Electronic Supplementary Material (ESI) for Analytical Methods

Optimization of solid phase extraction chromatography for the separation of Np from U and Pu using experimental design tools in Complex Matrices

Electronic Supplementary Information

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Table S1. Extraction data for the 2^3 half-fractional factorial experiment in the Step A.

R	**A**	**S**	**^{237}Np ext., %**	**^{242}Pu ext., %**	**^{238}U ext., %**
TEVA	0	10	14.2	96.9	42.8
DGA	2	10	11.5	96.0	6.1*
TEVA	2	0	16.8	2.5	-15.7*
DGA	0	0	23.4	98.1	95.3
TEVA	2	0	18.4	-2.7	0.7
TEVA	2	0	18.2	12.5	-1.0
DGA	0	0	24.7	98.4	98.7
TEVA	0	10	14.9	93.6	43.5
DGA	2	10	16.0	97.0	63.2
DGA	0	0	25.3	98.3	98.2
TEVA	0	10	14.9	92.4	45.4
DGA	2	10	17.2	96.9	61.9

R: resin; **A**: HNO_3 acidity (pH); **S**: sulfamic acid (mM). *Value not considered after residual analysis.

Table S2. Extraction data for the 2^3 half-fractional factorial experiment in Step B.

R	**A**	**S**	**^{237}Np ext., %**	**^{238}U ext., %**
UTEVA	2	10	13.7	30.6
DGA	0	10	15.6	97.9
DGA	2	30	10.8	25.7
DGA	0	10	16.9	85.6
UTEVA	2	10	14.7	29.8
UTEVA	0	30	14.5	86.8
UTEVA	0	30	11.8	92.9
DGA	2	30	12.2	17.2
DGA	0	10	15.0	83.2
UTEVA	2	10	12.6	29.5
UTEVA	0	30	13.0	85.6
DGA	2	30	9.7	14.4

R: resin; **A**: HNO_3 acidity (pH); **S**: sulfamic acid (mM)

Table S3. Extraction data for the full 2^3 factorial experiment in Step A.

A	**S**	**V**	**^{237}Np Ext., %**	**^{242}Pu Ext., %**	**^{238}U Ext., %**
2	12	6	15.6	92.5	32.5
1	8	8	10.2	92.2	47.8
2	4	10	6.1	91.8	10.8
1	8	8	5.7*	92.1*	24.1*
0	4	10	9.9	93.7	95.9
0	12	10	9.9	94.2	95.3
0	12	6	8.4	94.5	98.1
2	12	10	9.0	92.6	23.0
1	8	8	10.8	92.7	47.9
1	8	8	10.7	92.8	48.5
2	4	6	13.2	93.1	32.9
0	4	6	18.8	94.3	97.8

A: HNO_3 acidity (pH); **S**: sulfamic acid (mM); **V**: volume (mL). *Value not considered after residual analysis.

Table S4. Extraction data for the full 2^3 factorial experiment in Step B.

A	S	V	^{237}Np Ext., %	^{238}U Ext., %
2	10	10	6.8	-1.2
2	30	10	4.5	-9.5
0	30	6	5.5	99.5
1	20	8	2.5	100.0
2	30	6	6.5	99.9
0	10	6	6.2	100.1
0	10	10	-6.5	100.1
1	20	8	3.3	99.6
2	10	6	8.0	100.0
1	20	8	4.2	100.0
1	20	8	4.4	100.1
0	30	10	-4.1	100.2

A: HNO_3 acidity (pH); **S**: sulfamic acid (mM); **V**: volume (mL)

Table S5. Analysis of Variance for the 2^3 full factorial experiment in Step A for ^{237}Np extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
Straight line model	S_M= 110.7275	6	18.4546	F S_M/S_R 2.2494	p-value 0.1958
Residual	S_R= 41.0217 { S_L=23.0517, S_E=17.9700 }	5 { 2, 3 }	{ 11.5258, 5.9900 }	F S_L/S_E 0.2899	0.2899
Total	S_T= 151.7492	11		R^2	0.729675

Table S6. Analysis of Variance for the 2^3 full factorial experiment in Step A for ^{242}Pu extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
Straight line model	S_M= 6.6675	6	1.1113	F S_M/S_R 2.1194	p-value 0.2136
Residual	S_R= 2.6217 { S_L= 2.2517, S_E=0.3700 }	5 { 2, 3 }	{ 1.1258, 0.1233 }	F S_L/S_E 9.1284	0.0530
Total	S_T= 9.2892	11		R^2	0.717772

Table S7. Analysis of Variance for the 2^3 full factorial experiment in Step A for ^{238}U extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
Straight line model	S_M= 10667.908	6	1777.98	F S_M/S_R 6.407	p-value 0.030*
Residual	S_R= 1387.622 { S_L= 956.535, S_E=431.088 }	5 { 2, 3 }	{ 478.268, 143.696 }	F S_L/S_E 3.328	0.173
Total	S_T= 12055.530	11		R^2	0.884897

*Significant result

Table S8. Analysis of Variance for the 2^3 full factorial experiment in Step B for ^{237}Np extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
				F_{S_M/S_R}	p-value
Straight line model	S_M= 208.138	6	34.690	39.858	0.0005*
Residual	S_R= 4.352 { S_L=2.052, S_E=2.300 }	5 { 2, 3 }	{ 1.026, 0.767 }	F_{S_L/S_E} 1.338	0.3840
Total	S_T= 212.490	11		R^2	0.979521

*Significant result

Table S9. Analysis of Variance for the 2^3 full factorial experiment in Step B for ^{238}U extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
				F_{S_M/S_R}	p-value
Straight line model	S_M= 16662.258	6	2777.04	7.494	0.0215*
Residual	S_R= 1852.803 { S_L= 1852.655, S_E=0.148 }	5 { 2, 3 }	{ 926.328, 0.049 }	F_{S_L/S_E} 18840.56	<0.0001*
Total	S_T= 18515.060	11		R^2	0.89993

*Significant result

Table S10. Additional extraction data for the augmented 2^3 full factorial experiment in Step A.

A	**S**	**V**	**^{237}Np Ext., %**	**^{242}Pu Ext., %**	**^{238}U Ext., %**
1	1.5	8	9.9	93.1	49.1
2.6	8	8	11.6	92	26.7
1	8	11.3	5.7	91.8	33.3
1	8	8	8.9	91.5	20.9
1	14.5	8	11.7	92.8	48.4
1	8	8	11.8	92.6	48.6
-0.6	8	8	*	88.7	99.8
1	8	4.7	20.5	93.3	71.5

A: HNO_3 concentration (pH); **S**: sulfamic acid concentration (mM); **V**: volume (mL)

Table S11. Additional extraction data for the augmented 2^3 full factorial experiment in Step B.

A	**S**	**V**	**^{237}Np Ext., %**	**^{238}U Ext., %**
0	20	8	2.8	100.2
1	10	8	2.5	100.1
2	20	8	3.5	99.9
1	20	8	5.1	100.1
1	20	6	8.9	100.1
1	30	8	3.2	100.1
1	20	8	3.0	100.1
1	20	10	7.7	61.3

A: HNO_3 acidity (pH); **S**: sulfamic acid concentration (mM); **V**: volume (mL)

Table S12. Analysis of Variance for the augmented 2^3 full factorial experiment in Step A for ^{237}Np extraction.

Source	Sum of Squares		Degrees of Freedom		Mean Square		Significance analysis	
Quadratic model	S_M= 224.4668		9		24.9408		F S_M/S_R 4.1680	p-value 0.0225*
Residual	S_R= 53.8543	S_L=30.3460 S_E=23.5083	9	4 5	11.5258 5.9900		F S_L/S_E 1.9236	0.3032
Total	S_T= 278.3211		18				R^2	0.808503

*Significant result

Table S13. Analysis of Variance for the augmented 2^3 full factorial experiment in Step A.2 for ^{242}Pu extraction.

Source	Sum of Squares		Degrees of Freedom		Mean Square		Significance analysis	
Quadratic model	S_M= 11.8947		9		1.3216		F S_M/S_R 6.6196	p-value 0.0048*
Residual	S_R= 1.7969	S_L=0.6086 S_E=1.1883	9	4 5	0.1521 0.2377		F S_L/S_E 0.6401	0.6568
Total	S_T= 13.6916		18				R^2	0.868759

*Significant result

Table S14. Analysis of Variance for the augmented 2^3 full factorial experiment in Step A.2 for ^{238}U extraction.

Source	Sum of Squares		Degrees of Freedom		Mean Square		Significance analysis	
Quadratic model	S_M= 13318.401		9		1479.82		F S_M/S_R 11.8785	p-value 0.0005*
Residual	S_R= 1121.223	S_L=234.950 S_E=886.273	9	4 5	58.737 177.255		F S_L/S_E 0.3314	0.8465
Total	S_T= 14439.624		18				R^2	0.922351

*Significant result

Table S15. Analysis of Variance for the augmented 2^3 full factorial experiment in Step B for ^{237}Np extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
Quadratic model	S_M= 234.367	9	26.048	F S_M/S_R	p-value
				19.094	0.0002*
Residual	S_R= 10.910 { S_L=6.135, S_E=4.775 }	8 { 3, 5 }	{ 2.045, 0.955 }	F S_L/S_E	
				2.142	0.2135
Total	S_T= 245.278	17		R^2	0.955518

*Significant result

Table S16. Analysis of Variance for the augmented 2^3 full factorial experiment in Step B for ^{238}U extraction.

Source	Sum of Squares	Degrees of Freedom	Mean Square	Significance analysis	
Quadratic model	S_M= 19570.878	9	2174.54	F S_M/S_R	p-value
				87.107	<0.0001 *
Residual	S_R= 199.712 { S_L=199.524, S_E=0.188 }	8 { 3, 5 }	{ 58.737, 177.255 }	F S_L/S_E	
				1765.695	<0.0001 *
Total	S_T= 19770.589	17		R^2	0.989899

*Significant result

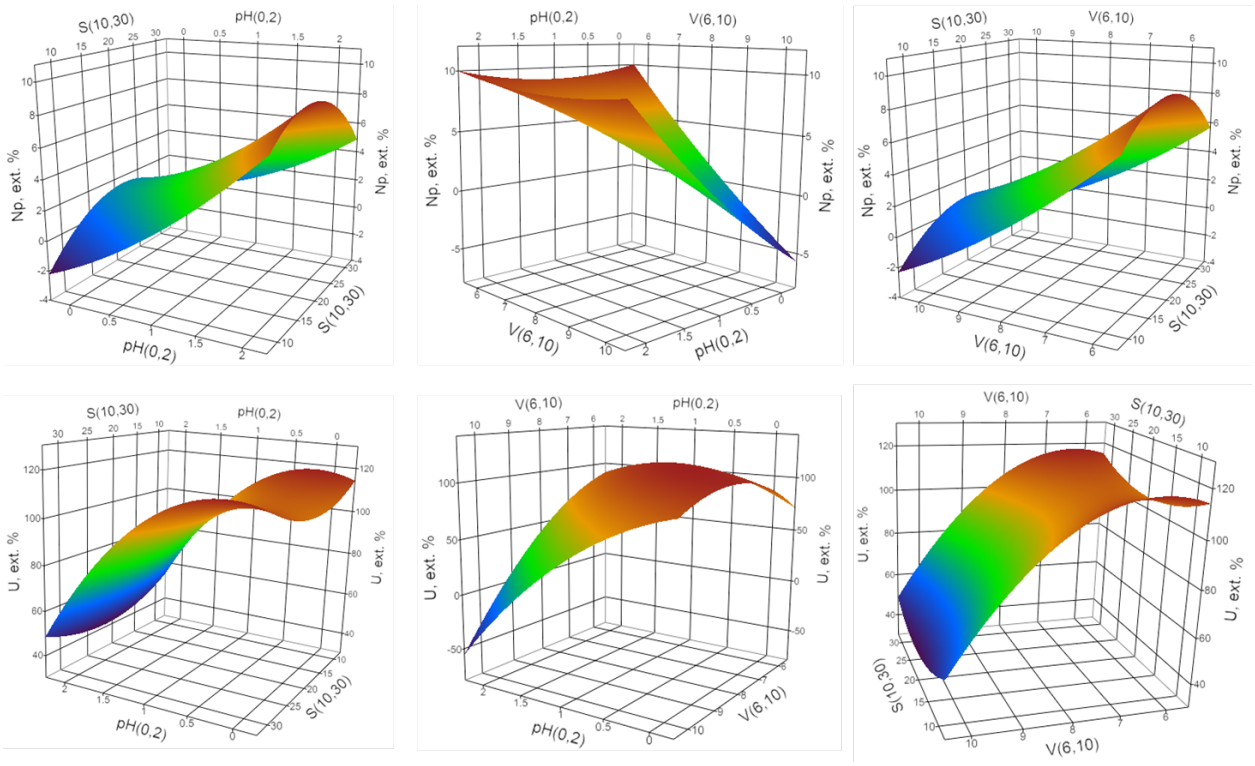

Figure S1. Surface plots generated from the augmented 2^3 full factorial experiment extraction data using the central composite design in Step B. **A**: HNO_3 acidity (pH); **S**: sulfamic acid (mM); **V**: volume (mL).

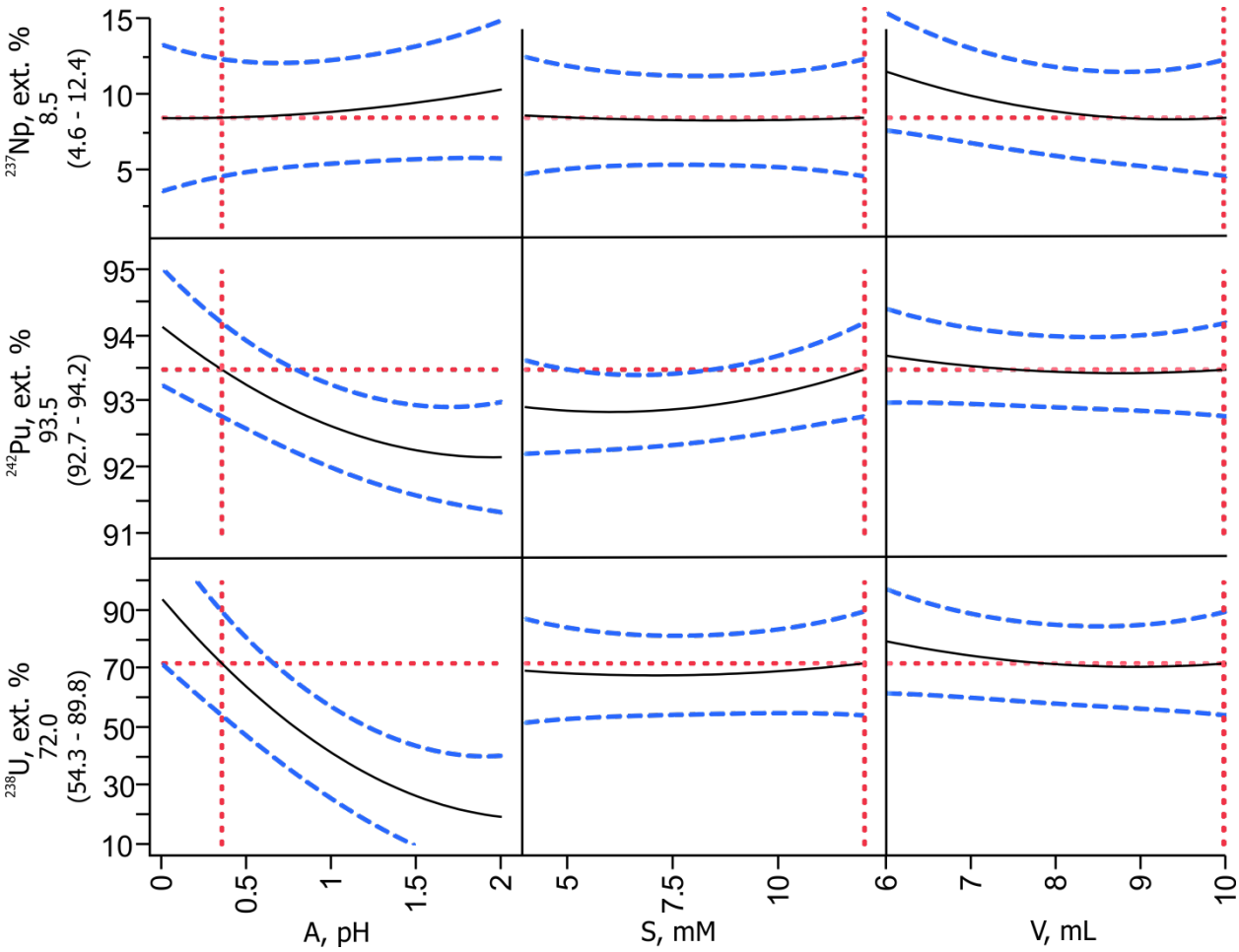

Figure S2. Profile of the predicted responses generated from the calculated quadratic models using the augmented 2^3 full factorial experiment extraction data and the central composite design in Step A. **A**: HNO_3 acidity (pH); **S**: sulfamic acid (mM); **V**: volume (mL). Black full lines: predicted mean response. Blue dotted lines: 95% confidence intervals for the mean response. Red dotted lines: fixed factor values (vertical) and expected extraction response (horizontal). Y-axis values: response mean and confidence interval values for fixed factor levels: HNO_3 acidity of pH 0.35, sulfamic acid 12 mM and volume 10 mL.

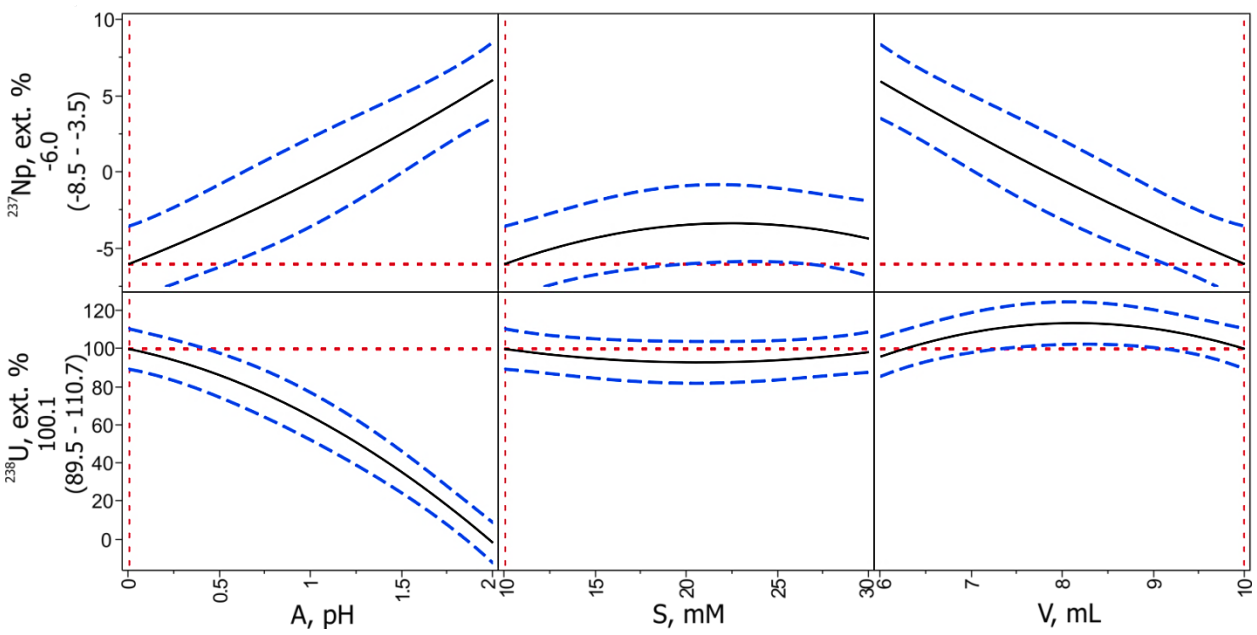

Figure S3. Profile of the predicted responses generated from the calculated quadratic models using the augmented 2^3 full factorial experiment extraction data using the central composite design in Step B. **A**: HNO_3 acidity (pH); **S**: sulfamic acid (mM); **V**: volume (mL). Black full lines: predicted mean response. Blue dotted lines: 95% confidence intervals for the mean response. Red dotted lines: fixed factor values (vertical) and expected extraction response (horizontal). *Y*-axis values: response mean and confidence interval values for fixed factor levels: HNO_3 acidity of pH 0, sulfamic acid 10 mM and volume 10 mL.

Example of main effects calculation

Main effect = $\bar{y}_+ - \bar{y}_-$

$\bar{y}_+$ is the average response on one face of the cube corresponding to the plus level of the factor

$\bar{y}_-$ is the average response on the opposite face of the cube for its minus level of the factor

Resin	**Coded units**	**^{237}Np ext., %**
TEVA	+	14.2
DGA	-	11.5
TEVA	+	16.8
DGA	-	23.4
TEVA	+	18.4
TEVA	+	18.2
DGA	-	24.7
TEVA	+	14.9
DGA	-	16.0
DGA	-	25.3
TEVA	+	14.9
DGA	-	17.2
	Total	-20.7
	Divisor	6
	Average	-3.5

$$\text{Resin effect} = \frac{14.2 + 16.8 + 18.4 + 18.2 + 14.9 + 14.9}{6} - \frac{11.5 + 23.4 + 24.7 + 16.0 + 25.3 + 17.2}{6}$$

$$\text{Resin effect} = -3.5$$

Example of interaction effects calculation

Two-factor interaction

A	S	A, coded units	S, coded units	Interaction, A x S	^{237}Np Ext., %
2	12	+	+	+	15.6
2	4	+	-	-	6.1
0	4	-	-	+	9.9
0	12	-	+	-	9.9
0	12	-	+	-	8.4
2	12	+	+	+	9.0
2	4	+	-	-	13.2
0	4	-	-	+	18.8
			Total		15.7
			Divisor		4
			Average		3.9

A: HNO_3 concentration (M); **S**: sulfamic acid concentration (mM)

$$\text{Interaction AxS effect} = \frac{15.6 + 9.9 + 9.0 + 18.8}{4} - \frac{6.1 + 9.9 + 8.4 + 13.2}{4}$$

$$\text{Interaction AxS effect} = 3.9$$

Estimate of standard error of the effects from replicate runs

- Estimate the variance σ^2 from samples.

$$s_+^2 = \frac{\sum(y_+ - \bar{y}_+)^2}{n_+ - 1}$$

$$s_-^2 = \frac{\sum(y_- - \bar{y}_-)^2}{n_- - 1}$$

- Assume a common σ^2. Then a pooled s^2 can be calculated.

$$s^2 = \frac{\sum(y_+ - \bar{y}_+)^2 + \sum(y_- - \bar{y}_-)^2}{n_+ + n_- - 2}$$

$$V(\bar{y}_+ - \bar{y}_-) = \frac{\sigma^2}{n_+} + \frac{\sigma^2}{n_-} = s^2\left(\frac{1}{n_+} + \frac{1}{n_-}\right)$$

- Standard error

$$S.E.(effect) = \sqrt{V(\bar{y}_+ - \bar{y}_-)} = s\sqrt{\frac{1}{n_+} + \frac{1}{n_-}}$$

Estimate the standard error of the effects from replicate center points

$$s_{cp}^2 = \frac{\sum\left(y_{cp} - \bar{y}_{cp}\right)^2}{n_{cp} - 1}$$

$$S.E.(effect) = \sqrt{s_{cp}^2}$$

Establish the significance of an effect

The challenge is to determine a threshold ratio effect/S.E.(effect) value above which we can consider the effect significant. On, NIID assumptions, each ratio effect/S.E.(effect) will form a *t* distribution with ν degrees of freedom (d.f.). The number of d.f. depends on how many times each

experiment was replicated; a duplicate experiment provides one d.f. and an experiment performed in triplicate provides two d.f.

As an example, if we consider the half-fractional factorial experimental data of ^{237}Np extraction in Step A, we tested four different set of conditions in triplicate. So, the number of d.f. is 8, since each set of conditions provides two d.f. Then, for $\nu = 8$ a significant value of t at the 5% level is 2.3, that is, $\Pr(|t_8|) > 2.3) = 0.05$; thus the 95% confidence interval for an effect would be given by the estimated effect ± 2.3 x S.E.(effect).