

Solketal production in a solvent-free continuous flow process: scaling from laboratory to bench size

1.1 Preliminary tests

The experimental work in batch reactors was performed using ethanol as solvent. In order to ensure that there was no interaction between the reactants and the solvent, all final mixtures were analyzed by GC-FID. One of these effluent chromatograms is shown in Fig. S1. As can be verified, there is not a significant signal of any products except for solketal and solketal-ISO (C5 and C6, respectively) and no condensation products involving ethanol were detected. The same can be asserted with acetone, which could be involved in aldolic condensation in an acidic medium. The signals corresponding to the aldolic condensation product (4-hidroxi-4-methyl-pentanone, known as di-acetone-alcohol and 4-methylpent-3-en-2-one, mesityl oxide) can be considered negligible compared to the initial acetone amount.

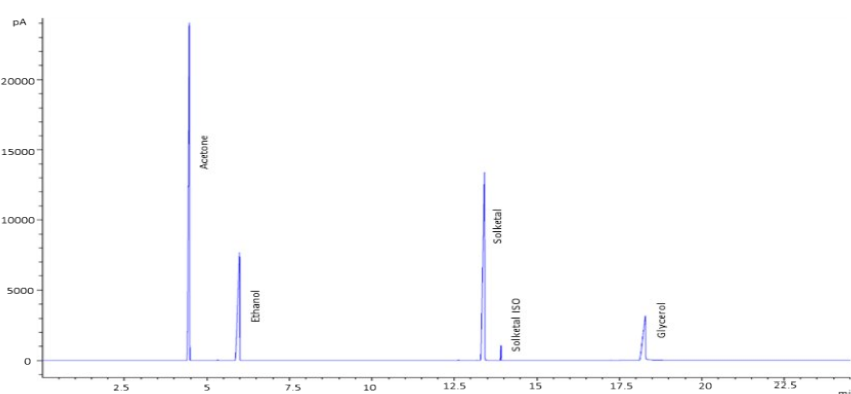


Fig. S1. Acetalization effluent chromatogram

Based on these observations, and taking into account that the proportion of dioxolane and dioxane was C5/C6 of 99/1 and there were no significant differences in their characteristics, the conversion (X_{Glyc}) was considered as the formation of both isomers

as the desired product throughout this study. Hence, from the fact that there were no undesirable reactions, selectivity (S) could be considered as 100 %, and therefore conversion (X) was equal to yield (Y).

Table S1A - Experimental data Figure 5

Test 1:150 rpm		Test 2:250 rpm		Test 3:350 rpm	
t (min)	X _{Glyc}	t (min)	X _{Glyc}	t (min)	X _{Glyc}
0	0	0	0.00	0	0
2.5	0.16	2	0.19	1.5	0.17
5	0.28	5	0.32	5	0.30
5.5	0.37	8	0.45	6	0.40
7.5	0.44	10	0.52	7.5	0.47
10	0.50	12	0.56	10	0.52
12.5	0.53	15	0.59	12.5	0.56
15	0.57	18	0.61	15	0.58
17.5	0.59	20	0.63	17.5	0.60
20	0.61	30	0.64	20	0.61
22.5	0.62	45	0.65	25	0.62
25	0.64			30	0.64
30	0.65			35	0.65
35	0.66			40	0.65
40	0.65			45	0.65
45	0.65			45	0.65

Table S1B - Experimental data Figure 5

Test 1: 323 K, 3 wt.% cat, MR _{A/G} =2, 150 rpm				
t (min)	C _{Glyc} (mol/L)	C _{Acet} (mol/L)	C _{solketal} (mol/L)	C _{wat} (mol/L)
0	3.59	7.18	0.00	0.07
2.5	3.03	6.62	0.56	0.64
5	2.59	6.18	1.00	1.07
5.5	2.26	5.85	1.33	1.40
7.5	2.01	5.60	1.58	1.65
10	1.82	5.41	1.77	1.85
12.5	1.67	5.26	1.92	1.99
15	1.56	5.15	2.03	2.10
17.5	1.47	5.06	2.11	2.19
20	1.41	5.00	2.18	2.25
22.5	1.36	4.95	2.23	2.30
25	1.30	4.89	2.28	2.36
30	1.26	4.85	2.33	2.41
35	1.23	4.82	2.36	2.43
40	1.24	4.83	2.34	2.42
45	1.24	4.83	2.34	2.42

Table S1C - Experimental data Figure 5

Test 2: 323 K, 3 wt.% cat, $MR_{A/G}=2$, 250 rpm				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	3.589	7.178	0.000	0.074
2	2.907	6.496	0.682	0.756
5	2.440	6.029	1.148	1.222
8	1.974	5.563	1.615	1.689
10	1.723	5.311	1.866	1.940
12	1.579	5.168	2.010	2.084
15	1.471	5.060	2.117	2.191
18	1.400	4.988	2.189	2.263
20	1.328	4.917	2.261	2.335
30	1.292	4.881	2.297	2.371
45	1.256	4.845	2.333	2.407

Table S1D - Experimental data Figure 5

Test 3: 323 K, 3 wt.% cat, $MR_{A/G}=2$, 350 rpm				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	3.59	7.18	0.00	0.07
1.5	2.97	6.55	0.62	0.70
5	2.50	6.09	1.09	1.17
6	2.15	5.74	1.44	1.51
7.5	1.90	5.49	1.69	1.76
10	1.72	5.31	1.87	1.94
12.5	1.59	5.18	2.00	2.07
15	1.50	5.09	2.08	2.16
17.5	1.44	5.03	2.15	2.22
20	1.39	4.98	2.19	2.27
25	1.36	4.95	2.23	2.30
30	1.29	4.88	2.30	2.37
35	1.25	4.84	2.34	2.41
40	1.24	4.83	2.35	2.42
45	1.24	4.83	2.34	2.42
45	1.24	4.83	2.34	2.42

Table S2A - Experimental data Figure 6

Test 4: $D_p < 160 \mu\text{m}$		Test 5: $160 \mu\text{m} < D_p < 500 \mu\text{m}$		Test 6: $500 \mu\text{m} < D_p < 1\text{mm}$	
t (min)	X_{Glyc}	t (min)	X_{Glyc}	t (min)	X_{Glyc}
0	0.00	0	0	0	0.00
2.5	0.15	2.5	0.16	1.5	0.13
5	0.27	5	0.28	3	0.24
6	0.38	6	0.38	6	0.34
7.5	0.47	7.5	0.45	7.5	0.42
10	0.54	10	0.52	10	0.49
15	0.67	15	0.62	15	0.61
20	0.74	17.5	0.69	20	0.69
25	0.77	20	0.74	25	0.75
30	0.79	30	0.78	30	0.78
40	0.80	40	0.81	35	0.81
45	0.81	50	0.83	40	0.83
50	0.84	60	0.84	50	0.85
60	0.84			60	0.85

Table S2B - Experimental data Figure 6

Test 4: 323 K, 3 wt.% cat, $MR_{A/G}=6$, $D_p < 160 \mu\text{m}$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	C_{solketal} (mol/L)	C_{wat} (mol/L)
0	1.75	10.47	0.00	0.08
2	1.49	10.22	0.26	0.34
4	1.27	10.00	0.48	0.56
6	1.08	9.81	0.66	0.74
8	0.93	9.66	0.82	0.90
10	0.80	9.53	0.94	1.03
15	0.58	9.31	1.17	1.25
20	0.46	9.19	1.29	1.37
25	0.40	9.13	1.35	1.43
30	0.37	9.10	1.38	1.46
35	0.35	9.08	1.39	1.48
40	0.33	9.06	1.41	1.50
50	0.28	9.01	1.47	1.55

Table S2C - Experimental data Figure 6

Test 5: 323 K, 3 wt.% cat, $MR_{A/G}=6$, $160 \mu\text{m} < D_p < 500 \mu\text{m}$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	C_{solketal} (mol/L)	C_{wat} (mol/L)
0	1.15	11.53	0.00	0.08
2	0.97	11.35	0.18	0.26
4	0.83	11.21	0.32	0.41
6	0.72	11.10	0.44	0.52
8	0.63	11.01	0.52	0.61
10	0.56	10.94	0.60	0.68
15	0.44	10.82	0.72	0.80
20	0.36	10.74	0.80	0.88
25	0.30	10.68	0.86	0.94
30	0.25	10.63	0.90	0.99
35	0.22	10.60	0.94	1.02
40	0.19	10.58	0.96	1.04
50	0.28	9.01	1.47	1.55

Table S2D - Experimental data Figure 6

Test 6: 323 K, 3 wt.% cat, $MR_{A/G}=6$, $D_p < 1 \text{ mm}$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	C_{solketal} (mol/L)	C_{wat} (mol/L)
0	1.75	10.47	0.00	0.08
2	1.51	10.23	0.24	0.32
4	1.31	10.04	0.44	0.52
6	1.14	9.87	0.60	0.68
8	1.01	9.74	0.74	0.82
10	0.90	9.62	0.85	0.93
15	0.68	9.41	1.06	1.14
20	0.53	9.26	1.21	1.29
25	0.42	9.15	1.32	1.40
30	0.34	9.07	1.40	1.48
35	0.30	9.02	1.45	1.53
40	0.28	9.01	1.47	1.55
50	0.28	9.01	1.47	1.55

Table S3A - Experimental data Figure 7

Test 9: RM10		Test 8: RM6		Test 7:RM2	
t (min)	X _{Glyc}	t (min)	X _{Glyc}	t (min)	X _{Glyc}
0	0.00	0	0.00	0	0.00
4	0.08	8	0.19	4	0.12
8	0.15	15	0.34	12	0.22
15	0.21	30	0.45	15	0.30
25	0.27	45	0.54	22	0.37
20	0.33	50	0.60	25	0.42
35	0.38	60	0.65	30	0.47
30	0.42	75	0.69	35	0.50
40	0.46	90	0.72	40	0.53
50	0.50	95	0.76	45	0.56
45	0.53	120	0.78	50	0.58
55	0.56	130	0.81	60	0.63
60	0.59	140	0.82	90	0.65
80	0.66	150	0.84	110	0.67
90	0.71	180	0.86	130	0.68
120	0.78	240	0.87	150	0.69
180	0.86			170	0.69
240	0.90			190	0.70
270	0.91			200	0.70
320	0.91				

Table S3B - Experimental data Figure 7

Test 9: 298 K, 3 wt.% cat, MR _{A/G} =10				
t (min)	C _{Glyc} (mol/L)	C _{Acet} (mol/L)	C _{solketal} (mol/L)	C _{wat} (mol/L)
0	1.15	11.53	0.00	0.08
5	1.06	11.45	0.09	0.17
10	0.98	11.36	0.17	0.25
15	0.91	11.29	0.24	0.33
20	0.84	11.22	0.31	0.40
25	0.78	11.16	0.38	0.46
30	0.72	11.10	0.43	0.52
35	0.67	11.05	0.48	0.57
40	0.62	11.00	0.53	0.62
45	0.58	10.96	0.58	0.66
50	0.54	10.92	0.61	0.70
55	0.50	10.88	0.65	0.73
60	0.47	10.85	0.68	0.77
75	0.39	10.77	0.76	0.85
90	0.33	10.71	0.82	0.91
120	0.25	10.63	0.90	0.99
180	0.16	10.54	0.99	1.08
240	0.12	10.50	1.04	1.12
270	0.11	10.49	1.05	1.13
320	0.11	10.49	1.05	1.13

Table S3C - Experimental data Figure 7

Test 8: 298 K, 3 wt.% cat, $MR_{A/G}=6$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	1.75	10.47	0.00	0.08
8	1.41	10.14	0.34	0.42
15	1.15	9.88	0.59	0.68
30	0.96	9.68	0.79	0.87
45	0.81	9.54	0.94	1.02
50	0.70	9.42	1.05	1.13
60	0.61	9.34	1.14	1.22
75	0.54	9.27	1.20	1.28
90	0.49	9.22	1.25	1.33
95	0.42	9.15	1.33	1.41
120	0.39	9.11	1.36	1.44
130	0.33	9.06	1.41	1.49
140	0.31	9.04	1.43	1.51
150	0.29	9.02	1.45	1.53
180	0.28	9.01	1.47	2.55
240	0.26	8.99	1.48	1.56

Table S3D - Experimental data Figure 7

Test 7: 298 K, 3 wt.% cat, $MR_{A/G}=2$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	3.59	7.18	0.00	0.07
4	3.16	6.75	0.43	0.51
12	2.80	6.39	0.79	0.86
15	2.51	6.09	1.08	1.16
22	2.26	5.85	1.32	1.40
25	2.07	5.66	1.52	1.60
30	1.91	5.50	1.68	1.76
35	1.78	5.37	1.81	1.89
40	1.67	5.26	1.92	1.99
45	1.59	5.18	2.00	2.08
50	1.52	5.11	2.07	2.15
60	1.35	4.93	2.24	2.32
90	1.25	4.84	2.34	2.41
110	1.19	4.78	2.40	2.47
130	1.15	4.74	2.44	2.51
150	1.12	4.71	2.47	2.54
170	1.10	4.68	2.49	2.57
190	1.08	4.66	2.51	2.59
200	1.08	4.67	2.51	2.59

Table S4A - Experimental data Figure 8

Test 10: 298 K		Test 11: 308 K		Test 12: 323 K	
t (min)	X _{Glyc}	t (min)	X _{Glyc}	t (min)	X _{Glyc}
0	0.00	0	0.00	0	0.00
10	0.20	10	0.30	15	0.46
30	0.35	30	0.50	20	0.70
40	0.45	40	0.63	35	0.80
45	0.55	60	0.70	60	0.86
60	0.63	75	0.82	75	0.89
75	0.68	90	0.86	90	0.90
90	0.72	120	0.89	120	0.90
100	0.75	150	0.90	180	0.90
120	0.81	180	0.91	240	0.90
150	0.85	240	0.91	300	0.90
160	0.87	300	0.91		
180	0.89				
240	0.91				
300	0.91				

Table S4B - Experimental data Figure 8

Test 10: 298 K, 3 wt.% cat, MR _{A/G} =10				
t (min)	C _{Glyc} (mol/L)	C _{Acet} (mol/L)	C _{solketal} (mol/L)	C _{wat} (mol/L)
0	0.91	9.08	0.00	0.07
10	0.73	8.90	0.18	0.26
30	0.59	8.77	0.32	0.39
40	0.50	8.68	0.41	0.48
45	0.41	8.59	0.50	0.57
60	0.34	8.51	0.57	0.65
75	0.29	8.47	0.62	0.69
90	0.25	8.43	0.65	0.73
100	0.23	8.40	0.68	0.76
120	0.17	8.35	0.74	0.81
150	0.14	8.31	0.77	0.85
160	0.12	8.29	0.79	0.87
180	0.10	8.28	0.81	0.88
240	0.09	8.26	0.82	0.90
300	0.09	8.26	0.82	0.90

Table S4C - Experimental data Figure 8

Test 11: 308 K, 3 wt.% cat, $MR_{A/G}=10$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	0.91	9.08	0.00	0.07
10	0.64	8.81	0.27	0.35
30	0.45	8.63	0.45	0.53
40	0.34	8.52	0.57	0.64
60	0.27	8.45	0.64	0.71
75	0.16	8.34	0.74	0.82
90	0.13	8.30	0.78	0.86
120	0.10	8.28	0.81	0.88
150	0.09	8.27	0.82	0.89
180	0.08	8.26	0.83	0.90
240	0.08	8.26	0.83	0.90
300	0.08	8.26	0.83	0.90

Table S4D - Experimental data Figure 8

Test 12: 323 K, 3 wt.% cat, $MR_{A/G}=10$				
t (min)	C_{Glyc} (mol/L)	C_{Acet} (mol/L)	$C_{solketal}$ (mol/L)	C_{wat} (mol/L)
0	0.91	9.08	0.00	0.07
15	0.49	8.67	0.42	0.49
20	0.27	8.45	0.64	0.71
35	0.18	8.36	0.73	0.80
60	0.13	8.30	0.78	0.86
75	0.10	8.28	0.81	0.88
90	0.09	8.27	0.82	0.89
120	0.09	8.27	0.82	0.89
180	0.09	8.27	0.82	0.89
240	0.09	8.27	0.82	0.89
300	0.09	8.27	0.82	0.89

Table S5A - Experimental data Figure 9

Test 14: 5%		Test 2: 3%		Test 13: 1%	
t (min)	X _{Glyc}	t (min)	X _{Glyc}	t (min)	X _{Glyc}
0	0.00	0	0.00	0	0.00
2	0.31	2	0.21	4	0.15
5	0.48	4	0.35	8	0.27
7	0.56	8	0.45	15	0.35
10	0.60	10	0.52	20	0.43
15	0.64	12	0.56	30	0.47
20	0.65	15	0.59	25	0.52
30	0.65	18	0.61	35	0.55
45	0.65	20	0.63	40	0.57
		30	0.64	45	0.59
		45	0.65	55	0.60
				60	0.62
				70	0.62
				90	0.65
				120	0.65

Table S5B - Experimental data Figure 9

Test 13: 323 K, 5 wt.% cat, MR _{A/G} =2				
t (min)	C _{Glyc} (mol/L)	C _{Acet} (mol/L)	C _{solketal} (mol/L)	C _{wat} (mol/L)
0	3.59	7.18	0.00	0.07
2	2.48	6.07	1.11	1.19
5	1.87	5.46	1.72	1.80
7	1.58	5.17	2.01	2.08
10	1.44	5.02	2.15	2.23
15	1.29	4.88	2.30	2.37
20	1.26	4.84	2.33	2.41
30	1.26	4.84	2.33	2.41
45	1.26	4.84	2.33	2.41

Table S5C - Experimental data Figure 9

Test 14: 323 K, 1 wt.% cat, MR _{A/G} =2				
t (min)	C _{Glyc} (mol/L)	C _{Acet} (mol/L)	C _{solketal} (mol/L)	C _{wat} (mol/L)
0	3.589	7.178	0.000	0.074
2	2.835	6.424	0.754	0.828
4	2.333	5.922	1.256	1.330
8	1.974	5.563	1.615	1.689
10	1.723	5.311	1.866	1.940
12	1.579	5.168	2.010	2.084
15	1.471	5.060	2.117	2.191
18	1.400	4.988	2.189	2.263
20	1.328	4.917	2.261	2.335
30	1.292	4.881	2.297	2.371
45	1.256	4.845	2.333	2.407

Table S6 - Experimental / estimated data Figure 10

323 K		308 K		298 K	
dXdt_exp	dXdt_est	dXdt_exp	dXdt_est	dXdt_exp	dXdt_est
0.049	0.051	0.028	0.028	0.017	0.017
0.043	0.045	0.024	0.024	0.014	0.014
0.038	0.039	0.021	0.021	0.012	0.012
0.034	0.034	0.018	0.018	0.010	0.010
0.030	0.029	0.015	0.015	0.008	0.008
0.026	0.025	0.013	0.013	0.006	0.006
0.023	0.022	0.011	0.011	0.005	0.005
0.020	0.019	0.009	0.009	0.004	0.004
0.017	0.016	0.008	0.008	0.004	0.004
0.015	0.014	0.007	0.007	0.003	0.003
0.013	0.012	0.006	0.006	0.003	0.003
0.011	0.010	0.004	0.005	0.002	0.002
0.010	0.009	0.003	0.004	0.002	0.002
0.008	0.007	0.002	0.003	0.001	0.001
0.007	0.006	0.002	0.002	0.001	0.001
0.006	0.005	0.002	0.001	0.001	0.001
0.005	0.005	0.001	0.001		
0.004	0.003	0.001	0.000		
0.003	0.002	0.000	0.000		
0.002	0.002				
0.001	0.001				
0.001	0.000				
0.000	0.000				

Table S7 - Experimental/estimated data Figure 12

dXdt_exp	dXdt_est	dXdt_exp	dXdt_est	dXdt_exp	dXdt_est
0.022	0.021	0.068	0.061	0.030	0.035
0.017	0.016	0.058	0.051	0.021	0.021
0.013	0.013	0.049	0.043	0.015	0.015
0.010	0.010	0.040	0.036	0.010	0.011
0.007	0.008	0.033	0.029	0.008	0.009
0.006	0.006	0.019	0.018	0.006	0.007
0.004	0.005	0.010	0.011	0.005	0.005
0.003	0.004	0.005	0.007	0.003	0.002
0.003	0.004	0.002	0.004	0.002	0.000
0.002	0.003	0.002	0.003	0.000	0.000
0.002	0.003	0.003	0.002	0.000	0.000
0.002	0.002	0.000	0.000	0.089	0.101
0.002	0.002	0.026	0.029	0.069	0.073
0.001	0.002	0.022	0.024	0.053	0.053
0.001	0.001	0.018	0.020	0.040	0.038
0.001	0.001	0.015	0.016	0.031	0.028
0.001	0.001	0.012	0.013	0.023	0.021
0.001	0.001	0.010	0.011	0.018	0.016
0.001	0.000	0.008	0.009	0.014	0.012
0.000	0.000	0.007	0.008	0.010	0.006
0.000	0.000	0.005	0.007	0.008	0.006
0.000	0.000	0.004	0.006	0.006	0.004
0.000	0.000	0.003	0.005	0.003	0.002
0.076	0.072	0.002	0.003	0.002	0.000
0.062	0.060	0.001	0.002	0.001	0.000
0.052	0.051	0.001	0.001		
0.043	0.043	0.000	0.001		
0.035	0.036	0.000	0.000		
0.030	0.030	0.000	0.000		
0.020	0.018	0.000	0.000		
0.015	0.013	0.000	0.000		
0.011	0.008	0.034	0.034		
0.008	0.004	0.028	0.027		
0.004	0.001	0.023	0.022		
0.000	0.000	0.018	0.018		
0.000	0.000	0.015	0.015		
0.088	0.072	0.012	0.012		
0.070	0.061	0.010	0.010		
0.055	0.051	0.008	0.008		
0.043	0.043	0.006	0.007		
0.034	0.036	0.005	0.005		
0.027	0.031	0.000	0.004		
0.017	0.020	0.003	0.003		
0.012	0.013	0.003	0.003		
0.009	0.008	0.002	0.002		
0.007	0.005	0.001	0.001		
0.005	0.003	0.000	0.001		
0.003	0.001	0.000	0.001		
0.000	0.000	0.099	0.101		
0.080	0.072	0.075	0.074		

Table S8 – Experimental/estimated data Figure 14

313 K		323 K		333 K	
X _{Glyc_exp}	X _{Glyc_est}	X _{Glyc_exp}	X _{Glyc_est}	X _{Glyc_exp}	X _{Glyc_est}
0.56	0.5	0.73	0.75	0.85	0.84
0.57	0.5	0.78	0.75	0.77	0.77
0.68	0.64	0.74	0.77	0.78	0.81
0.68	0.66	0.66	0.66	0.88	0.85
0.69	0.59	0.78	0.78	0.84	0.85
		0.52	0.56	0.86	0.85
		0.62	0.66	0.85	0.91
		0.77	0.78	0.86	0.86
		0.61	0.66		
		0.9	0.86		
		0.82	0.84		
		0.87	0.85		
		0.86	0.85		
		0.87	0.89		
		0.91	0.89		
		0.83	0.85		

Estimation of the confidence intervals:

After estimating the kinetic and thermodynamic parameters (ps_{est}) as has been previously described, the results obtained were analyzed in statistical terms, determining the uncertainty of these parameters based on confidence intervals, following the method described by Portillo et al [1]. These intervals provide a range of values where the value of the parameters (ps) is found with a probability of $1-\alpha$ (confidence level). The confidence intervals are estimated according to:

$$ps = ps_{est} \pm t_{\alpha/2, Ndf} \cdot \sqrt{Tr(V_{ps})}$$

Where is the vector of the estimated parameters $t_{\alpha/2, Ndf}$ is the value of the student t distribution with Ndf degrees of freedom and V_{ps} is the variance-covariance matrix of the parameters.

Close to the minimum of the objective function, by Taylor series approximation to the quadratic term, the objective function is described in the equation:

$$\Phi(ps) \approx \Phi(ps_{est}) + \nabla \Phi_{ps=ps_{est}} (ps - ps_{est})^T + \frac{1}{2} (ps - ps_{est})^T \cdot H_{ps=ps_{est}} (ps - ps_{est})$$

With

$$\nabla \Phi = \frac{\partial \Phi}{\partial ps_k} \quad \text{and} \quad H = \frac{\partial^2 \Phi}{\partial ps_k \partial ps_l}$$

Where $\nabla \Phi$ is the objective function gradient, and H its hessian matrix. At the minimum or optimum point, the gradient of the objective function is zero:

$$\nabla \Phi_{ps=ps_{est}} = 0$$

By assuming that the errors estimation of these parameters follow a normal distribution, V_{ps} has been estimated from the hessian matrix evaluated at the optimum point since the inverse of hessian at the optimum point is a good estimator of the covariance matrix of the estimated parameters.

$$H_{ps} = 2 \cdot V_{ps}^{-1}$$

This relation is intuitive since the sensitivity of the objective function in the optimal versus quadratic deviations in the parameters is given by the Hessian matrix

$$\Phi(ps) - \Phi(ps_{est}) \approx \frac{1}{2} (ps - ps_{est})^T \cdot H_{ps=ps_{est}} (ps - ps_{est})$$

For the determination of the covariance matrix from the Hessian, it can be previously defined the Jacobian matrix J of the residuals as:

$$J(ps) = \begin{bmatrix} J_1 \\ J_2 \\ \dots \\ J_N \end{bmatrix}_{(N \times C) \times p}$$

With

$$J_j = \begin{bmatrix} \frac{\partial r_{1j}}{\partial ps_1} & \dots & \frac{\partial r_{1j}}{\partial ps_p} \\ \dots & \dots & \dots \\ \frac{\partial r_{cj}}{\partial ps_1} & \dots & \frac{\partial r_{cj}}{\partial ps_p} \end{bmatrix}$$

It can be demonstrated that $\nabla \Phi = 2 \cdot J^T \cdot r$, from :

$$\nabla \Phi = \frac{\partial \Phi}{\partial ps} = \frac{\partial \sum_{i=1}^C \sum_{j=1}^N r_{ij}^2}{\partial ps} = 2 \cdot J^T \cdot \frac{\partial r_{ij}}{\partial ps} = 2 \cdot J^T \cdot r$$

With

$$r = \begin{bmatrix} r_1 \\ r_2 \\ \dots \\ r_{c_j} \end{bmatrix}$$

Where

$$r_j = \begin{bmatrix} r_{1j} \\ \dots \\ r_{cj} \end{bmatrix}$$

The Hessian matrix can be expressed in terms of the Jacobian matrix through the equation:

$$H(ps) = \frac{\partial^2 ps}{\partial ps_k \partial ps_l} = \frac{\partial^2}{\partial ps_k \partial ps_l} \sum_{i=1}^C \sum_{j=1}^N (r_{ij})^2 = 2 \cdot \sum_{i=1}^C \sum_{j=1}^N \frac{\partial r_{ij}}{\partial ps_k} \frac{\partial r_{ij}}{\partial ps_l} + 2 \cdot \sum_{i=1}^C \sum_{j=1}^N r_{ij} \frac{\partial^2 r_{ij}}{\partial ps_k \partial ps_l};$$

$$H(ps) = 2 \cdot J^T \cdot J + 2 \cdot \sum_{i=1}^C \sum_{j=1}^N r_{ij} \frac{\partial^2 r_{ij}}{\partial ps_k \partial ps_l};$$

From this expression, it can be verified that the second term of the Hessian is multiplied by the residuals (r_{ij}). At the optimal point, the values of the residuals must be not-significant, so this second term of Eq. 6.16 can be neglected, giving rise to which is known as the Gauss-Newton approximation of the Hessian:

$$H(ps_{est}) = 2 \cdot J^T \cdot J$$

Therefore, the covariance matrix has been calculated using the equation

$$V_{ps}^{-1} = \frac{1}{2} \cdot H(ps_{est}) \approx J^T \cdot J \rightarrow V_{ps} \approx (J^T \cdot J)^{-1}$$

According to this, it is not necessary to determine derivatives of second order for the calculation of the covariance matrix.