

Supporting Information

**Physiologically Based Pharmacokinetic Model for the
Biotransportation of Arsenic in Marine Medaka (*Oryzias melastigma*)**

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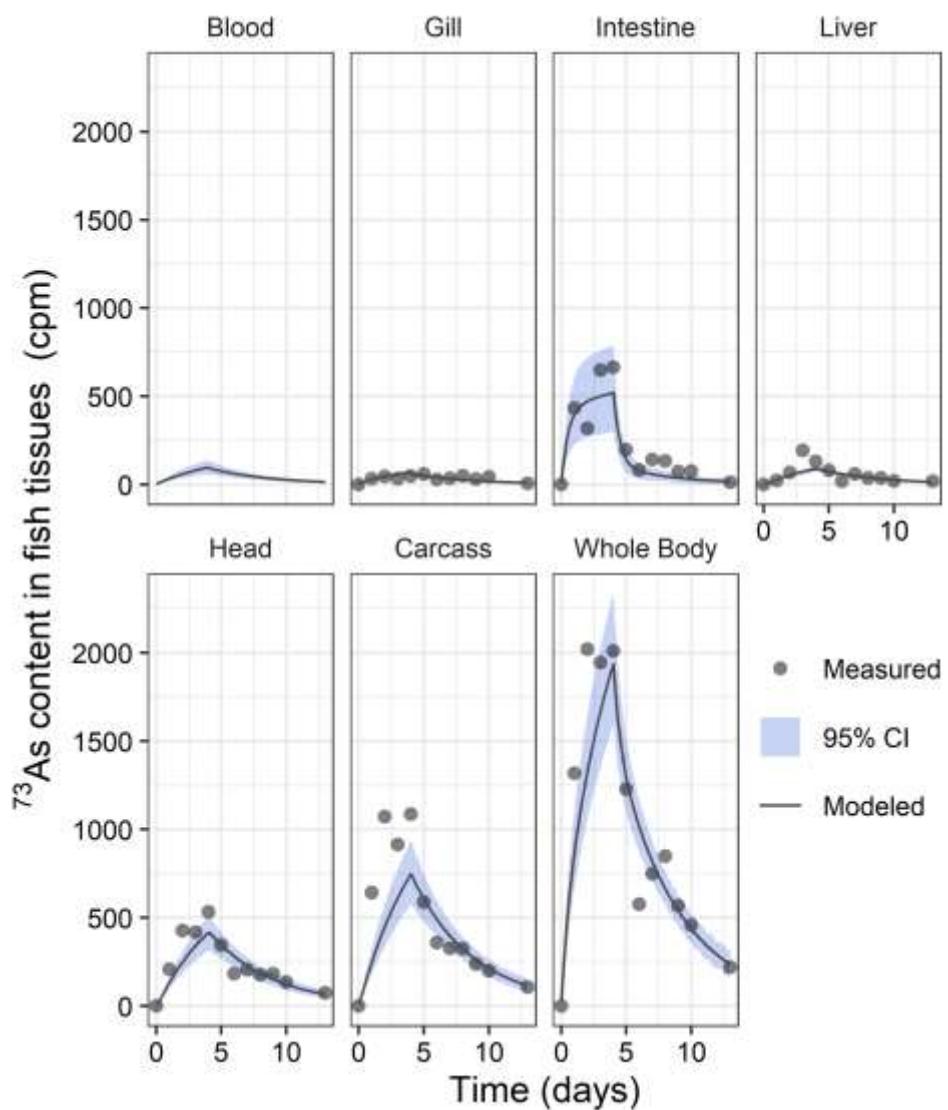


Figure S1 The content of ^{73}As radioactivity (cpm) distributed in different tissues of marine medaka during the 4 d exposure and the subsequent 9 d depuration

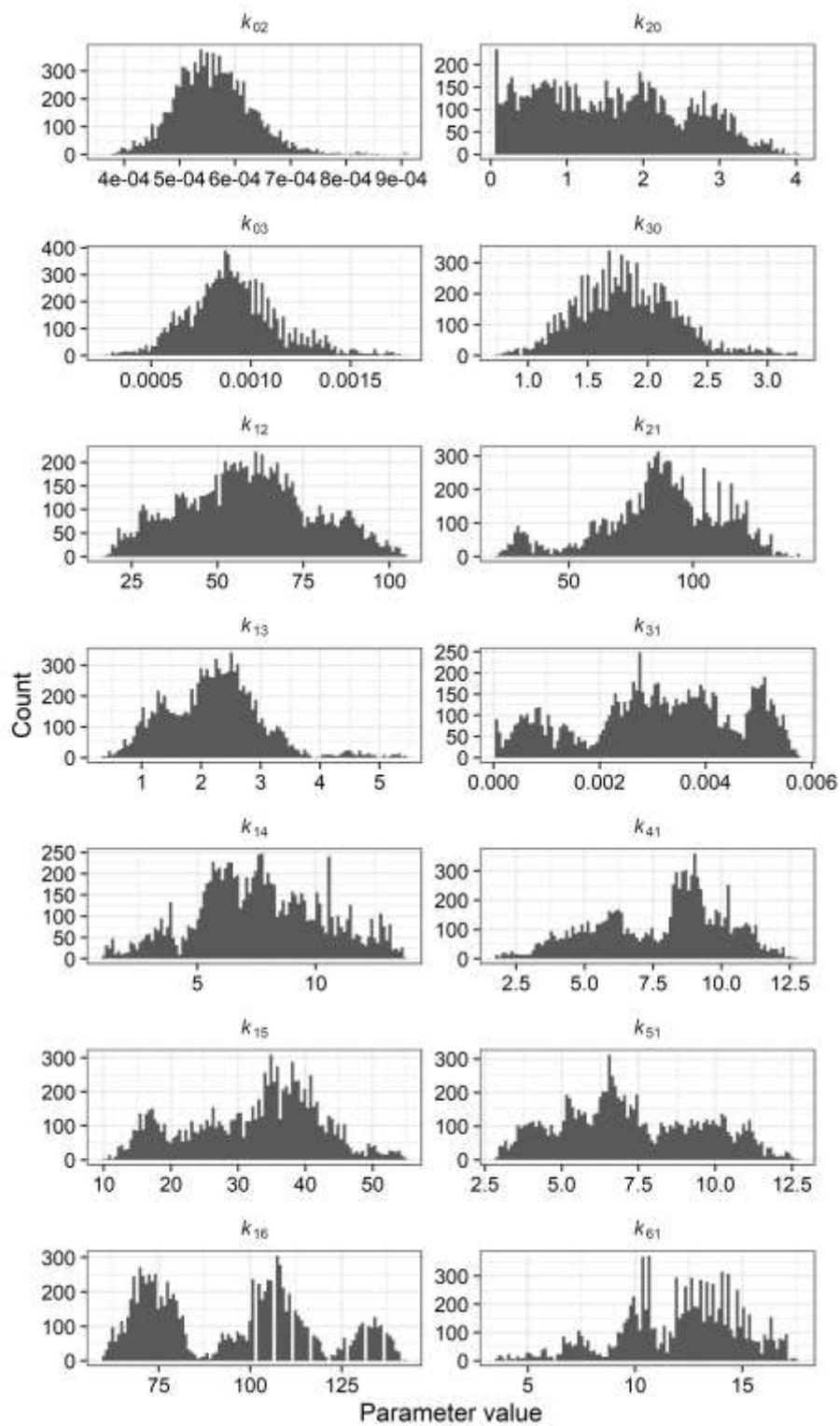


Figure S2 The posterior distribution of the model parameters. The parameter values are from the parameter samples generated by the MCMC fitting and are the first 10000 skipped values (skip interval = 2) after 50% burn in

Table S1 Average fresh weight of fish tissues used for the modeling. The weight values were the sum of eight fish, which were sampled at each time point. Weight of blood was not measured and was estimated by assuming 40 µL of blood for 1 g of fresh tissue weight.

Tissue	Fresh weight (g)
Blood	0.0661
Gill	0.0298
Intestine	0.0958
Liver	0.0445
Head	0.389
Carcass	1.08
Whole body	1.65

Table S2 Total As and As species concentrations ($\mu\text{g g}^{-1}$) in brine shrimp

	As concentrations ($\mu\text{g/g}$)					
	As(III)	As(V)	MMA	DMA	AsB	Total As
brine shrimp	0.40 \pm 0.03	0.54 \pm 0.10	0.27 \pm 0.05	0.40 \pm 0.06	5.11 \pm 0.21	6.72 \pm 0.31

Table S3 As species concentrations ($\mu\text{g g}^{-1}$) in gill, intestine, liver, head, and carcass tissues of marine medaka after waterborne exposure for 4 d and depuration for 9 d

		As species concentrations ($\mu\text{g g}^{-1}$)				
		As(III)	As(V)	MMA	DMA	AsB
Gill						
Exposure	1	0.26 \pm 0.05	0.11 \pm 0.02	0.16 \pm 0.01	0.11 \pm 0.01	1.61 \pm 0.21
	2	0.25 \pm 0.01	0.13 \pm 0.05	0.12 \pm 0.03	0.09 \pm 0.01	1.55 \pm 0.06
	3	0.37 \pm 0.02	0.15 \pm 0.02	0.20 \pm 0.02	0.11 \pm 0.01	2.00 \pm 0.02
	4	0.58 \pm 0.01	0.38 \pm 0.01	0.14 \pm 0.01	0.10 \pm 0.01	2.19 \pm 0.04
Depuration	5	0.06 \pm 0.01	0.25 \pm 0.02	0.09 \pm 0.01	0.04 \pm 0.00	2.01 \pm 0.03
	6	0.07 \pm 0.02	0.23 \pm 0.04	0.07 \pm 0.01	0.04 \pm 0.01	2.11 \pm 0.02
	7	0.08 \pm 0.01	0.23 \pm 0.02	0.10 \pm 0.01	0.04 \pm 0.01	1.99 \pm 0.01
	8	0.17 \pm 0.02	0.30 \pm 0.01	0.22 \pm 0.02	0.03 \pm 0.01	2.04 \pm 0.01
	9	0.09 \pm 0.02	0.27 \pm 0.02	0.04 \pm 0.02	0.05 \pm 0.01	2.15 \pm 0.02
	10	0.05 \pm 0.02	0.23 \pm 0.01	0.07 \pm 0.02	0.07 \pm 0.01	2.06 \pm 0.01
	13	0.10 \pm 0.04	0.34 \pm 0.02	0.07 \pm 0.01	0.05 \pm 0.01	1.67 \pm 0.01
Intestine						
Exposure	1	0.35 \pm 0.01	1.91 \pm 0.01	0.06 \pm 0.00	0.10 \pm 0.01	1.82 \pm 0.01
	2	0.37 \pm 0.01	1.79 \pm 0.02	0.06 \pm 0.00	0.12 \pm 0.00	1.92 \pm 0.03
	3	0.48 \pm 0.02	1.85 \pm 0.01	0.05 \pm 0.00	0.20 \pm 0.00	2.19 \pm 0.01
	4	0.31 \pm 0.00	2.39 \pm 0.00	0.08 \pm 0.01	0.04 \pm 0.00	3.15 \pm 0.07
Depuration	5	0.07 \pm 0.00	0.25 \pm 0.01	0.03 \pm 0.01	0.10 \pm 0.01	2.98 \pm 0.06
	6	0.07 \pm 0.01	0.21 \pm 0.00	0.03 \pm 0.00	0.12 \pm 0.00	3.41 \pm 0.01
	7	0.08 \pm 0.01	0.23 \pm 0.01	0.04 \pm 0.00	0.11 \pm 0.01	3.14 \pm 0.03
	8	0.06 \pm 0.01	0.18 \pm 0.05	0.00 \pm 0.00	0.04 \pm 0.00	3.23 \pm 0.05
	9	0.14 \pm 0.02	0.26 \pm 0.05	0.02 \pm 0.00	0.17 \pm 0.00	2.66 \pm 0.06
	10	0.05 \pm 0.01	0.19 \pm 0.03	0.09 \pm 0.00	0.11 \pm 0.01	2.63 \pm 0.01
	13	0.02 \pm 0.01	0.07 \pm 0.01	0.01 \pm 0.00	0.02 \pm 0.01	2.90 \pm 0.03
Liver						
Exposure	1	0.35 \pm 0.01	1.82 \pm 0.01	0.68 \pm 0.01	0.77 \pm 0.01	0.88 \pm 0.01
	2	0.31 \pm 0.03	1.42 \pm 0.01	0.47 \pm 0.03	0.55 \pm 0.01	0.65 \pm 0.01
	3	0.12 \pm 0.01	1.14 \pm 0.01	0.55 \pm 0.01	0.63 \pm 0.01	0.58 \pm 0.03
	4	0.79 \pm 0.01	1.88 \pm 0.03	0.41 \pm 0.01	0.41 \pm 0.01	1.48 \pm 0.02
Depuration	5	0.42 \pm 0.01	0.61 \pm 0.05	0.51 \pm 0.00	0.78 \pm 0.02	1.02 \pm 0.02
	6	0.36 \pm 0.01	0.56 \pm 0.03	0.42 \pm 0.01	0.82 \pm 0.01	1.11 \pm 0.04
	7	0.38 \pm 0.01	0.61 \pm 0.02	0.46 \pm 0.01	0.90 \pm 0.01	1.25 \pm 0.03
	8	0.47 \pm 0.02	0.67 \pm 0.06	0.41 \pm 0.01	0.99 \pm 0.02	1.38 \pm 0.01
	9	0.50 \pm 0.05	0.43 \pm 0.02	0.60 \pm 0.02	0.61 \pm 0.01	1.26 \pm 0.03
	10	0.73 \pm 0.02	0.35 \pm 0.03	0.36 \pm 0.01	0.67 \pm 0.03	1.53 \pm 0.02
	13	0.14 \pm 0.01	0.36 \pm 0.03	0.39 \pm 0.00	0.17 \pm 0.05	1.92 \pm 0.03
Head						
Exposure	1	0.21 \pm 0.00	0.02 \pm 0.00	0.01 \pm 0.00	0.00 \pm 0.00	1.41 \pm 0.21
	2	0.24 \pm 0.01	0.03 \pm 0.00	0.00 \pm 0.00	0.00 \pm 0.00	1.45 \pm 0.13

	3	0.30±0.01	0.01±0.00	n.d.	n.d.	1.53±0.11
	4	0.16±0.01	0.03±0.00	0.01±0.01	0.00±0.00	1.66±0.15
Depuration	5	0.06±0.00	0.06±0.00	0.03±0.00	0.02±0.01	1.49±0.10
	6	0.07±0.00	0.03±0.01	0.03±0.01	0.02±0.00	1.50±0.05
	7	0.07±0.00	0.03±0.01	0.03±0.01	0.02±0.00	1.50±0.23
	8	0.10±0.01	0.02±0.00	0.02±0.01	0.01±0.01	1.58±0.25
	9	0.05±0.00	0.05±0.00	0.03±0.00	0.01±0.00	1.52±0.07
	10	0.05±0.00	0.06±0.01	0.03±0.00	0.04±0.00	1.49±0.11
	13	0.04±0.01	0.02±0.00	0.02±0.01	0.02±0.00	1.41±0.30
				Carcass		
Exposure	1	0.20±0.00	0.08±0.01	0.01±0.01	0.01±0.00	1.61±0.15
	2	0.17±0.01	0.05±0.00	0.01±0.02	0.02±0.01	1.45±0.09
	3	0.20±0.01	0.09±0.04	0.02±0.01	0.02±0.00	1.72±0.24
	4	0.19±0.01	0.05±0.02	0.02±0.01	0.01±0.00	1.57±0.52
Depuration	5	0.03±0.01	0.04±0.01	0.01±0.00	0.01±0.00	1.51±0.05
	6	0.04±0.01	0.04±0.01	0.01±0.00	0.01±0.00	1.55±0.06
	7	0.03±0.02	0.04±0.01	0.01±0.01	0.01±0.00	1.62±0.10
	8	0.04±0.00	0.02±0.01	0.01±0.00	0.01±0.00	1.65±0.12
	9	0.02±0.00	0.05±0.02	0.01±0.00	0.02±0.01	1.72±0.19
	10	0.03±0.00	0.04±0.01	0.00±0.00	0.01±0.00	1.62±0.30
	13	0.02±0.01	0.01±0.00	0.02±0.02	0.02±0.00	1.96±0.34

Table S4 As species distribution (%) in head, carcass, gill, intestine, and liver tissues of marine medaka after waterborne exposure for 4 d and depuration for 9 d

		As species distribution (%)				
		As(III)	As(V)	MMA	DMA	AsB
Gill						
Exposure	1	11.5±0.03	4.98±0.90	6.93±1.01	4.98±0.25	71.6±1.47
	2	11.6±0.12	5.89±0.11	5.70±0.37	4.10±0.36	72.7±0.99
	3	13.1±0.21	5.41±0.85	7.09±0.24	3.73±0.24	70.7±0.37
	4	17.2±0.65	11.3±0.55	4.03±0.09	2.88±0.63	64.7±0.42
Depuration	5	2.30±0.87	10.1±1.20	3.65±0.08	1.44±0.25	82.6±0.68
	6	2.70±0.55	9.05±0.42	2.78±0.10	1.63±0.20	83.8±1.17
	7	3.33±0.64	9.49±0.26	4.15±0.27	1.44±0.17	81.6±1.07
	8	6.21±0.54	10.8±0.24	7.85±0.21	1.02±0.08	74.1±2.01
	9	3.38±0.21	10.4±0.51	1.37±0.20	1.79±0.09	83.0±1.85
	10	1.87±0.05	9.40±0.26	2.85±0.23	2.96±0.15	82.9±2.47
	13	4.48±1.21	15.4±0.31	3.23±0.14	2.11±0.06	74.7±1.52
Intestine						
Exposure	1	8.28±0.25	45.1±0.99	1.44±0.09	2.38±0.01	42.8±1.45
	2	8.58±0.16	42.0±0.55	1.50±0.01	2.87±0.02	45.0±0.92
	3	10.1±1.01	38.8±0.10	1.05±0.05	4.18±0.06	45.9±1.55
	4	5.20±0.69	40.1±0.24	1.35±0.04	0.63±0.04	52.7±1.35
Depuration	5	1.89±0.55	7.37±0.36	0.87±0.04	2.94±0.04	86.9±0.62
	6	1.93±0.15	5.55±0.51	0.65±0.03	3.02±0.03	88.9±0.86
	7	2.26±0.25	6.27±0.42	1.00±0.01	3.04±0.07	87.4±0.99
	8	1.57±0.10	5.02±0.74	0.09±0.01	1.08±0.07	92.2±0.90
	9	4.29±0.23	8.07±0.62	0.61±0.06	5.34±0.05	81.7±1.01
	10	1.72±0.30	6.31±0.15	2.96±0.01	3.51±0.05	85.5±1.32
	13	0.78±0.25	2.40±0.41	0.24±0.03	0.54±0.01	96.0±1.03
Liver						
Exposure	1	7.68±0.13	40.4±0.25	15.2±0.25	17.1±0.13	19.6±1.01
	2	9.17±0.32	41.6±0.35	13.8±0.51	16.2±0.25	19.2±0.92
	3	3.87±0.15	37.7±0.40	18.3±0.13	20.9±0.31	19.2±0.66
	4	15.9±0.10	37.8±0.36	8.23±0.21	8.26±0.26	29.8±0.71
Depuration	5	12.4±0.10	18.3±0.41	15.3±0.92	23.5±0.34	30.4±0.37
	6	10.9±0.07	17.3±0.21	12.9±0.66	25.0±0.47	33.9±0.49
	7	10.5±1.03	17.0±0.32	12.8±0.52	25.0±0.25	34.7±0.16
	8	12.0±1.32	17.1±0.10	10.4±0.72	25.3±0.21	35.1±1.52
	9	14.6±1.09	12.7±0.32	17.8±0.65	18.0±0.35	37.0±1.07
	10	20.2±0.51	9.52±0.51	9.76±0.52	18.4±0.33	42.2±1.55
	13	4.81±0.64	12.1±1.25	13.1±0.62	5.68±0.31	64.3±1.10
Head						
Exposure	1	12.9±0.21	1.27±0.06	0.36±0.04	0.24±0.03	85.3±1.25

Depuration	2	13.6±0.01	1.43±0.04	0.17±0.05	0.06±0.03
	3	16.1±0.03	0.63±0.07	n.d.	n.d.
	4	8.76±0.13	1.71±0.03	0.75±0.02	0.15±0.01
	5	3.52±0.10	3.34±0.05	1.52±0.04	0.97±0.05
	6	3.97±0.11	2.08±0.02	1.53±0.04	1.10±0.02
	7	4.29±0.03	2.05±0.03	1.75±0.05	1.21±0.03
	8	5.68±0.014	1.21±0.06	0.98±0.03	0.83±0.03
	9	2.75±0.03	2.92±0.05	1.58±0.03	0.73±0.02
	10	3.04±0.10	3.44±0.02	1.66±0.02	2.11±0.03
	13	2.37±0.13	1.23±0.03	1.43±0.03	1.15±0.02
				Carcass	
Exposure	1	10.2±0.15	3.94±0.89	0.63±0.02	0.47±0.07
	2	9.89±0.21	3.00±0.51	0.59±0.14	0.88±0.02
	3	9.89±1.28	4.58±1.23	0.73±0.25	0.88±0.18
	4	10.2±2.81	2.53±1.76	0.93±0.13	0.33±0.02
Depuration	5	1.94±2.10	2.26±0.24	0.38±0.21	0.69±0.01
	6	2.21±0.20	2.14±0.32	0.61±0.13	0.43±0.02
	7	1.47±0.30	2.41±0.24	0.70±0.09	0.47±0.03
	8	2.37±0.36	1.33±0.02	0.41±0.05	0.52±0.05
	9	1.16±0.10	2.98±1.59	0.28±0.11	0.83±0.14
	10	1.66±0.17	2.19±0.02	0.18±0.09	0.30±0.17
	13	0.80±0.39	0.50±0.24	1.19±0.05	0.35±0.06
					97.2±1.49

Table S5 Total As concentrations in gill, intestine, liver, head, and carcass tissues of marine medaka^a

		Total As concentrations ($\mu\text{g/g}$)				
	Days	Gill	Intestine	Liver	Head	Carcass
Exposure	1	2.19 \pm 0.11	4.01 \pm 0.21	4.45 \pm 0.32	1.68 \pm 0.06	1.91 \pm 0.14
	2	1.94 \pm 0.08	4.36 \pm 0.09	3.01 \pm 0.05	1.76 \pm 0.05	1.54 \pm 0.13
	3	2.89 \pm 0.15	4.87 \pm 0.13	3.55 \pm 0.14	1.82 \pm 0.11	1.98 \pm 0.20
	4	3.32 \pm 0.09	5.68 \pm 0.07	4.92 \pm 0.09	1.99 \pm 0.04	2.01 \pm 0.23
Depuration	5	2.54 \pm 0.21	4.08 \pm 0.30	3.31 \pm 0.11	1.67 \pm 0.18	1.73 \pm 0.18
	6	2.91 \pm 0.14	4.42 \pm 0.15	3.62 \pm 0.15	1.75 \pm 0.08	1.71 \pm 0.56
	7	2.50 \pm 0.08	3.28 \pm 0.10	3.53 \pm 0.18	1.72 \pm 0.14	1.73 \pm 0.69
	8	2.49 \pm 0.10	3.48 \pm 0.24	3.55 \pm 0.25	1.69 \pm 0.21	1.69 \pm 0.12
	9	2.60 \pm 0.24	3.39 \pm 0.06	3.45 \pm 0.20	1.68 \pm 0.07	1.75 \pm 0.15
	10	2.45 \pm 0.09	3.22 \pm 0.14	3.26 \pm 0.17	1.75 \pm 0.10	1.60 \pm 0.21
	13	2.38 \pm 0.08	2.97 \pm 0.25	2.85 \pm 0.05	1.57 \pm 0.06	1.80 \pm 0.13

^aValues are means \pm SD (n= 3).

Estimation maximum likelihood values and the 95% credible intervals of the PBPK model parameters in OpenModel

The PBPK model of As in fish was implemented in the software OpenModel (version 2.4.2). The software is developed by Neil Crout at the University of Nottingham and is freely available at the website: <http://openmodel.info/>.

Below are the detailed procedures of the model implementation and parameter estimation.

1. Implementing the PBPK model with OpenModel code

1.1 OpenModel code of the PBPK model

```
//Arsenic in water-----
water=C_water.Cw(t)

//blood, Compartment 1-----
Q_blood.rate=k31*Q_intes+k41*Q_liver+k21*Q_gill+k51*Q_head+k61*Q_res
t-(k13+k14+k12+k15+k16)*Q_blood

//gill, Compartment 2-----
Q_gill.rate=k02*water+k12*Q_blood-(k21+k20)*Q_gill

//intestine, Compartment 3-----
Q_intes.rate=k13*Q_blood-k31*Q_intes+k03*water-k30*Q_intes

//liver, Compartment 4-----
Q_liver.rate=k14*Q_blood-k41*Q_liver

//head, Compartment 5-----
Q_head.rate=k15*Q_blood-k51*Q_head

//carcass, Compartment 6-----
Q_rest.rate=k16*Q_blood-k61*Q_rest

//whole fish-----
Q_whole=Q_blood+Q_intes+Q_liver+Q_gill+Q_head+Q_rest

C_blood=Q_blood/0.0661
C_intes=Q_intes/0.0958
C_liver=Q_liver/0.0445
C_gill=Q_gill/0.0298
C_head=Q_head/0.389
C_rest=Q_rest/1.08

C_whole=(Q_blood+Q_intes+Q_liver+Q_gill+Q_head+Q_rest)/1.65
```

1.2 OpenModel code of the PBPK model (view in the OpenModel interface)



The screenshot shows the OpenModel interface with the title "Model Design(Fish As PBPK.OMMLx)". The menu bar includes File, Edit, View, Model, Debug, Help. Below the menu is a toolbar with buttons for Previous, Save, Syntax, Evaluate, Graph, Table, Map, Model, and Estimate. A "Trace" button is also present. The main window displays a hierarchical tree on the left and a code editor on the right.

Hierarchical Tree:

- FishAsPBPK
- Modules
 - Module1
- Parameterizations
 - Initial
 - MCMC_prior
 - MCMC_post
- Data Sheets
 - data_0
 - C_water
 - data_C
 - Ends

Code Editor (Module1):

```
Module[Module1];
Symbols initial Mem;
1 //As in water
2 water=C_water.CWt();
3
4 //blood, Compartment 1-
5 Q_blood.rate=k31*Q_intes+k41*Q_liver+k51*Q_gill+k61*Q_head+k61*Q_rest-(k13+k14+k12+k15+k16)*Q_blood
6 //gill, Compartment 2-
7 Q_gill.rate=k02*water+k12*Q_blood-(k21+k20)*Q_gill
8
9 //intestine, Compartment 3-
10 Q_intes.rate=k13*Q_blood-k31*Q_intes+k03*water=k30*Q_intes
11
12 //liver, Compartment 4-
13 Q_liver.rate=k14*Q_blood-k41*Q_liver
14
15 //head, Compartment 5-
16 Q_head.rate=k15*Q_blood=k51*Q_head
17
18 //carcass, Compartment 6-
19 Q_rest.rate=k16*Q_blood=k61*Q_rest
20
21 //whole fish-
22 Q_whole=Q_blood+Q_intes+Q_liver+Q_gill+Q_head+Q_rest
23
24 //code below converts Q (mass of As) into C (concentration of As)
25 C_blood=Q_blood/0.0661
26 C_intes=Q_intes/0.0958
27 C_liver=Q_liver/0.0449
28 C_gill=Q_gill/0.0298
29 C_head=Q_head/0.389
30 C_rest=Q_rest/1.06
31
32 C_whole=(Q_blood+Q_intes+Q_liver+Q_gill+Q_head+Q_rest)/1.65
```

2. Defining the symbols

2.1 Symbols defined in the model

Symbols	Definition	Unit
Variables		
C_blood	concentration of ^{73}As in the blood	cpm g^{-1} fresh weight
C_gill	concentration of ^{73}As in the gill	cpm g^{-1} fresh weight
C_head	concentration of ^{73}As in the head	cpm g^{-1} fresh weight
C_intes	concentration of ^{73}As in the intestine	cpm g^{-1} fresh weight
C_liver	concentration of ^{73}As in the liver	cpm g^{-1} fresh weight
C_rest	concentration of ^{73}As in the carcass	cpm g^{-1} fresh weight
C_whole	concentration of ^{73}As in the whole fish	cpm g^{-1} fresh weight
Q_whole	quantity of ^{73}As in the whole fish	cpm
water	concentration of ^{73}As in water	cpm L^{-1}
ODEs (Ordinary differential equations)		
Q_blood	quantity of ^{73}As in the blood	cpm
Q_gill	quantity of ^{73}As in the gill	cpm
Q_head	quantity of ^{73}As in the head	cpm
Q_intes	quantity of ^{73}As in the intestine	cpm
Q_liver	quantity of ^{73}As in the liver	cpm
Q_rest	quantity of ^{73}As in the carcass	cpm
Parameters		
k02	water to gill	L d^{-1}
k20	gill to water	d^{-1}
k03	water to intestine	L d^{-1}
k30	intestine to water	d^{-1}
k12	blood to gill	d^{-1}
k21	gill to blood	d^{-1}
k13	blood to intestine	d^{-1}
k31	intestine to blood	d^{-1}
k14	blood to liver	d^{-1}
k41	liver to blood	d^{-1}
k15	blood to head	d^{-1}
k51	head to blood	d^{-1}
k16	blood to carcass	d^{-1}
k61	carcass to blood	d^{-1}

2.2 Symbols defined in the model (view in the OpenModel interface)

Model Design:[Fish As PBPK.OMMLx]

File Edit View Model Debug Help

Previous Save Syntax Evaluate Graph... Table... Map... Merit Estimate

Fish As PBPK

Modules

Module1

Parameterisations

Initial

MCMC_prior

MCMC_post

Data Sheets

data_Q

C_water

data_C

Grids

Module [Module1]

Symbols Initial Main

Add Remove Rename Trace

Module1

Variables

- C_blood
- C_gill
- C_head
- C_intes
- C_liver
- C_rest
- C_whole
- Q_whole
- water

ODEs

- Q_blood
- Q_gill
- Q_head
- Q_intes
- Q_liver
- Q_rest

Parameters

- k02
- k03
- k12
- k13
- k14
- k15
- k16
- k20
- k21
- k30
- k31
- k41
- k51
- k61

Description:

Units:

Information:

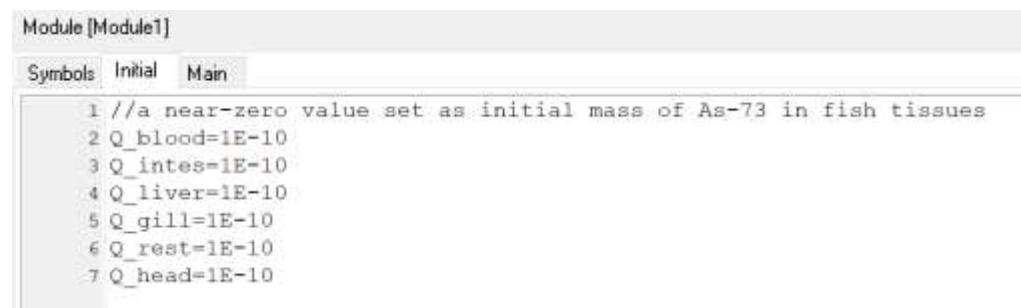
3. Settings of initial values

3.1 Initial values of ODEs

```
Q_blood=1E-10
Q_intes=1E-10
Q_liver=1E-10
Q_gill=1E-10
Q_rest=1E-10
Q_head=1E-10
```

The initial quantity of the radioactive tracer ^{73}As in fish tissues was zero. A very small and non-zero value (10^{-10} CPM) was set as the initial quantity. This value is negligible compared to the bioaccumulated ^{73}As ; however, this non-zero value was needed to avoid technical errors in parameter estimation.

3.2 Initial values of ODEs (view in the OpenModel interface)



```
Module [Module1]
Symbols Initial Main
1 //a near-zero value set as initial mass of As-73 in fish tissues
2 Q_blood=1E-10
3 Q_intes=1E-10
4 Q_liver=1E-10
5 Q_gill=1E-10
6 Q_rest=1E-10
7 Q_head=1E-10
```

3.3 Initial values of parameters (view in the OpenModel interface)

Rough estimates were used as initial values of the parameters, which were optimized by fitting to observed ^{73}As bioaccumulation data.

Model Design:[Fish As PBPK.OMMLx]

File Edit View Model Debug Help

Previous Save Syntax Evaluate Graph... Table... Map... Melt Estimate

FishAs PBPK

Modules

Module1

Parameterisations

Initial

MCMC_prior

MCMC_post

Data Sheets

Grids

Descriptors Default Specifications Parameter Values Covariance

Fish As PBPK

Modules

Module1

Sym	Value	Distribution	Constraint
k02	0.0001	default	default
k03	0.0001	default	default
k12	5	default	default
k13	6	default	default
k14	4	default	default
k15	1	default	default
k16	6	default	default
k20	3	default	default
k21	4	default	default
k30	4	default	default
k31	0.5	default	default
k41	0.5	default	default
k51	2	default	default
k61	2	default	default

4. Optimizing the parameters

4.1 Least squares optimization

The parameters were firstly optimized using least-squares method with the Marquardt algorithm. Below are the best-fit estimates.

Previous	Save	Syntax	Evaluate	Graph...	Table...	Map...	Merr...	Estimate
			Descriptors	Default Specifications	ParameterValues	Covariance		
				Fish As PBPK				
				Modules				
				Module1				
				Parameterizations				
				Initial				
				MCMC_prior				
				MCMC_post				
				Data Sheets				
				Gids				

Symbol	Value	Distribution	Constraint	User Distribution
k02	0.00049641	user defined	default	normal mean=0.0004964 (absolute); sd=0.001997 (absolute)
k03	0.00073032	user defined	default	normal mean=0.0007303 (absolute); sd=0.0004879 (absolute)
k12	32.57498	user defined	default	normal mean=32.57 (absolute); sd=1737 (absolute)
k13	1.577143	user defined	default	normal mean=1.577 (absolute); sd=73.15 (absolute)
k14	3.104405	user defined	default	normal mean=3.104 (absolute); sd=133.2 (absolute)
k15	10.64303	user defined	default	normal mean=10.64 (absolute); sd=453.1 (absolute)
k16	16.70229	user defined	default	normal mean=16.7 (absolute); sd=715.6 (absolute)
k20	1.789616	user defined	default	normal mean=1.79 (absolute); sd=8.903 (absolute)
k21	42.14971	user defined	default	normal mean=42.15 (absolute); sd=852.7 (absolute)
k30	1.371284	user defined	default	normal mean=1.371 (absolute); sd=1.538 (absolute)
k31	0.00125	user defined	default	normal mean=0.00125 (absolute); sd=1.549 (absolute)
k41	2.862323	user defined	default	normal mean=2.862 (absolute); sd=70.39 (absolute)
k51	2.185269	user defined	default	normal mean=2.185 (absolute); sd=42.83 (absolute)
k61	2.079571	user defined	default	normal mean=2.08 (absolute); sd=39.2 (absolute)

4.2 Markov chain Monte Carlo (MCMC) optimization

The parameters were further optimized using the MCMC method with the Metropolis–Hastings algorithm. Parameter values and distributions from the least-squares optimization (see above) were used as prior settings. Default settings, except that 20000 (instead of 10000) iterations, were used in the estimation. Below are the maximums likelihood estimates of the parameters.

Model Design:[Fish As PBPK.OMM].x					
	File	Edit	View	Model	Debug
	Previous	Save	Syntax	Evaluate	Graph...
	Table...	Map...	Mexit	Estimate	
▼ FishAs PBPK	Descriptors	Default Specifications	Parameter Values	Covariance	
└ Modules	Fish As PBPK	Modules	Symbol	Value	Distribution
Module1					
└ Parametrisations					
Initial					
MCMC_prior					
MCMC_post					
Data Sheets					
Grids					

The parameter samples generated by the MCMC fitting include 5000 combinations of parameter values after 50% burn in and being skipped with the interval of 2 (see Fig. S2 for the distribution of parameters). The 2.5 percentile to 97.5 percentile of each parameter were calculated based on the parameter samples, and were accepted as the 95% credible intervals (Table 1).