)

John Wambaugh

Source

Wambaugh et al. (2019)

References

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

`wambaugh2019.seem3` *ExpoCast SEEM3 Consensus Exposure Model Predictions for Chemical Intake Rates*

Description

These data are a subset of the Bayesian inferences reported by Ring et al. (2019) (doi:10.1021/acs.est.8b04056) for a consensus model of twelve exposure predictors. The predictors were calibrated based upon their ability to predict intake rates inferred National Health and Nutrition Examination Survey (NHANES). They reflect the population median intake rate (mg/kg body weight/day), with uncertainty.

These data are a subset of the Bayesian inferrences reported by Ring et al. (2019) for a consensus model of twelve exposue predictors. The predictors were calibrated based upon their ability to predict intake rates inferred National Health and Nutrition Examination Survey (NHANES). They reflect the populaton median intake rate (mg/kg body weight/day), with uncertainty.

Usage

```
wambaugh2019.seem3

wambaugh2019.seem3
```

Format

A data frame with 385 rows and 38 variables:

A data frame with 385 rows and 38 variables:

Author(s)

John Wambaugh

Source

Wambaugh et al. (2019)

Wambaugh et al. (2019)

References

Ring CL, Arnot JA, Bennett DH, Egeghy PP, Fantke P, Huang L, Isaacs KK, Jolliet O, Phillips KA, Price PS, others (2018). "Consensus modeling of median chemical intake for the US population based on predictions of exposure pathways." *Environmental science & technology*, **53**(2), 719–732. doi:10.1021/acs.est.8b04056.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

Ring CL, Arnot JA, Bennett DH, Egeghy PP, Fantke P, Huang L, Isaacs KK, Jolliet O, Phillips KA, Price PS, others (2018). "Consensus modeling of median chemical intake for the US population based on predictions of exposure pathways." *Environmental science & technology*, **53**(2), 719–732. doi:10.1021/acs.est.8b04056.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

`wambaugh2019.tox21` *Tox21 2015 Active Hit Calls (EPA)*

Description

The ToxCast and Tox21 research programs employ batteries of high-throughput assays to assess chemical bioactivity in vitro. Not every chemical is tested through every assay. Most assays are conducted in concentration response, and each corresponding assay endpoint is analyzed statistically to determine if there is a concentration-dependent response or "hit" using the ToxCast Pipeline. Most assay endpoint-chemical combinations are non-responsive. Here, only the hits are treated as potential indicators of bioactivity. This bioactivity does not have a direct toxicological interpretation. The October 2015 release (invitrodb_v2) of the ToxCast and Tox21 data were used for this analysis. This object contains just the chemicals in Wambaugh et al. (2019) and only the quantiles across all assays for the ACC.

The ToxCast and Tox21 research programs employ batteries of high-throughput assays to assess chemical bioactivity in vitro. Not every chemical is tested through every assay. Most assays are conducted in concentration response, and each corresponding assay endpoint is analyzed statistically to determine if there is a concentration-dependent response or "hit" using the ToxCast Pipeline. Most assay endpoint-chemical combinations are non-responsive. Here, only the hits are treated as potential indicators of bioactivity. This bioactivity does not have a direct toxicological interpretation. The October 2015 release (invitrodb_v2) of the ToxCast and Tox21 data were used for this analysis. This object contains just the chemicals in Wambaugh et al. (2019) and only the quantiles across all assays for the ACC.

Usage

```
wambaugh2019.tox21
```

```
wambaugh2019.tox21
```

Format

A data.table with 401 rows and 6 columns

A data.table with 401 rows and 6 columns

Author(s)

John Wambaugh

References

Kavlock R, Chandler K, Houck K, Hunter S, Judson R, Kleinstreuer N, Knudsen T, Martin M, Padilla S, Reif D, others (2012). "Update on EPA's ToxCast program: providing high throughput decision support tools for chemical risk management." *Chemical research in toxicology*, **25**(7), 1287–1302.

Tice RR, Austin CP, Kavlock RJ, Bucher JR (2013). "Improving the human hazard characterization of chemicals: a Tox21 update." *Environmental health perspectives*, **121**(7), 756–765.

Richard AM, Judson RS, Houck KA, Grulke CM, Volarath P, Thillainadarajah I, Yang C, Rathman J, Martin MT, Wambaugh JF, others (2016). "ToxCast chemical landscape: paving the road to 21st century toxicology." *Chemical research in toxicology*, **29**(8), 1225–1251.

Filer DL, Kothiya P, Setzer RW, Judson RS, Martin MT (2017). "tcpl: the ToxCast pipeline for high-throughput screening data." *Bioinformatics*, **33**(4), 618–620.

Wambaugh JF, Wetmore BA, Ring CL, Nicolas CI, Pearce RG, Honda GS, Dinallo R, Angus D, Gilbert J, Sierra T, others (2019). "Assessing toxicokinetic uncertainty and variability in risk prioritization." *Toxicological Sciences*, **172**(2), 235–251. doi:10.1093/toxsci/kfz205.

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Tice, Raymond R., et al. "Improving the human hazard characterization of chemicals: a Tox21 update." Environmental health perspectives 121.7 (2013): 756-765.

Richard, Ann M., et al. "ToxCast chemical landscape: paving the road to 21st century toxicology." Chemical research in toxicology 29.8 (2016): 1225-1251.

Filer, Dayne L., et al. "tcpl: the ToxCast pipeline for high-throughput screening data." Bioinformatics 33.4 (2016): 618-620.

Wambaugh, John F., et al. "Assessing Toxicokinetic Uncertainty and Variability in Risk Prioritization." Toxicological Sciences 172.2 (2019): 235-251.

`wang2018` *Wang et al. 2018 Wang et al. (2018) screened the blood of 75 pregnant women for the presence of environmental organic acids (EOAs) and identified mass spectral features corresponding to 453 chemical formulae of which 48 could be mapped to likely structures. Of the 48 with tentative structures the identity of six were confirmed with available chemical standards.*

Description

Wang et al. 2018 Wang et al. (2018) screened the blood of 75 pregnant women for the presence of environmental organic acids (EOAs) and identified mass spectral features corresponding to 453 chemical formulae of which 48 could be mapped to likely structures. Of the 48 with tentative structures the identity of six were confirmed with available chemical standards.

Wang et al. 2018 Wang et al. (2018) (doi:10.1289/EHP2920) screened the blood of 75 pregnant women for the presence of environmental organic acids (EOAs) and identified mass spectral features corresponding to 453 chemical formulae of which 48 could be mapped to likely structures. Of the 48 with tentative structures the identity of six were confirmed with available chemical standards.

Usage

```
wang2018
```

```
wang2018
```

Format

data.frame

data.frame

Source

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

Kapraun DF, Sfeir M, Pearce RG, Davidson-Fritz SE, Lumen A, Dallmann A, Judson RS, Wambaugh JF (2022). "Evaluation of a rapid, generic human gestational dose model." *Reproductive Toxicology*, **113**, 172–188. doi:10.1016/j.reprotox.2022.09.004.

References

Wang A, Gerona RR, Schwartz JM, Lin T, Sirota M, Morello-Frosch R, Woodruff TJ (2018). "A Suspect Screening Method for Characterizing Multiple Chemical Exposures among a Demographically Diverse Population of Pregnant Women in San Francisco." *Environmental Health Perspectives*, **126**(7), 077009. doi:10.1289/EHP2920.

Wang A, Gerona RR, Schwartz JM, Lin T, Sirota M, Morello-Frosch R, Woodruff TJ (2018). "A Suspect Screening Method for Characterizing Multiple Chemical Exposures among a Demographically Diverse Population of Pregnant Women in San Francisco." *Environmental Health Perspectives*, **126**(7), 077009. doi:10.1289/EHP2920.

`Wetmore2012` *Published toxicokinetic predictions based on in vitro data from Wetmore et al. 2012.*

Description

This data set overlaps with Wetmore.data and is used only in Vignette 4 for steady state concentration.

This data set overlaps with Wetmore.data and is used only in Vignette 4 for steady state concentration.

Usage

```
Wetmore2012
```

```
Wetmore2012
```

Format

A data.frame containing 13 rows and 15 columns.

A data.frame containing 13 rows and 15 columns.

References

Wetmore BA, Wambaugh JF, Ferguson SS, Sochaski MA, Rotroff DM, Freeman K, Clewell III HJ, Dix DJ, Andersen ME, Houck KA, others (2012). "Integration of dosimetry, exposure, and high-throughput screening data in chemical toxicity assessment." *Toxicological Sciences*, **125**(1), 157–174. doi:10.1093/toxsci/kfr254.

Wetmore BA, Wambaugh JF, Ferguson SS, Sochaski MA, Rotroff DM, Freeman K, Clewell III HJ, Dix DJ, Andersen ME, Houck KA, others (2012). "Integration of dosimetry, exposure, and high-throughput screening data in chemical toxicity assessment." *Toxicological Sciences*, **125**(1), 157–174. doi:10.1093/toxsci/kfr254.

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