Supplementary Information

Prospects for finding Junge variability-lifetime relationships for micropollutants in the Danube river.

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Contents

Monitoring stations in the Danube river as used for STREAM-EU

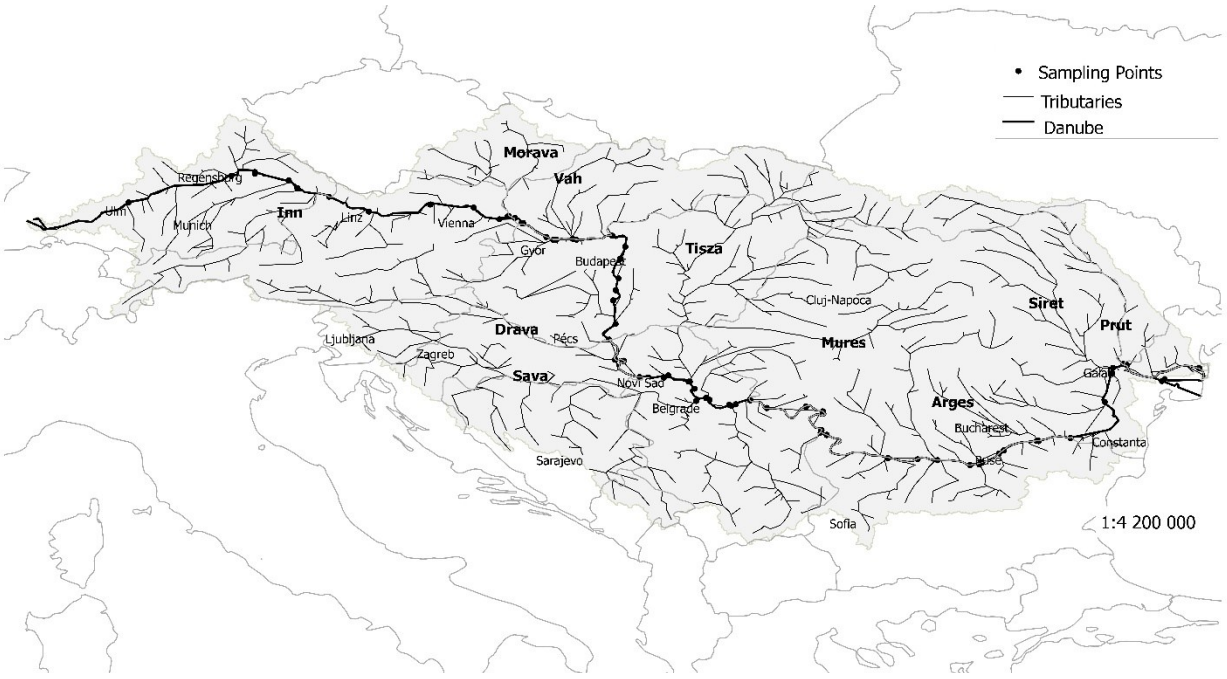
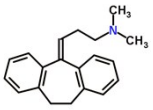
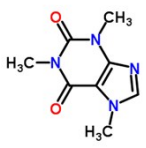
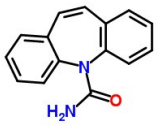
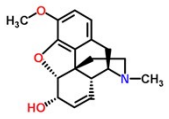
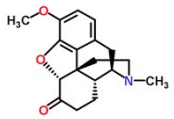
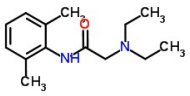
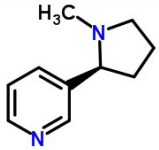
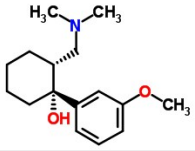
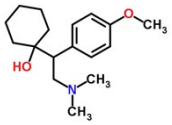


Figure S1. Map used in Lindim, et. al.[1] displaying the 68 sampling points along the Danube river that were modeled in STREAM-EU[1, 2]. The daily concentrations of 4 hypothetical micropollutants were modeled in these stations for the year 2013 and used to calculate spatial and temporal Junge variability-lifetime relationships.

Properties of the monitored micropollutants that were used in the empirical Junge relationship

Table S1. Micropollutants monitored by Croatian Waters in the third Joint Danube Survey (JDS3-CW) and their relevant properties.

Compound	**CAS**	**Chemical group and function**	**Structure** ‡	**log D_{OW}** *	**Main ionic form at *pH* 6.5-8.5***	**log K_{AW}** +
Amitriptyline	50-48-6	Pharmaceutical: Antidepressant		2.48	Cationic	–5.55
Caffeine	58-08-2	Stimulant		-0.55	Neutral	–8.83

Carbamazepine	298-46-4	Pharmaceutical: Anti-epileptic		2.77	Neutral	–8.35
Codeine	76-57-3	Pharmaceutical: Analgesic/ opioid		-0.45	Cationic	–11.51
Hydrocodone	125-29-1	Pharmaceutical: Analgesic		0.73	Cationic	–9.58
Lidocaine	137-58-6	Pharmaceutical: Anesthetic		2.33	Cationic	–8.27
Nicotine	54-11-5	Stimulant		-0.04	Cationic	–6.91
Tramadol	27203-92-5	Pharmaceutical: Analgesic/ opioid		0.62	Cationic	–9.20
Venlafaxine	93413-69-5	Pharmaceutical: Antidepressant		1.22	Cationic	–9.08

Note: ‡ obtained from ChemSpider. * Obtained from ChemAxon Chemicalize web-based software (www.chemicalize.com). Distribution coefficient (log D_{OW}) was obtained at pH 7.4, main ionic form was deduced from the software-estimated strongest acidic or basic *pKa* + Calculated from Henry's Law constant at 25°C obtained from EPI Suite V4.11[3]

Method used to fit measured concentrations of JDS3-CW to log-normal distributions and to estimate the measurements below LOQ.

The empirical relative standard deviation (σ/μ) for spatial variability was calculated for the nine micropollutants measured in the JDS3 (Table S1). To avoid bias in the estimation of means and standard deviations calculated only from measurements above LOQ, we imputed values below LOQ by fitting the concentration measurements to log-normal distributions and extrapolating values in the lower tail (as recommended for censored data [4, 5]) and not from the parameters of the fitted log-normal distribution.

Concentrations in (ng/L) obtained for compounds measured in the JDS3-CW were first log-transformed and then inverse-ranked from highest to smallest, meaning that if N concentrations were below LOQ, then the

highest concentration corresponding to rank 68 and the lowest to 68-N. An empirical cumulative probability (Y) was calculated for each log-concentration with Equation S1.

$$Y = rank / 68 \qquad \text{Eq. S1.}$$

A modeled cumulative probability (Y') according to a normal distribution was calculated with initial estimated values for the mean (μ) and standard deviation of Y ().

Based on a method described in Reference 3, the squared error between each Y and Y' was calculated and summed. Using the "Solver" tool in Excel, the first estimates of $\mu_{\text{fit-lognorm}}$ and $\sigma_{\text{fit-lognorm}}$ were changed in order to minimize the sum of squared errors.[6]

The N concentrations below LOQ were then calculated using the optimized $\mu_{\text{fit-lognorm}}$ and $\sigma_{\text{fit-lognorm}}$ and combined with the original concentration measurements for the subsequent calculation of σ / μ intended for the calibration of the empirical Junge relationship. The $\mu_{\text{fit-lognorm}}$ and $\sigma_{\text{fit-lognorm}}$ were not back-transformed and used directly for the calculation of σ / μ, because this is known to cause bias in the estimation of central-tendency and dispersion parameters of small skewed samples.[4, 5]

Figure S2 shows the graphical visualization of the fitting.

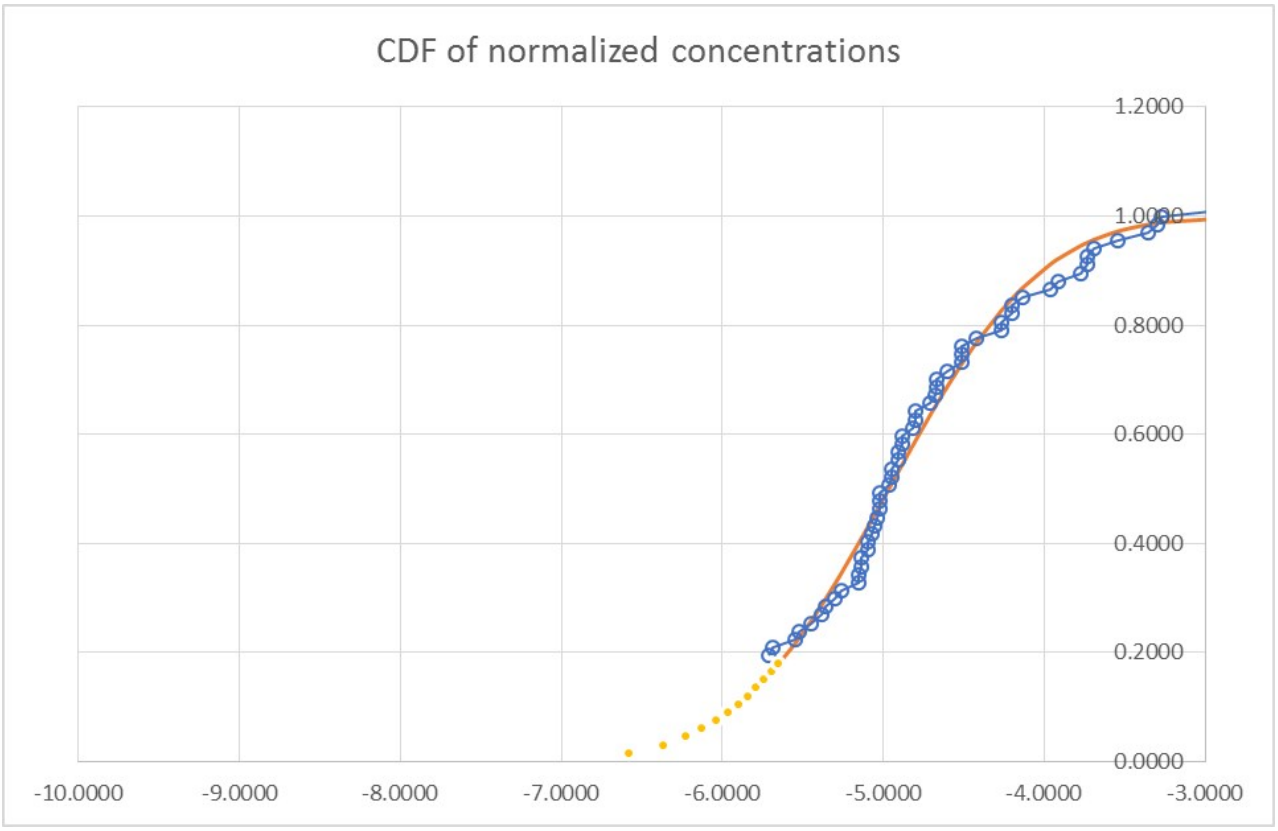


Figure S2. Cumulative distribution function for the log-normal concentrations measured in the JDS3-CW (in blue), the fitted normal distribution (in orange) and the imputed concentrations below LOQ (in yellow).

A single arithmetic mean, standard deviation and subsequently the relative standard deviation σ/μ, were calculated for each micropollutant using the concentrations measurements above the LOQ (in blue) combined with the imputed data below the LOQ (in yellow) (as recommended for censored data [4, 5]) and not from the parameters of the fitted log-normal distribution (in orange).

Compounds where all concentrations were close to LOQ (i.e. sulfamethoxazole) were excluded for this part of analysis due to the low resolution and measurement error.

Evaluation of sorption of cationic compounds to soil and sediment (K_d calculation).

Seven of the compounds used in the empirical Junge relationship (shown in Tables S1 and S6) occur mainly as cationic species in freshwater. Sorption of cationic pharmaceuticals to soil and sediment is higher compared to neutral pharmaceuticals with similar K_{OW}, and thus sorption might be underestimated by a criteria based only on D_{OW}. Therefore sediment-water partition coefficients (K_d) were calculated according to Droge [7] to assess degree of sorption to sediment and dissolved matter from the distribution coefficient D_{OW}. The estimated K_d of the seven cationic compounds is lower than the K_d calculated with the sorption criteria we used (i.e., log D_{OW} < 4, see SI), so therefore we decided these chemicals meet our criteria and can be included in this study.

The distribution coefficient (K_d) was calculated using two approaches:

1) Using a refined sorption model for organic cations to soil and clay (Eq. S4), by calculating D_{OC} (Eq. S2Eq. S2 [7] $\log D_{OC} = 1.53Vx + 0.32NA_i - 0.27$) and K_{CEC} (Eq. S3) from the micropollutant molecule volume V_X and surface area NA_i [7]

Eq. S2 [7] $\log D_{OC} = 1.53Vx + 0.32NA_i - 0.27$

Eq. S3 [7] $\log K_{CEC,clay} = 1.22Vx + 0.22NA_i + 1.09$

Eq. S4 [7] $K_d = K_{CEC,clay} \cdot (CEC_{soil} - 3.4 \cdot f_{OC}) + f_{OC} \cdot D_{OC}$

2) Using a calculated from a traditional linear regression between D_{OC} and D_{OW} (Eq. S5)[8], and then using this D_{OC} for calculation of K_d as in Equation S4.

Eq. S5 [8] $D_{OC} = 10^{0.31 \log Dow + 2.78}$

The average and maximum concentrations of dissolved organic carbon (DOC) measurements from JDS3-CW were taken into account for the calculations of K_d and since the exact composition of the DOC in the Danube river is unknown, the properties of standard Eurosoils ES-1 and ES-5[7] were used.

Table S2. Average and maximum dissolved organic matter (DOM) parameters obtained from the JDS3-CW data.[9]

	DOM	
average	2.98	mg/L
maximum	5.50	mg/L

Table S3. Standard Eurosoil 1 and 5 (ES-1 and ES-5) characteristics used on the K_d calculations according to Reference 6. ES-1 is the standard soil with highest content of clay and lowest f_{OC}, and ES5 the one with highest f_{OC} and lowet clay content.[7]

Soil type	**f_{oc}**		**CEC_{soil}**		**CEC_{clay}**	
ES-1	0.013	kg oc / kg solid dw	0.299	mmol/kg	0.2548	mol/kg
ES-5	0.0925	kg oc / kg solid dw	0.327	mmol/kg	0.0125	mol/kg

Table S4. Calculation of K_d for two different types of soil (ES-1 and ES-5) and average or maximum dissolved organic matter (DOM) measured in the Danube during the JDS3. The K_d of the compounds in the empirical Junge relationship do not exceed the K_d of the theoretical D_{OW} limit chosen.

					ES-1, average DOM		ES-5, average DOM		ES-1, maximum DOM		ES-5, maximum DOM	
Compound	**log D_{OW}**	**log D_{OC}**	**log D_{OC}**	**log K_{CEC}**	**log K_d**	**log K_d**	**log K_d**	**log K_d**	**log K_d**	**log K_d**	**log K_d**	**log K_d**
		(Eq S5)	(Eq S2)	(Eq S3)	(Eq S5+S4)	(Eq S2+S4)	(Eq S5+S4)	(Eq S2+S4)	(Eq S5+S4)	(Eq S2+S4)	(Eq S5+S4)	(Eq S2+S4)
Amitriptyline	2.48	3.55	3.82	4.88	-1.23	-1.23	-2.42	-2.33	-0.97	-0.96	-2.16	-2.07
Caffeine	-0.55	2.61	1.45	3.46	-2.64	-2.66	-3.66	-3.94	-2.37	-2.39	-3.39	-3.67
Carbamazepine	2.77	3.64	2.50	4.30	-1.79	-1.82	-2.71	-3.08	-1.52	-1.55	-2.45	-2.82
Codeine	-0.45	2.64	3.63	4.72	-1.40	-1.39	-2.68	-2.50	-1.13	-1.12	-2.42	-2.24
Hydrocodone	0.73	3.01	3.63	4.72	-1.40	-1.39	-2.65	-2.50	-1.13	-1.12	-2.38	-2.24
Lidocaine	2.33	3.50	3.20	4.38	-1.72	-1.73	-2.75	-2.87	-1.45	-1.46	-2.48	-2.61
Nicotine	-0.04	2.77	2.15	3.54	-2.55	-2.57	-3.54	-3.77	-2.29	-2.30	-3.27	-3.51
Tramadol	0.62	2.97	3.77	4.84	-1.28	-1.27	-2.55	-2.38	-1.02	-1.00	-2.29	-2.11
Venlafaxine	1.22	3.16	3.68	4.77	-1.35	-1.34	-2.59	-2.45	-1.08	-1.07	-2.32	-2.19
Theoretical sorption limit	**4**	**4.02**	**3.82**	**4.88**	**-1.22**	**-1.23**	**-2.24**	**-2.33**	**-0.95**	**-0.96**	**-1.98**	**-2.07**

STREAM-EU concentration predictions for the JDS3 monitoring campaign

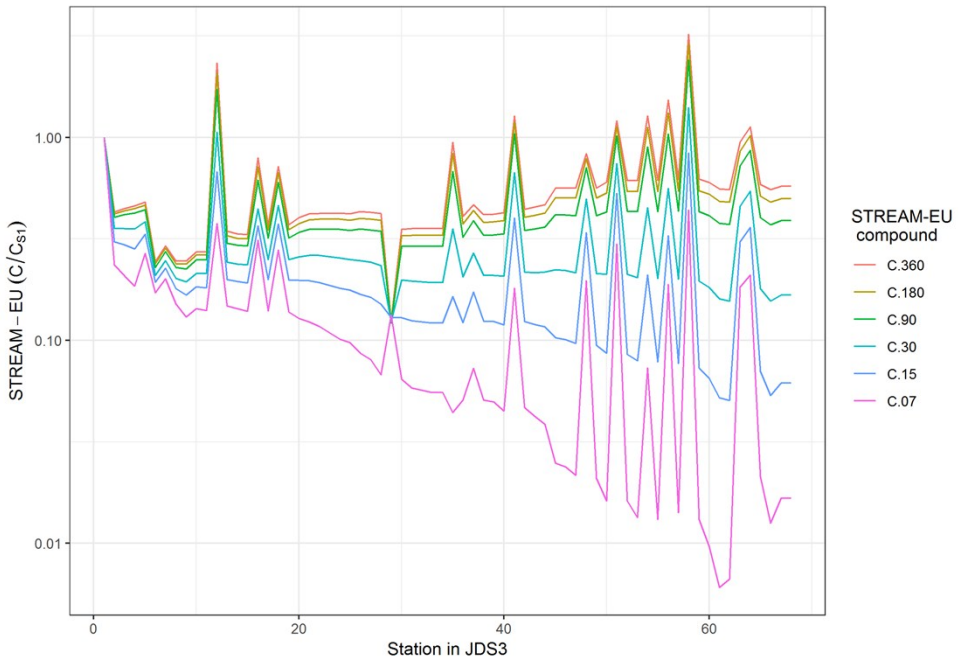


Figure S3. Normalized concentrations predicted for the corresponding date and station sampled during the third Joint Danube Survey (JDS3). The normalization was relative to the concentration of the compound in the first station (S1)

The normalized modeled concentrations ($C/C_{station\ 1}$) have more variation for compounds with shorter half-life (i.e. C07 with $\tau = 7$ days), than for longer half-lives (i.e. C360 with $\tau = 360$ days). Variation is similar for the three most persistent hypothetical compounds with half-lives of 90, 180 and 360 days.

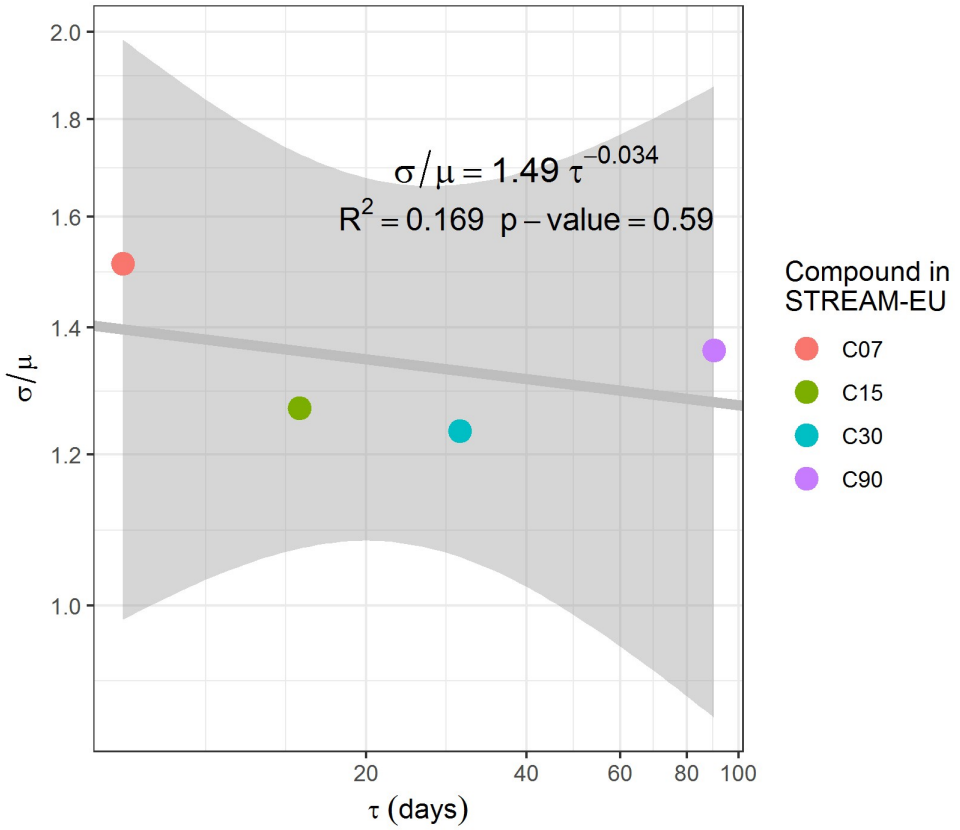


Figure S4. Junge relationship of STREAM-EU concentrations predicted for dates and location of measurements performed in the Joint Danube Survey (JDS3). Only the four compounds with shortest half-lives (7, 15, 30 and 90 days) were used to derive this relationship.

Junge relationships from STREAM-EU synthetic data

Table S5. Summary of Junge relationships for four hypothetical chemicals with concentrations modeled by STREAM-EU. The parameter *a* represents the intercept, and *b* the slope of the Junge relationships. The temporal relationships were calculated for 67 monitoring stations along the Danube river, the spatial relationships were calculated daily for the year 2013.

	Temporal relationships Mean (5^{th} ,95^{th} percentiles)	**Spatial relationship Mean (5^{th}, 95^{th} percentiles)**
Total number	67	365
a	1.33 (0.62, 2.98)	1.32 (0.99, 1.89)
b	–0.327 (–0.651, –0.088)	–0.154 (–0.212, –0.103)
p-value (slope)	0.027 (0.002, 0.085)	0.079 (0.024 , 0.181)
R^2	0.95 (0.84, 0.99)	0.85 (0.67, 0.95)

Note: the 5th and 95th percentiles are shown instead of a confidence interval.

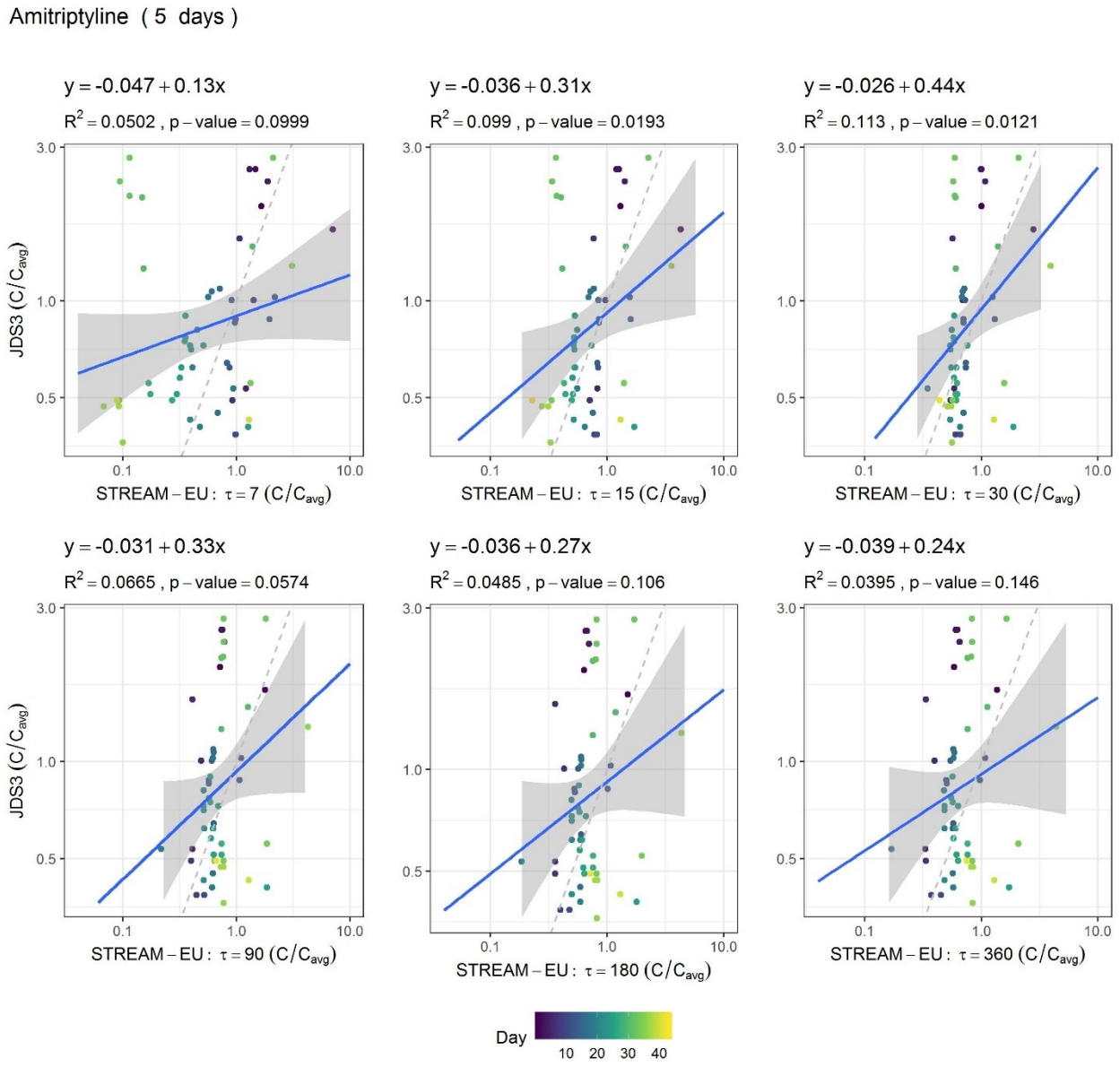
Relative standard deviation and half-lives of micropollutants

Table S6. Relative Standard Deviations (σ/μ) and half-lives (τ) of micropollutants used to generate an empirical spatial Junge relationship. σ/μ were calculated from concentrations measured in the JDS3-CW, imputing measurements below limits of quantification (LOQ). In cases where there were two or more half-lives reported in the literature τ is the geometric mean, and the 95% confidence factor (Cf) is reported as described in reference [10].

Micropollutant	**Empirical σ/μ in the Danube river**	**Literature τ (days)**	**Cf in τ**	**References for τ**
amitriptyline	0.8034	5.0	NA	[11]
caffeine	1.3448	5.7	3.39	[11-19]
carbamazepine	0.5461	181.8	2.37	[12, 14-20]
codeine	0.7877	34.6	1.03	[12, 21]
hydrocodone	0.7811	18.5	NA	[12]
lidocaine	1.0447	100.6	NA	[22]
nicotine	0.7773	3.2	NA	[12]
tramadol	1.0067	81.4	1.84	[22, 23]
venlafaxine	0.8945	44.7	3.43	[22, 24]

Several studies have experimental designs with replicates at different conditions (i.e. comparing different study sites[12]) and report more than one half-life for each compound. If this was the case, then the compiled half-lives were first averaged per compound and per study as the geometric mean. Second, all studies for each compound were pooled in order to compute a broad geometric mean for each micropollutant, this geometric mean is reported in the "literature τ ".

153 Concentrations of micropollutants in the JDS3 vs predicted concentrations for
154 hypothetical chemicals in STREAM-EU



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156 Figure S5. Normalized concentrations measured for amitriptyline in the JDS3 campaign compared to the
157 predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation
158 half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the
159 JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the
160 experimental half-life is shown in brackets.

161

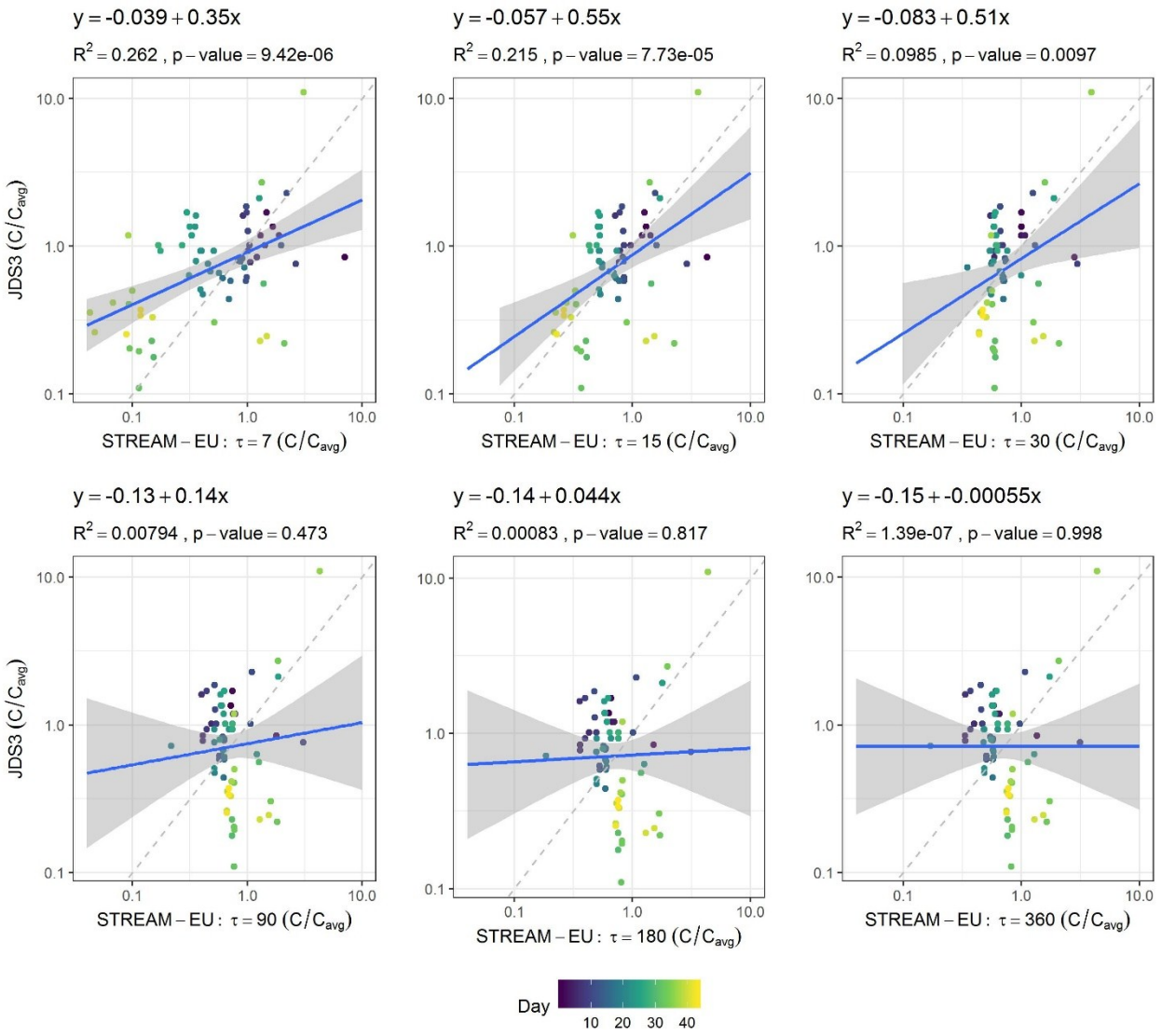
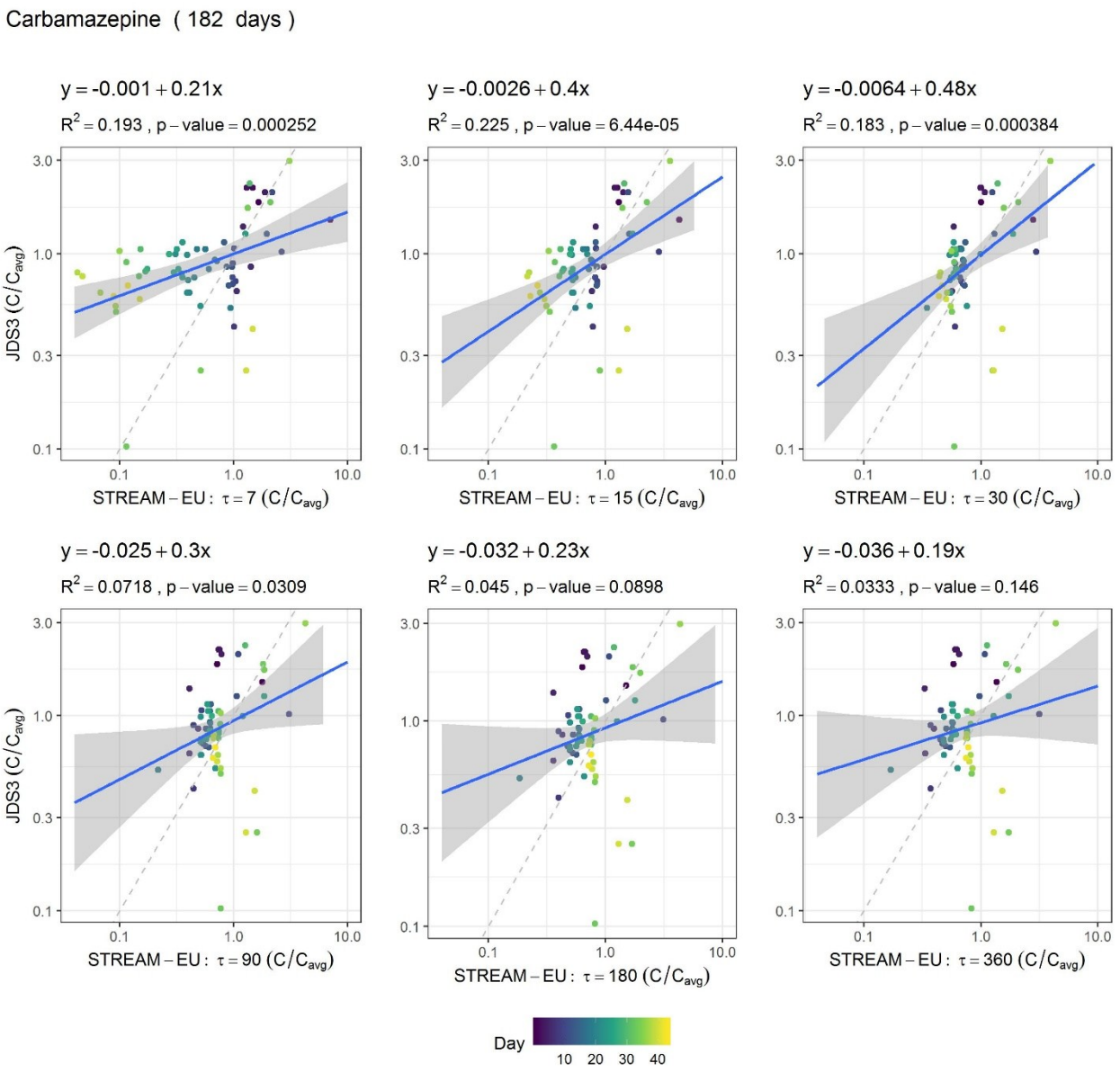


Figure S6. Normalized concentrations measured for caffeine in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.



169

170 Figure S7. Normalized concentrations measured for carbamazepine in the JDS3 campaign compared to the
171 predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation
172 half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the
173 JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the
174 experimental half-life is shown in brackets.

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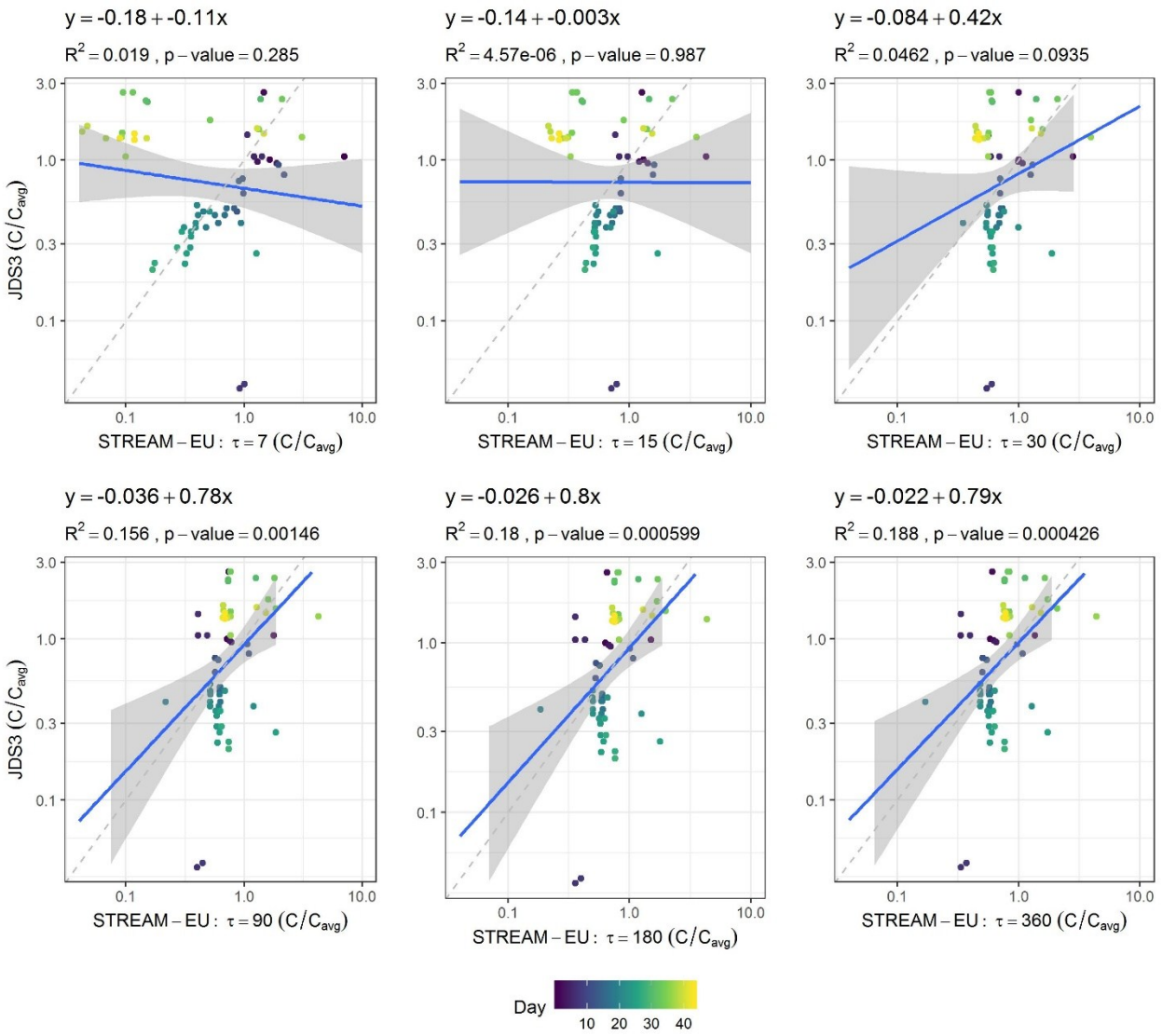


Figure S8. Normalized concentrations measured for codeine in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.

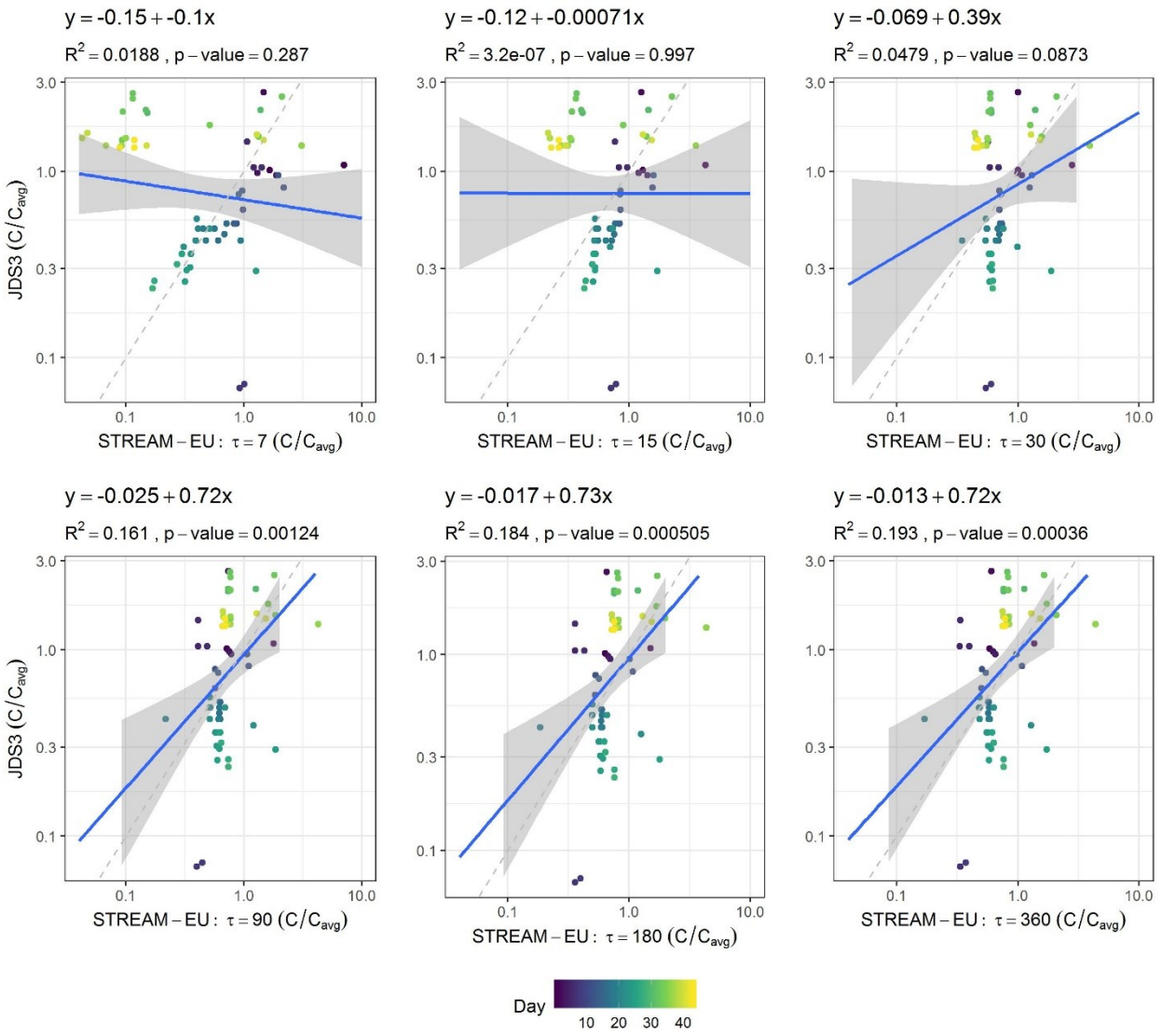


Figure S9. Normalized concentrations measured for hydrocodone in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.

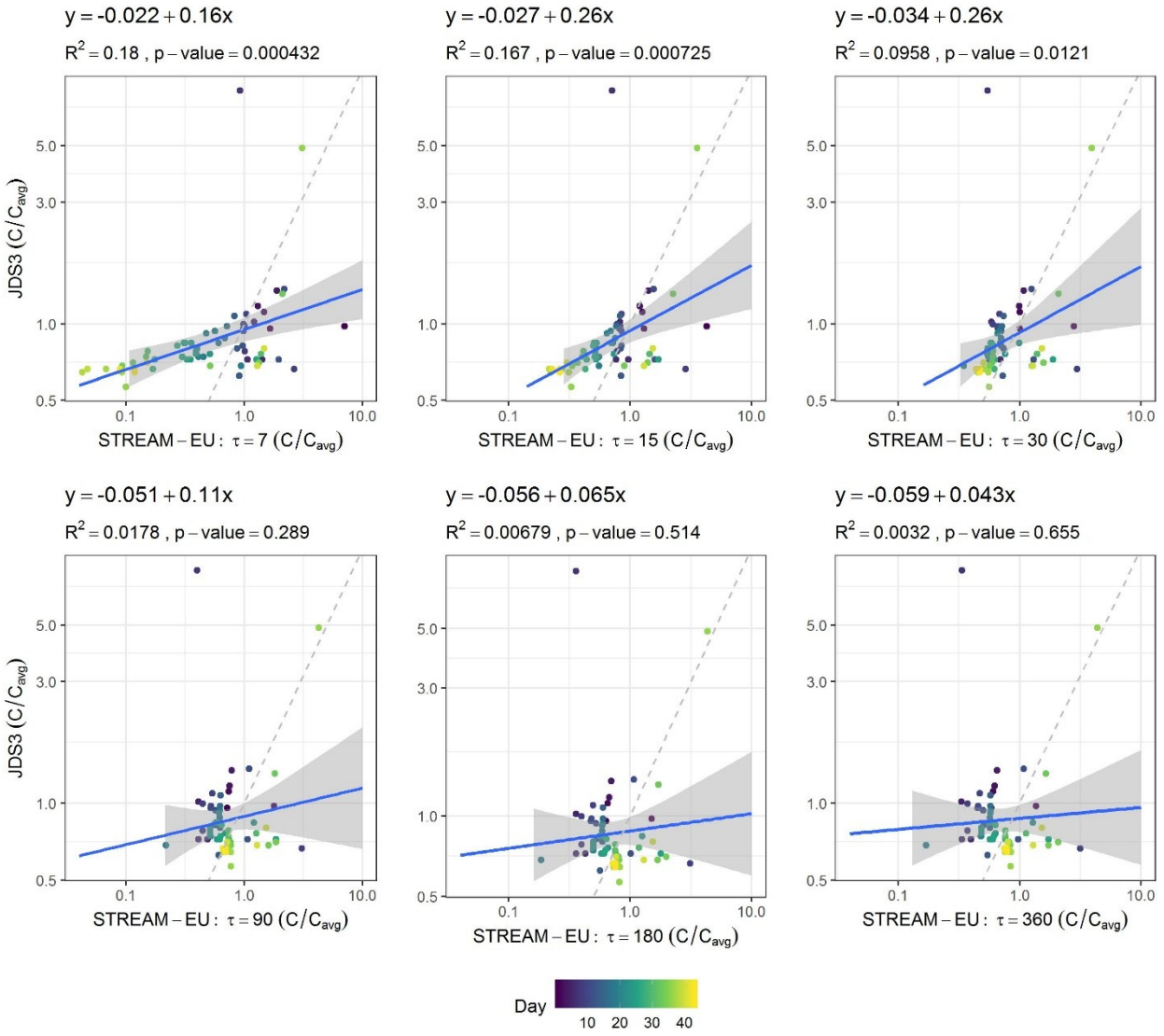
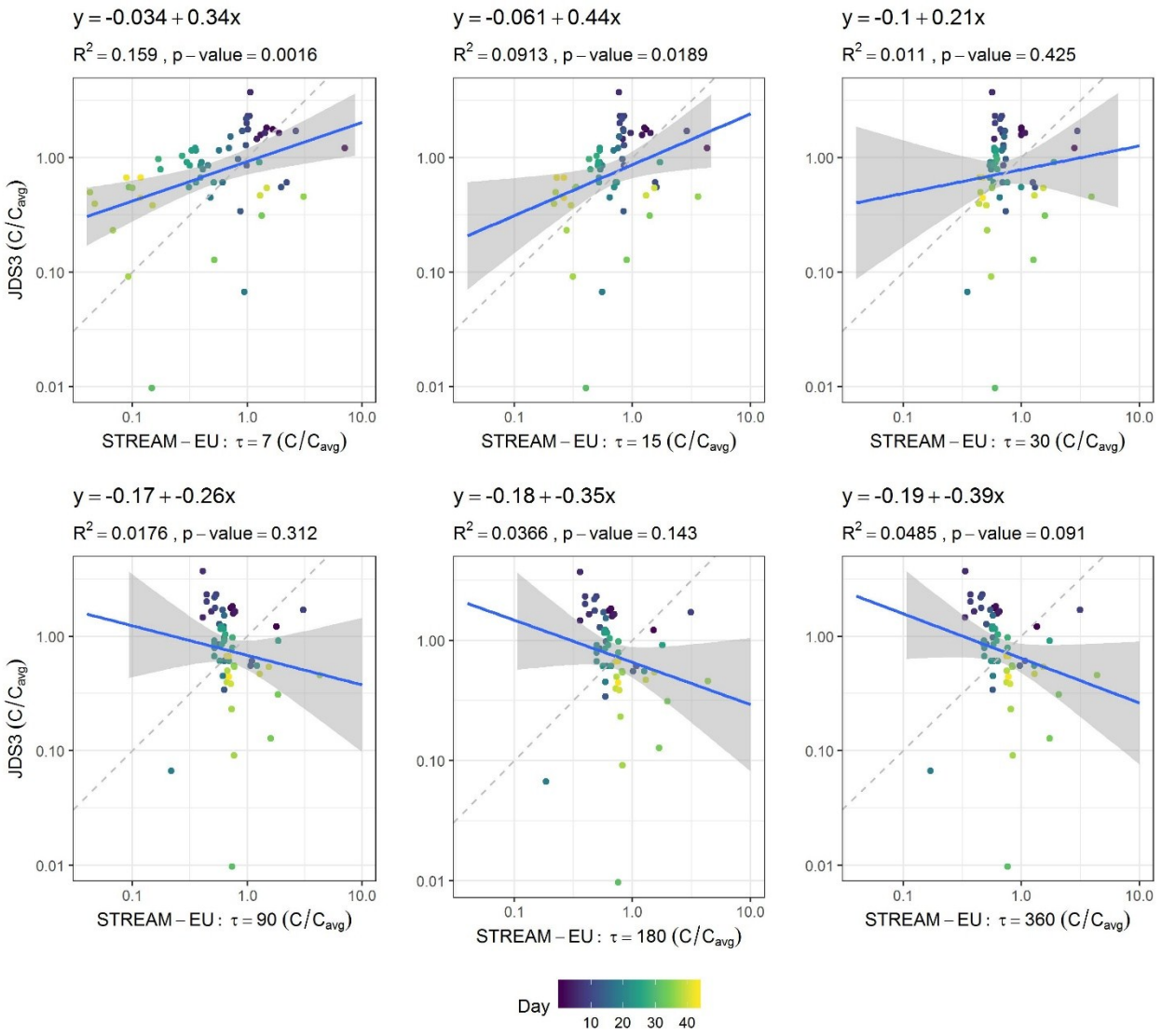


Figure S10. Normalized concentrations measured for lidocaine in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.



196

197 Figure S11. Normalized concentrations measured for nicotine in the JDS3 campaign compared to the
198 predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation
199 half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the
200 JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the
201 experimental half-life is shown in brackets.

202

Tramadol (81 days)

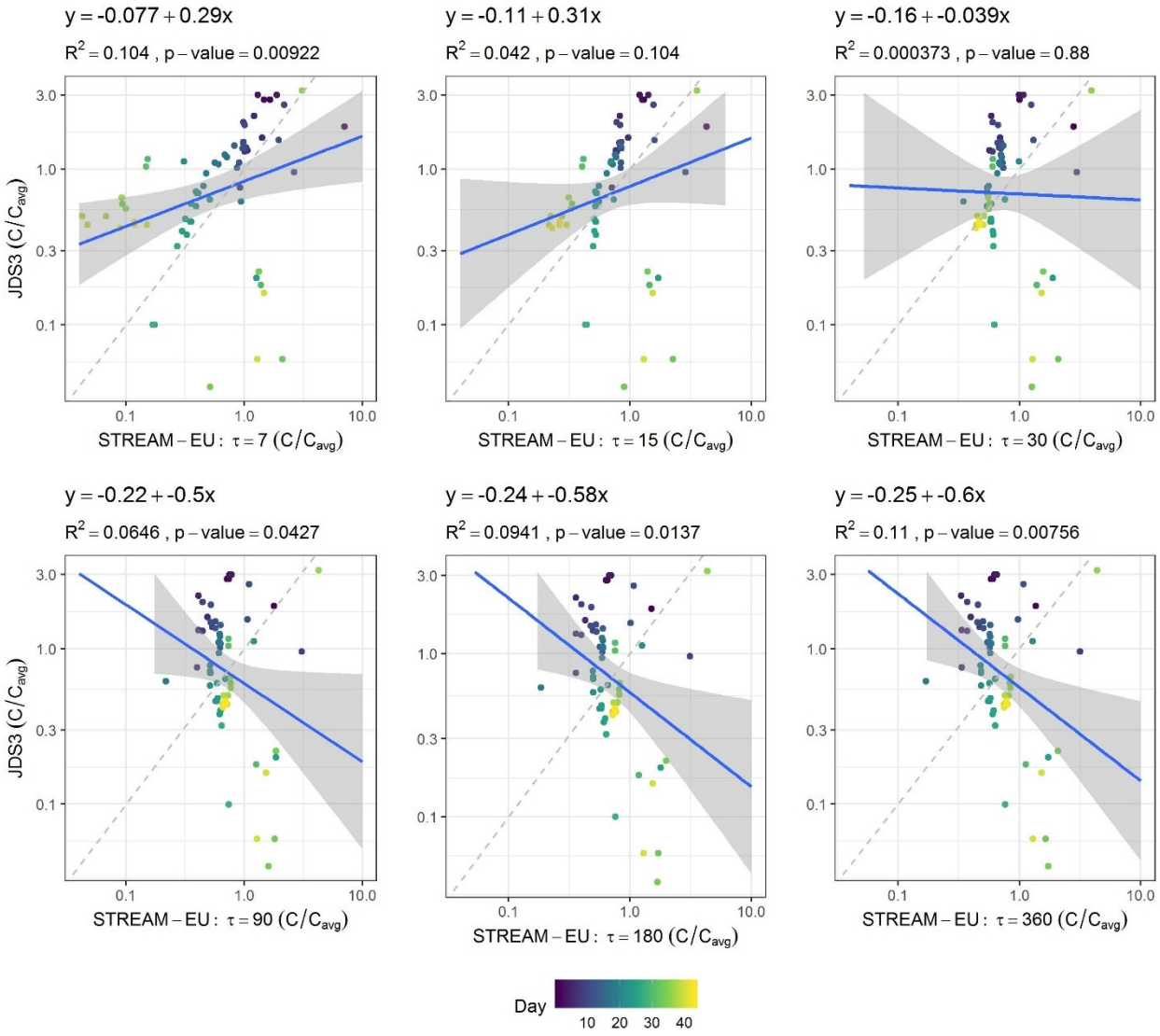


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Figure S12. Normalized concentrations measured for tramadol in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.

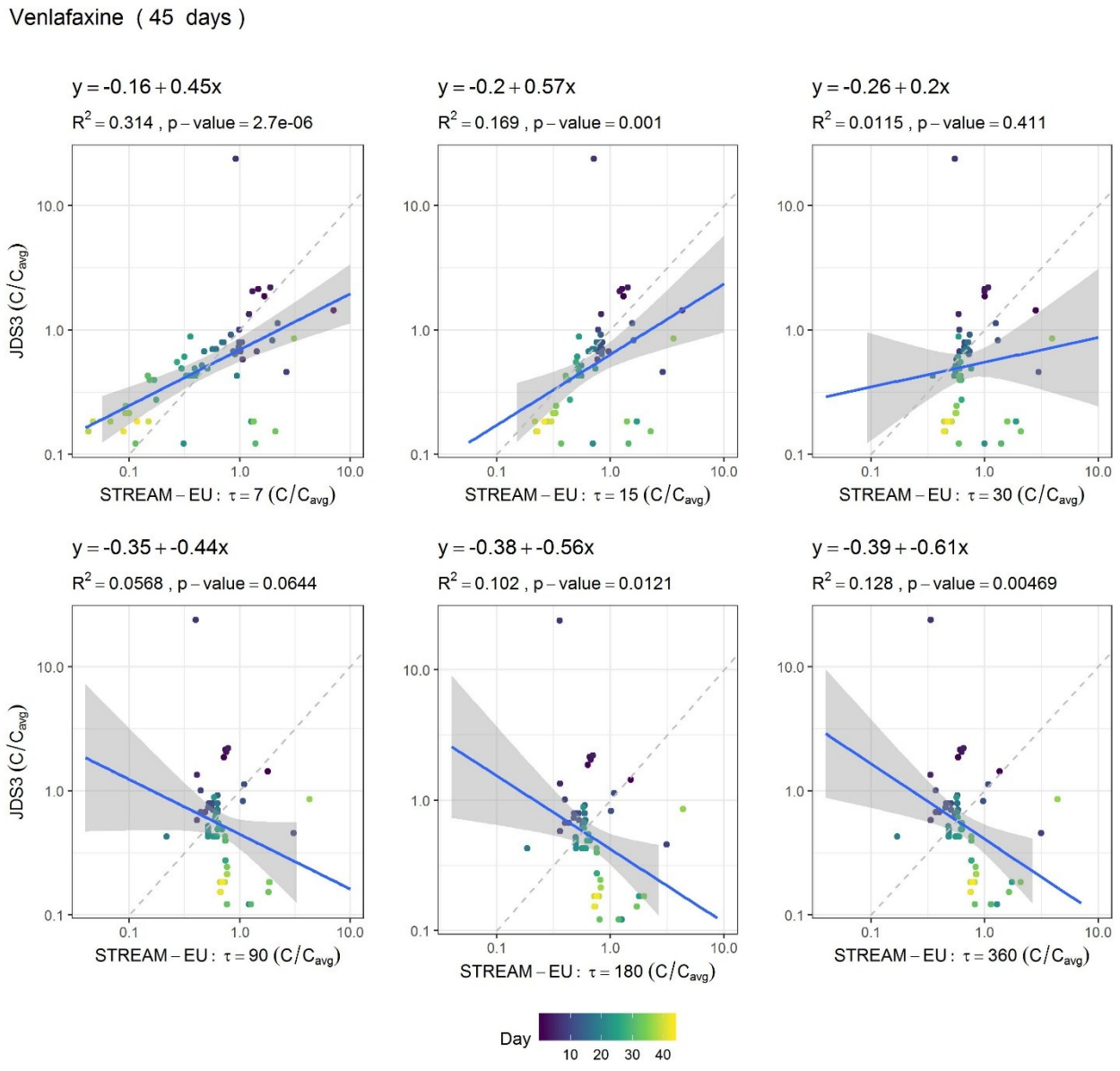

Figure S13. Normalized concentrations measured for venlafaxine in the JDS3 campaign compared to the predicted normalized concentrations in STREAM-EU of the six hypothetical chemicals with biodegradation half-lives of 7, 15, 30, 90, 180 and 360 days and for the corresponding date and station sampled during the JDS3. The normalization was relative to the average concentration of the compound. In the plot's title, the experimental half-life is shown in brackets.

REFERENCES

1. C. Lindim, I. T. Cousins and J. vanGils, Estimating emissions of PFOS and PFOA to the Danube River catchment and evaluating them using a catchment-scale chemical transport and fate model, *Environmental Pollution*, 2015, **207**, 97-106.
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