

Ranges for Parameters for Global Sensitivity Analysis

2/20/2015

Parameter	POINT	LOW	HIGH
QPC	212.4	149	276
DEADSPACE	0.238	0.166	0.309
RQPCO	0.8	0.6	1
FQG	0.16	0.112	0.208
FQL	0.09	0.063	0.117
FQF	0.05	0.035	0.065
FQK	0.15	0.105	0.195
QSKSA	0.58	0.406	0.754
FVBD	0.079	0.0553	0.1027
FVL	0.034	0.0238	0.0442
FVGI	0.0165	0.0116	0.0214
FVF	0.1	0.07	0.13
FVK	0.004	0.0028	0.0052
FSASK	0.75	0.5	1
VLUM	2.1	1.47	2.73
LSK	2	1.4	2.6
PBBDCM	15.97	11.179	20.761
PRPBDCM	1.93	1.351	2.509
PPPBDCM	0.78	0.546	1.014
PSKBDCM	2.91	2.037	3.783
PWSBDCM	6.25	4.375	8.125
PLBDCM	1.93	1.351	2.509
PGBDCM	1.93	1.351	2.509
PFBDCM	33.2	23.24	43.16
PKBDCM	2.08	1.456	2.704
KBDCM	0.18	0.126	0.234
V1CBDCM	41248.5	16500	66000 ~4-fold range
VFCBDCM	0.0079	0.00316	0.0124 ~4-fold range
KM1BDCM	221	100	330
KABDCM	8	0.6	16 Range based on Leavens et al. See RNB 1620 p. 183
AIREXCHANGE	15	10.5	19.5

VOLSHWR	2400	1680	3120
QW	582	407.4	756.6
TEMP	37	25.9	48.1
KOLA	504	352.8	655.2

Changes: (1) Not using BW and HEIGHT parameters due to dependencies on Skin Surface Area and QP

(2) Updated parameter values based on new/different data for V1CBDCM and KFCBDCM

(3) Set V1CBDCM to vary ~3-fold around central tendency estimate consistent with ~-fold variation in Zhao & Allis, 2002, Table 2

Fractional volume for richly and poorly perfused kept constant at 0.2 and 0.8, respectively to maintain mass balance.

Fractional blood flow for richly and poorly perfused kept constant at 0.75 and 0.25, respectively to maintain mass balance.

Fractional blood volume kept at 0.25 and 0.75 for arterial and venous, respectively to maintain mass balance.

Upper and lower limits for physiological volumes and flows set to +/- one SD, assuming CV of 30% (Tan et al., 2007).

Upper and lower limits for most chemical-specific parameters set to +/- one SD, assuming CV of 30%.

Upper and lower limits for shower model parameters also set to +/- one SD, assuming CV of 30%.

Global Sensitivity Analysis Morris Method Settings (Screening Analysis)

GSA Parameter Settings	
Parameter	Setting
p	100
jump	25
Ns	1000

P is the number of values in discretized parameter range (divides up parameter range into p-1 ranges or jump is the step size in computing effects (effectively computing a number of local sensitivities);

Ns is the number of samples

These algorithmic settings were selected to optimize performance of the analysis, i.e. multiple test runs

r hypercubes);

were done until no changes in dose metrics (model outputs) were observed.

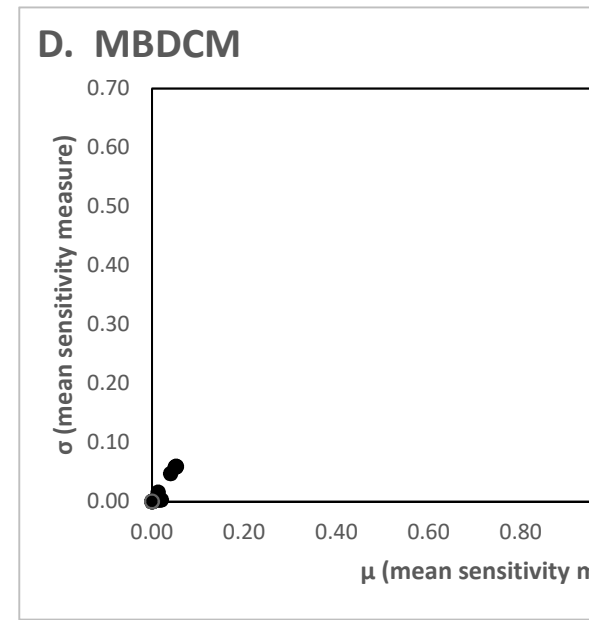
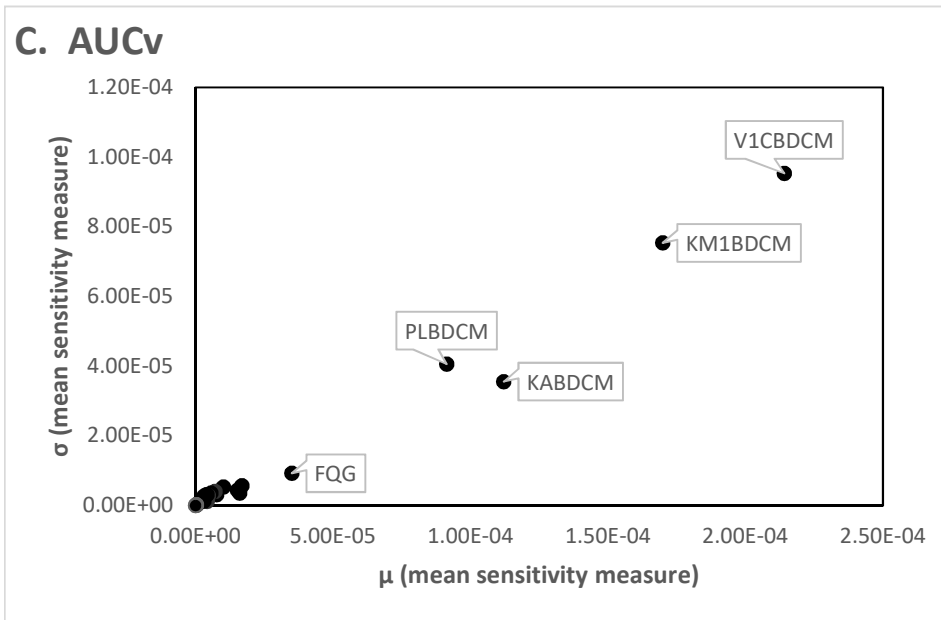
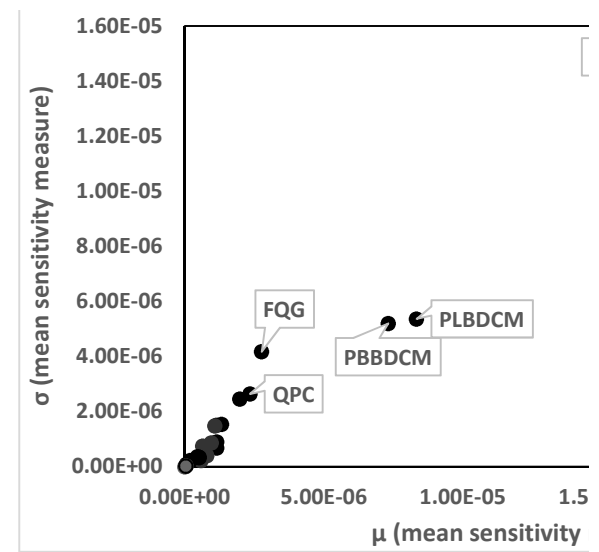
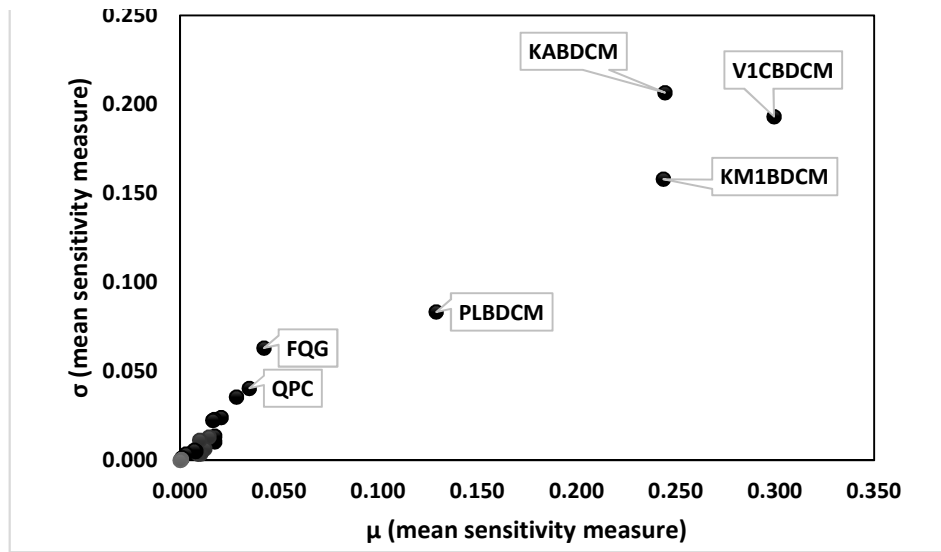
Oral BDCM 10 ppb Single 1/4 Liter Drink Summary Morris GSA Results

Response CvBDCM			Response Calv			Response AUCv		
Parameter	Mean	STDEV	Parameter	Mean	STDEV	Parameter	Mean	STDEV
V1CBDCM	0.299533	0.193159	V1CBDCM	1.97E-05	1.28E-05	V1CBDCM	2.14E-04	9.53E-05
KABDCM	0.244536	0.206664	KABDCM	1.62E-05	1.37E-05	KM1BDCM	1.70E-04	7.54E-05
KM1BDCM	0.243738	0.157995	KM1BDCM	1.58E-05	1.03E-05	KABDCM	1.12E-04	3.56E-05
PLBDCM	0.129190	0.083363	PLBDCM	8.34E-06	5.37E-06	PLBDCM	9.13E-05	4.06E-05
FQG	0.042310	0.063116	PBBDCM	7.32E-06	5.20E-06	FQG	3.50E-05	9.26E-06
QPC	0.034910	0.040488	FQG	2.77E-06	4.17E-06	FQL	1.69E-05	5.74E-06
RQPCO	0.028403	0.035592	QPC	2.35E-06	2.64E-06	RQPCO	1.60E-05	3.61E-06
FQL	0.020722	0.024021	RQPCO	1.98E-06	2.46E-06	QPC	1.52E-05	4.39E-06
QSKSA	0.017582	0.010388	FQL	1.33E-06	1.53E-06	QSKSA	1.01E-05	5.34E-06
PRBDCM	0.017453	0.013641	QSKSA	1.16E-06	6.79E-07	PRBDCM	7.65E-06	3.16E-06
PGBDCM	0.017320	0.022977	PRBDCM	1.15E-06	8.98E-07	FSASK	7.04E-06	4.04E-06
FVGI	0.016459	0.022421	PGBDCM	1.14E-06	1.51E-06	PBBDCM	5.54E-06	3.55E-06
FVBD	0.014527	0.013022	FVGI	1.08E-06	1.49E-06	PGBDCM	4.63E-06	2.82E-06
FSASK	0.012529	0.006455	FVBD	9.60E-07	8.68E-07	FVBD	4.27E-06	1.67E-06
PBBDCM	0.010396	0.003491	FSASK	7.95E-07	4.01E-07	PSKBDCM	4.27E-06	2.05E-06
DEADSPACE	0.009836	0.011247	DEADSPACE	6.49E-07	7.54E-07	DEADSPACE	4.22E-06	1.17E-06
PPBDCM	0.009035	0.003516	PPBDCM	5.87E-07	2.28E-07	LSK	4.16E-06	1.98E-06
FQF	0.008906	0.003618	FQF	5.80E-07	2.36E-07	PPBDCM	4.13E-06	3.13E-06
PSKBDCM	0.007902	0.005221	PSKBDCM	5.22E-07	3.43E-07	FQF	3.82E-06	3.04E-06
LSK	0.007885	0.004981	LSK	5.19E-07	3.28E-07	FVGI	3.10E-06	2.78E-06
FVL	0.007194	0.005713	FVL	4.60E-07	3.67E-07	FVL	3.00E-06	1.26E-06
FQK	0.003031	0.003495	FQK	1.99E-07	2.32E-07	FQK	4.56E-07	3.52E-07
PKBDCM	0.001093	0.001332	PKBDCM	7.05E-08	8.59E-08	PKBDCM	4.34E-07	1.66E-07
FVK	0.000809	0.001084	FVK	5.42E-08	7.28E-08	FVF	3.13E-07	2.14E-07
PFBDCM	0.000749	0.000404	PFBDCM	4.96E-08	2.67E-08	PFBDCM	2.71E-07	2.43E-07
FVF	0.000634	0.000256	FVF	4.20E-08	1.70E-08	FVK	1.27E-07	9.89E-08
VFCBDCM	0.000012	0.000008	VFCBDCM	7.94E-10	5.12E-10	VFCBDCM	8.83E-09	3.93E-09

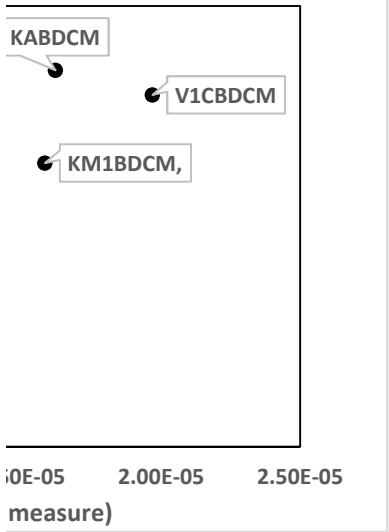
A. CvBDCM

0.250

B. Calv



Response	MBDCM	
Parameter	Mean	STDEV
KABDCM	1.492273	0.567559
PGBDCM	0.053374	0.059649
FVGI	0.052419	0.058746
FQG	0.052229	0.059768
QPC	0.050457	0.058506
RQPCO	0.040715	0.047763
V1CBDCM	0.020556	0.003050
KM1BDCM	0.016729	0.002481
DEADSPACE	0.013874	0.016196
PLBDCM	0.007942	0.001828
FQL	0.001359	0.000354
PBBDCM	0.000806	0.000459
FVL	0.000740	0.000960
QSKSA	0.000739	0.000398
PRBDCM	0.000599	0.000257
FSASK	0.000483	0.000284
PPBDCM	0.000352	0.000272
FVBD	0.000341	0.000144
PSKBDCM	0.000338	0.000171
FQF	0.000325	0.000264
LSK	0.000321	0.000160
FQK	0.000035	0.000026
PKBDCM	0.000034	0.000013
FVF	0.000028	0.000019
PFBDCM	0.000024	0.000022
FVK	0.000010	0.000007
VFCBDCM	0.000001	0.000000

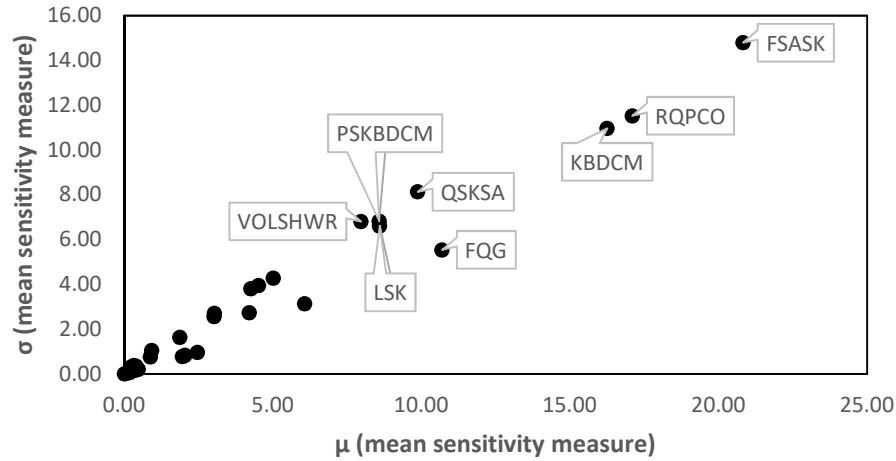


Showering 10 min BDCM 10 ppb Summary Morris GSA Results

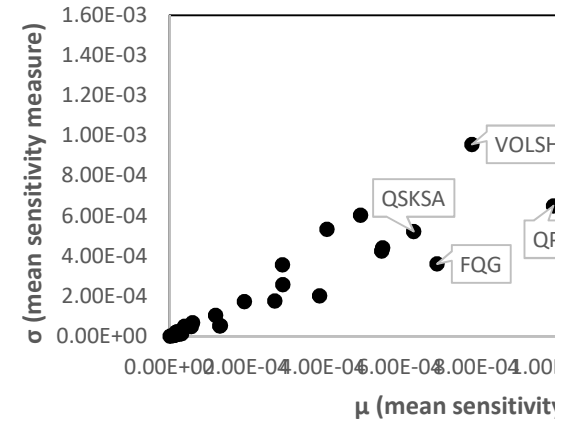
Response CvBDCM			Response Calv			Response AUCv		
Parameter	Mean	STDEV	Parameter	Mean	STDEV	Parameter	Mean	STDEV
FSASK	20.83	14.80	PBBDCM	1.67E-03	1.47E-03	FSASK	1.38E-02	7.06E-03
RQPCO	17.10	11.53	FSASK	1.35E-03	9.64E-04	RQPCO	1.09E-02	5.98E-03
KBDCM	16.26	10.97	RQPCO	1.25E-03	8.90E-04	KBDCM	1.07E-02	5.40E-03
QPC	15.40	9.92	KBDCM	1.04E-03	7.03E-04	QPC	8.75E-03	5.43E-03
FQG	10.70	5.55	QPC	1.00E-03	6.51E-04	FQG	6.39E-03	3.64E-03
QSKSA	9.88	8.14	VOLSHWR	7.88E-04	9.57E-04	VOLSHWR	5.60E-03	2.59E-03
LSK	8.60	6.62	FQG	6.97E-04	3.61E-04	QSKSA	4.99E-03	1.98E-03
PSKBDCM	8.58	6.82	QSKSA	6.36E-04	5.23E-04	FQL	3.59E-03	2.05E-03
VOLSHWR	7.97	6.81	PSKBDCM	5.55E-04	4.41E-04	KOLA	3.47E-03	1.60E-03
FQL	6.07	3.14	LSK	5.52E-04	4.25E-04	PSKBDCM	3.41E-03	1.49E-03
KOLA	5.02	4.28	KOLA	4.97E-04	6.04E-04	LSK	3.29E-03	1.49E-03
PRBDCM	4.53	3.96	AIREXCHANGE	4.09E-04	5.35E-04	AIREXCHANGE	2.90E-03	1.41E-03
AIREXCHANGE	4.26	3.81	FQL	3.90E-04	2.02E-04	DEADSPACE	2.45E-03	1.52E-03
DEADSPACE	4.21	2.75	PRBDCM	2.95E-04	2.58E-04	QW	2.11E-03	9.74E-04
FVBD	3.03	2.71	QW	2.94E-04	3.57E-04	PRBDCM	1.77E-03	8.00E-04
QW	3.02	2.57	DEADSPACE	2.74E-04	1.77E-04	PBBDCM	1.33E-03	8.35E-04
PBBDCM	2.47	0.97	FVBD	1.95E-04	1.73E-04	FVBD	1.03E-03	5.06E-04
FQF	2.05	0.84	FQF	1.32E-04	5.38E-05	PPBDCM	9.30E-04	7.00E-04
PPBDCM	1.96	0.79	PPBDCM	1.30E-04	5.24E-05	FQF	8.86E-04	7.02E-04
FVL	1.88	1.64	FVL	1.19E-04	1.04E-04	FVL	7.19E-04	3.24E-04
FQK	0.93	1.06	FQK	5.96E-05	6.76E-05	FVGI	3.44E-04	1.55E-04
FVGI	0.89	0.77	FVGI	5.63E-05	4.93E-05	V1CBDCM	2.76E-04	1.58E-04
V1CBDCM	0.47	0.22	TEMP	3.90E-05	5.10E-05	TEMP	2.76E-04	1.34E-04
TEMP	0.40	0.36	V1CBDCM	3.11E-05	1.43E-05	KM1BDCM	2.24E-04	1.28E-04
KM1BDCM	0.37	0.17	KM1BDCM	2.42E-05	1.11E-05	PLBDCM	1.18E-04	6.74E-05
PKBDCM	0.32	0.38	PKBDCM	2.04E-05	2.42E-05	PWSBDCM	1.15E-04	6.26E-05
FVK	0.25	0.32	FVK	1.64E-05	2.08E-05	FQK	1.09E-04	9.45E-05
PLBDCM	0.19	0.09	PLBDCM	1.29E-05	5.90E-06	PKBDCM	9.93E-05	4.62E-05
PWSBDCM	0.18	0.13	PWSBDCM	1.17E-05	8.35E-06	FVF	6.90E-05	4.71E-05
PFBDCM	0.18	0.09	PFBDCM	1.16E-05	6.12E-06	PFBDCM	6.67E-05	5.94E-05

FVF	0.14	0.06	FVF	9.17E-06	3.89E-06	FVK	3.01E-05	2.80E-05
PGBDCM	0.01	0.01	PGBDCM	8.02E-07	8.56E-07	PGBDCM	4.37E-06	2.04E-06

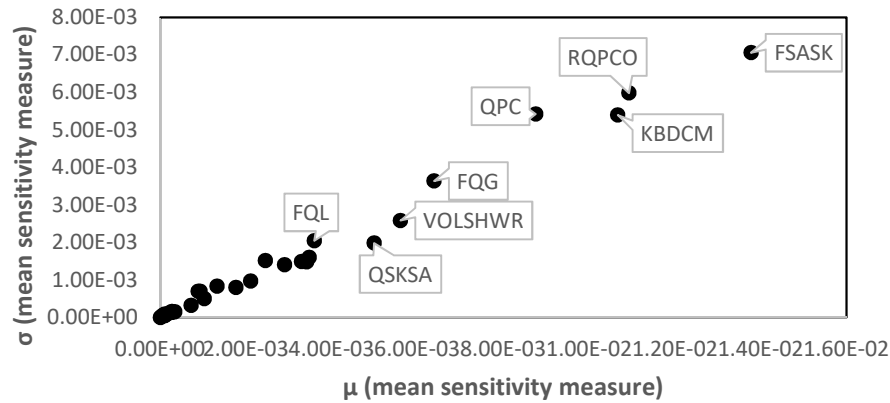
A. CvBDCM



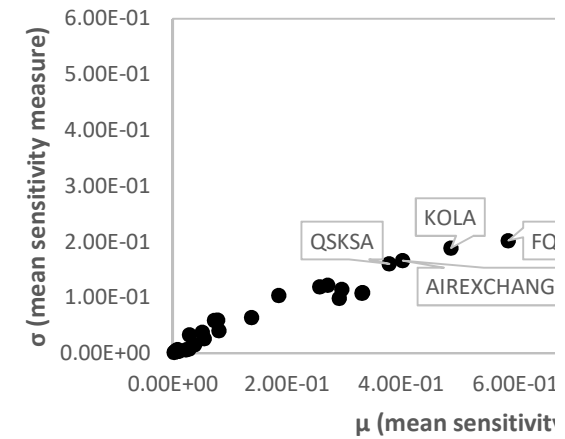
B. Calv



C. AUCv



D. MBDCM



Response	MBDCM	
	Mean	STDEV
FSASK	1.06E+00	5.71E-01
QPC	1.02E+00	3.47E-01
KBDCM	8.33E-01	4.45E-01
VOLSHWR	7.84E-01	3.04E-01
FQG	5.87E-01	2.02E-01
KOLA	4.87E-01	1.89E-01
AIREXCHANGE	4.03E-01	1.66E-01
QSKSA	3.79E-01	1.61E-01
RQPCO	3.32E-01	1.09E-01
FQL	3.31E-01	1.08E-01
QW	2.96E-01	1.15E-01
DEADSPACE	2.91E-01	9.92E-02
PSKBDCM	2.71E-01	1.22E-01
LSK	2.57E-01	1.19E-01
PBBDCM	1.85E-01	1.04E-01
PRBDCM	1.38E-01	6.46E-02
FVBD	8.06E-02	4.11E-02
PPBDCM	7.82E-02	6.00E-02
FQF	7.28E-02	5.91E-02
FVL	5.52E-02	2.63E-02
PGBDCM	5.17E-02	3.78E-02
TEMP	3.82E-02	1.58E-02
FVGI	2.89E-02	3.34E-02
V1CBDCM	2.86E-02	8.39E-03
KM1BDCM	2.28E-02	6.69E-03
PLBDCM	1.09E-02	4.03E-03
PWSBDCM	8.81E-03	5.04E-03
FQK	8.40E-03	7.04E-03
PKBDCM	7.74E-03	3.61E-03
FVF	5.96E-03	4.12E-03

PFBDCM	5.16E-03	4.70E-03
FVK	2.32E-03	2.05E-03

