Development and Characterisation of Completely Degradable Composite Tissue Engineering Scaffolds

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Appendix

Appendix Chapter 2

Composition nº	**Porosity (%)**	*Standard deviation*
1	**80,99**	*1,38*
2	**95,01**	*0,37*
3	**66,44**	*5,97*
4	**95,96**	*0,30*
5	**79,25**	*0,71*
6	**95,05**	*0,21*
7	**72,04**	*0,88*
8	**96,58**	*0,92*
9	**81,60**	*1,59*
10	**94,57**	*0,09*
11	**81,08**	*17,09**
12	**95,02**	*0,68*
13	**71,15**	*0,65*
14	**94,70**	*0,28*
15	**95,02**	*3,72*
16	**72,07**	*0,13*

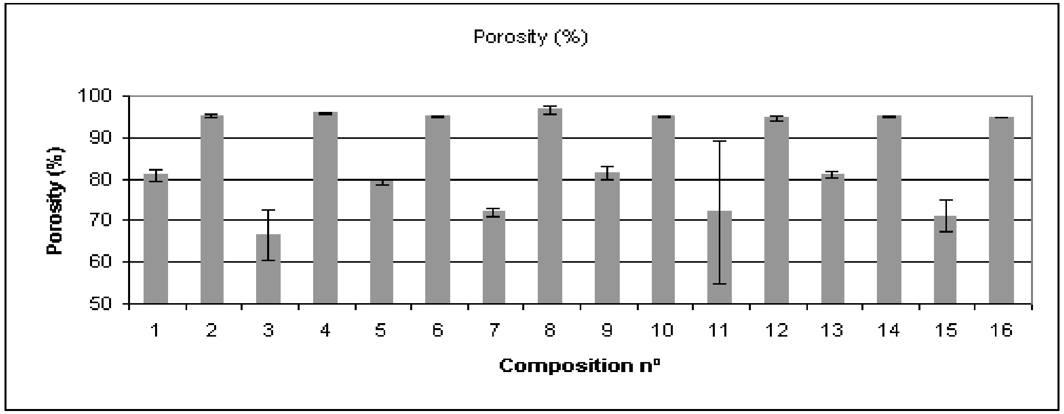
Table App2. 1: Porosity results for composition 1-16. Porosity was measured by mercury pycnometry. Composition nº 11 was very heterogeneous and thus had a large standard deviation.

Composition nº	**Stiffness (MPa)**	*Standard deviation*
1	**0.620**	*0.16*
2	**0.131**	*0.01*
3	**0.468**	*0.03*
4	**0.109**	*0.01*
5	**0.676**	*0.18*
6	**0.123**	*0.02*
7	**0.445**	*0.09*
8	**0.107**	*0.01*
9	**0.279**	*0.12*
10	**0.191**	*0.02*
11	**0.368**	*0.08*
12	**0.144**	*0.01*
13	**0.381**	*0.11*
14	**0.128**	*0.02*
15	**0.556**	*0.15*
16	**0.117**	*0.01*

Table App2. 2: Stiffness results for compositions 1-16. Stiffness was measured by compression tests.

Table App2. 3: Experiment Design Calculations for the factors influencing the porosity of the solvent cast scaffolds

Composition nº	NaCl wt%	NaCl particle size	Glass particle size	Glass wt%	Porosity (%)	s.d.
1	-1	-1	-1	1	80,99	1,38
2	1	-1	-1	1	95,01	0,37
3	-1	1	-1	1	66,44	5,97
4	1	1	-1	1	95,83	0,30
5	-1	-1	1	1	79,25	0,71
6	1	-1	1	1	95,05	0,21
7	-1	1	1	1	72,04	0,88
8	1	1	1	1	96,58	0,92
9	-1	-1	-1	-1	81,6	1,59
10	1	-1	-1	-1	95,02	0,09
11	-1	1	-1	-1	72,07	17,09
12	1	1	-1	-1	94,57	0,68
13	-1	-1	1	-1	81,08	0,65
14	1	-1	1	-1	95,02	0,28
15	-1	1	1	-1	71,15	3,72
16	1	1	1	-1	94,7	0,13



Response Vector   Factor Matrix

Porosity (%)	NaCl wt% = X1	NaCl particle size= X2	Glass particle size = X3	Glass wt% = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X3X4	X2X3X4	X1X2X4	X1X2X3X4
80,99	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
95,01	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	1	-1	1
66,44	-1	1	-1	1	-1	1	-1	-1	1	-1	1	1	-1	-1	1
95,83	1	1	-1	1	1	-1	1	-1	1	-1	-1	-1	-1	1	-1
79,25	-1	-1	1	1	1	-1	-1	-1	-1	1	1	-1	-1	1	1
95,05	1	-1	1	1	-1	1	1	-1	-1	1	-1	1	-1	-1	-1
72,04	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	1	-1	-1
96,58	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
81,6	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
95,02	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	-1	1	-1
72,07	-1	1	-1	-1	-1	1	1	-1	-1	1	1	-1	1	1	-1
94,57	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	1	1	-1	1
81,08	-1	-1	1	-1	1	-1	1	-1	1	-1	1	1	1	-1	-1
95,02	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	-1	1	1	1
71,15	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	-1	1	1
94,7	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1

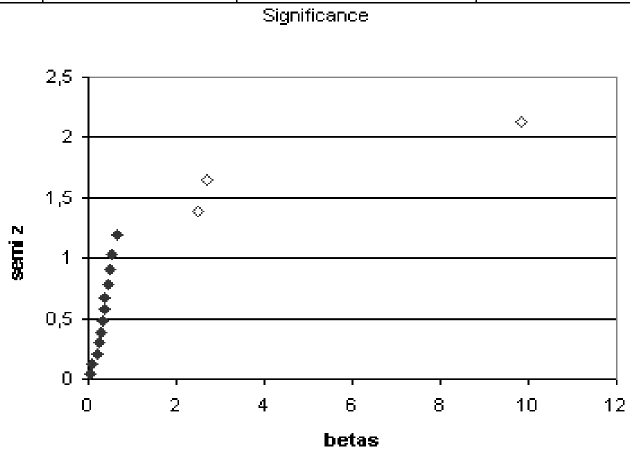
Calculation of the value of the βs (SUMPRODUCT of the response vector and the factor vector)

Factor	NaCl wt% = X1	NaCl particle size= X2	Glass particle size = X3	Glass wt% = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X3X4	X2X3X4	X1X2X4	X1X2X3X4
Coeficients (βs)	9,82	-2,48	0,21	-0,25	2,68	-0,09	0,65	0,49	0,05	0,37	-0,38	-0,29	0,52	0,34	-0,45

Calculations for the significance of the factors

Coeficients (βs)	absolute value β (in ascending order)	i	corrected accumulated frequencies	probability	semi z
9,8225	0,05125	1	0,033333	0,516666667	0,041789008
-2,4775	0,09375	2	0,100000	0,55	0,125661472
0,20875	0,20875	3	0,166667	0,583333333	0,210428652
-0,25125	0,25125	4	0,233333	0,616666667	0,296738563
2,675	0,29	5	0,300000	0,65	0,385321073
-0,09375	0,33875	6	0,366667	0,683333333	0,477040203
0,64625	0,3725	7	0,433333	0,716666667	0,57296802
0,48625	0,38125	8	0,500000	0,75	0,674490366
0,05125	0,4475	9	0,566667	0,783333333	0,783500127
0,3725	0,48625	10	0,633333	0,816666667	0,902734882
-0,38125	0,52	11	0,700000	0,85	1,036432877
-0,29	0,64625	12	0,766667	0,883333333	1,1918155
0,52	2,4775	13	0,833333	0,916666667	1,382995833
0,33875	2,675	14	0,900000	0,95	1,644853
-0,4475	9,8225	15	0,966667	0,983333333	2,128044798

non significant βs	significant βs
0,05125	
0,09375	
0,20875	
0,25125	
0,29	
0,33875	
0,3725	
0,38125	
0,4475	
0,48625	
0,52	
0,64625	
	2,4775
	2,675
	9,8225



SCR = 8*(Σ of non significant β)^2	27,613
SCEx= 8*(Σ of significant β)^2	1756,4022
SCT= (Σ of all β)	1784,0152
R^2=SCEx/SCT	0,98452199
average	85,4

Linear model : porosity = 85,4+9,8225*X1-2,4775*X2+2,675*X1X2

Error calculations

Linear model : porosity = 85,4+9,8225*X1-2,4775*X2+2,675*X1X2

βs	Porosity (%)	NaCl wt% = X1	NaCl particle size = X2	X1X2	Calculated Y =Y^	error = e (Y^-Y)
9,8225	80,99	-1	-1	1	80,73	0,26
-2,4775	95,01	1	-1	-1	95,025	-0,015
2,675	66,44	-1	1	-1	70,425	-3,985
	95,83	1	1	1	95,42	0,41
	79,25	-1	-1	1	80,73	-1,48
	95,05	1	-1	-1	95,025	0,025
	72,04	-1	1	-1	70,425	1,615
	96,58	1	1	1	95,42	1,16
	81,6	-1	-1	1	80,73	0,87
	95,02	1	-1	-1	95,025	-0,005
	72,07	-1	1	-1	70,425	1,645
	94,57	1	1	1	95,42	-0,85
	81,08	-1	-1	1	80,73	0,35
	95,02	1	-1	-1	95,025	-0,005
	71,15	-1	1	-1	70,425	0,725
	94,7	1	1	1	95,42	-0,72

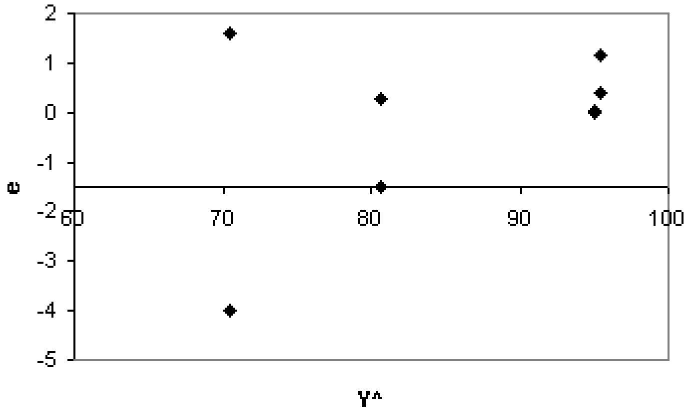
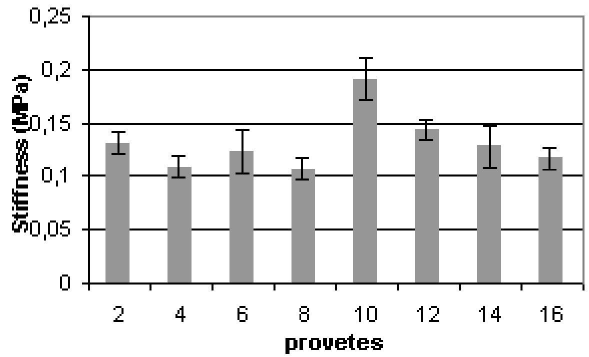


Table App2. 4: Experiment Design Calculations for the factors influencing the stiffness of the solvent cast scaffolds

Composistion nº	NaCl particle size	Glass particle size	Glass wt%	Stiffness (MPa)	*s.d.*
2	-	-	+	0,131	0,01
4	+	-	+	0,109	0,01
6	-	+	+	0,123	0,02
8	+	+	+	0,107	0,01
10	-	-	-	0,191002	0,02
12	+	-	-	0,143896	0,01
14	-	+	-	0,127898	0,02
16	+	+	-	0,116974	0,01



Response vector Factor matrix

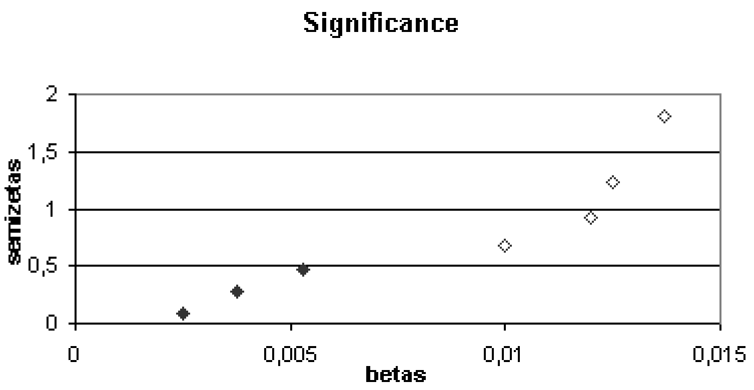
Stiffness (MPa)	NaCl particle size = X2	Glass particle size = X3	Glass wt%= X4	X2X3	X2X4	X3X4	X2X3X4
0,131	-1	-1	1	1	-1	-1	1
0,109	1	-1	1	-1	1	-1	-1
0,123	-1	1	1	-1	-1	1	-1
0,107	1	1	1	1	1	1	1
0,191002	-1	-1	-1	1	1	1	-1
0,143896	1	-1	-1	-1	-1	1	1
0,127898	-1	1	-1	-1	1	-1	1
0,116974	1	1	-1	1	-1	-1	-1

Calculation of the value of the βs (SUMPRODUCT of the response vector and the factor matrix)

Factors	**X2**	**X3**	**X4**	**X2X3**	**X2X4**	**X3X4**	**X2X3X4**
Coeficients (βs)	-0,01200375	-0,01250325	-0,01372125	0,00527275	0,00250375	0,01000325	-0,00377275

estimated βs	β abs ord	i	frec corr.	prob	semi z
-0,01200375	0,00250375	1	0,071429	0,535714286	0,08964207
-0,01250325	0,00377275	2	0,214286	0,607142857	0,2718798
0,01372125	0,00527275	3	0,357143	0,678571429	0,46370815
0,00527275	0,01000325	4	0,500000	0,75	0,67449037
-0,00250375	0,01200375	5	0,642857	0,821428571	0,92082246
-0,01000325	0,01250325	6	0,785714	0,892857143	1,24186727
0,00377275	0,01372125	7	0,928571	0,964285714	1,80274583

non significant βs	significant βs
0,00250375	
0,00377275	
0,00527275	
	0,01000325
	0,01200375
	0,01250325
	0,01372125



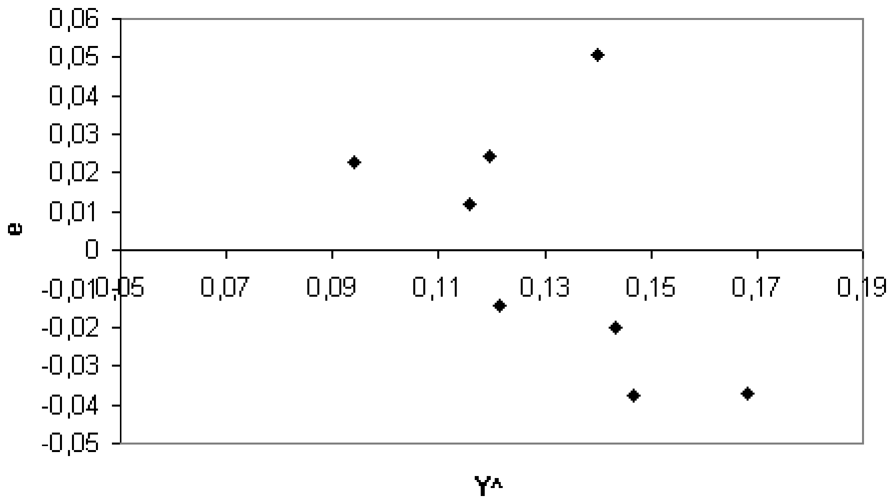
SCR = 8*(Σ of non significant β)^2	0,00038643
SCEx= 8*(Σ of significant β)^2	0,00471007
SCT= (Σ of all β)	0,00509651
R^2=SCEx/SCT	0,92417661
average	
mitja=	0,13122125

linear model = stiffness = 0,13122-0,01372X4-0,01250X3-0,0120X2+0,01X3X4

Error calculations

linear model = stiffness = 0,13122-0,01372X4-0,01250X3-0,0120X2+0,01X3X4

β's	Stiffness (MPa)	NaCl particle size = X2	Glass particle size = X3	Glass wt%= X4	X3X4	Y^	e
-0,01200375	0,131	-1	-1	-1	-0,131	0,16813907	-0,03713907
-0,01250325	0,109	1	-1	-1	0,109	0,14653235	-0,03753235
-0,01372125	0,123	-1	1	-1	-0,123	0,1432126	-0,0202126
0,01000325	0,107	1	1	-1	0,107	0,12150585	-0,01450585
	0,191002	-1	-1	1	-0,191002	0,14009636	0,05090564
	0,143896	1	-1	1	0,143896	0,11943893	0,02445707
	0,127898	-1	1	1	-0,127898	0,1157211	0,0121769
	0,116974	1	1	1	0,116974	0,09416312	0,02281088



Calculation of the volume fraction of PLA, G5 and NaCl in the composites.

The composite is made of PLA and 20wt% or 50wt% of glass particles.
The NaCl particles added to the mix measure either [80-210]μm or [295-590]μm.

The volume fraction of PLA, f_{PLA}, is:

$$f_{PLA} = \frac{Vol_{PLA}}{Vol_{Total}} = \frac{Vol_{PLA}}{Vol_{PLA} + Vol_{G5}} = \frac{M_{PLA}/\rho_{PLA}}{\frac{M_{PLA}}{\rho_{PLA}} + \frac{M_{G5}}{\rho_{G5}}}$$

At 20wt% of G5 glass, $4M_{G5}=M_{PLA}$;

$$20wt\% \longrightarrow f_{PLA} = \frac{M_{PLA}/\rho_{PLA}}{\frac{M_{PLA}}{\rho_{PLA}} + \frac{M_{G5}}{\rho_{G5}}} = \frac{4M_{G5}/\rho_{PLA}}{\frac{4M_{G5}}{\rho_{PLA}} + \frac{M_{G5}}{\rho_{G5}}} = \frac{4/\rho_{PLA}}{\frac{4}{\rho_{PLA}} + \frac{1}{\rho_{G5}}} = \frac{4\rho_{G5}}{4\rho_{G5} + \rho_{PLA}} = \frac{1}{1 + \frac{\rho_{PLA}}{4\rho_{G5}}}$$

At 50 wt% of G5 glass, $M_{G5}= M_{PLA}$;

$$50wt\% \longrightarrow f_{PLA} = \frac{M_{PLA}/\rho_{PLA}}{\frac{M_{PLA}}{\rho_{PLA}} + \frac{M_{G5}}{\rho_{G5}}} = \frac{M_{G5}/\rho_{PLA}}{\frac{M_{G5}}{\rho_{PLA}} + \frac{M_{G5}}{\rho_{G5}}} = \frac{1/\rho_{PLA}}{\frac{1}{\rho_{PLA}} + \frac{1}{\rho_{G5}}} = \frac{1\rho_{G5}}{1\rho_{G5} + \rho_{PLA}} = \frac{1}{1 + \frac{\rho_{PLA}}{\rho_{G5}}}$$

At 94 wt% of NaCl, and M_{comp}= 0.06M_{Total}; M_{NaCl}= 0.94M_{NaCl}

$$f_{comp} = \frac{Vol_{comp}}{Vol_{Total}} = \frac{Vol_{comp}}{Vol_{comp} + Vol_{NaCl}} = \frac{M_{comp}/\rho_{comp}}{M_{comp}/\rho_{comp} + M_{NaCl}/\rho_{NaCl}} = \frac{0.06M_{Total}/\rho_{comp}}{0.06M_{Total}/\rho_{Total} + 0.94M_{Total}/\rho_{NaCl}}$$

If ρ_{comp} at 20 wt% G5= 1.37 gcm^{-3}, If ρ_{comp} at 50 wt% G5= 1.71 gcm^{-3}, and ρ_{NaCl}=2.2 gcm^{-3}. The volume fraction of composite, f_{comp}, in each case would be:

$$20wt\% \longrightarrow f_{comp} = \frac{1}{1 + \frac{0.94\rho_{comp}}{0.06\rho_{NaCl}}} = 0.093 = 9.3\%$$

$$50wt\% \longrightarrow f_{comp} = \frac{1}{1 + \frac{0.94\rho_{comp}}{0.06\rho_{NaCl}}} = 0.075 = 7.5\%$$

In order to calculate the thickness of the pore wall, we will assume the NaCl particles are spherical and the average NaCl particle radius is: 145μm in the case of NaCl particles ranging between [80-210]μm, and 440μm in the case of NaCl particles ranging between [295-590]μm.

The volume of a NaCl particle would be:

$$Vol_{NaCl} \xrightarrow{d=440\mu m} \frac{4}{3}\pi\left(\frac{440}{2}\right)^3 = 45*10^6\ \mu m^3$$

$$Vol_{NaCl} \xrightarrow{d=145\mu m} \frac{4}{3}\pi\left(\frac{145}{2}\right)^3 = 1.6*10^6\ \mu m^3$$

The volume fraction of composite in the mix is:

$$f_{comp} = \frac{Vol_{comp}}{Vol_{Total}} = \frac{Vol_{comp}}{Vol_{comp} + Vol_{NaCl}}$$

$$f_{comp}Vol_{comp} + f_{comp}Vol_{NaCl} = Vol_{comp}$$

$$f_{comp}Vol_{NaCl} = Vol_{comp}(1 - f_{comp})$$

$$Vol_{NaCl} = Vol_{comp}\frac{(1 - f_{comp})}{f_{comp}}$$

$$Vol_{comp} = Vol_{NaCl}\frac{f_{comp}}{(1 - f_{comp})}$$

At 50wt% glass, f_{comp} = 7.5%.

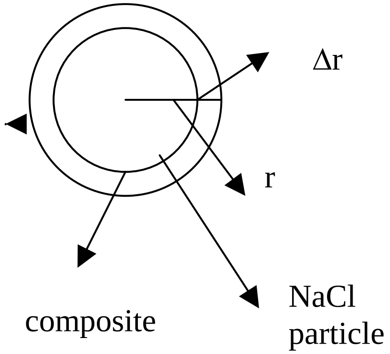
At large NaCl particle sizes, the volume of composite for each volume of NaCl is:

$$Vol_{comp} \xrightarrow{r=440\mu m} 45*10^6\frac{0.075}{(1-0.075)} = 3.6*10^6\ \mu m^3$$

At small NaCl particle sizes;

$$Vol_{comp} \xrightarrow{r=145\,\mu m} 1.6*10^{6}\frac{0.075}{(1-0.075)} = 0.13*10^{6}\,\mu m^{3}$$

If we assume each NaCl particle is surrounded by composite:



R= r+Δr

The total volume of the NaCl particle plus the composite coating for large NaCl particles at 50wt% of glass would be:

$$Vol_{Total}(NaCl + composite) \xrightarrow{d=440\,\mu m} = 4\pi R^{3} = 45*10^{6}\,\mu m^{3} + 3.6*10^{6}\,\mu m^{3} = 48.6*10^{6}\,\mu m^{3}$$

Taking: $Vol_{Total} = \frac{4}{3}\pi R^{3}$:

$$R = 227\mu m\,, \qquad \Delta r = 227 - \frac{440}{2} = 7\mu m$$

And the total volume of the NaCl particle plus the composite coating for small NaCl particles would be:

$$Vol_{Total}\,(NaCl + composite) \xrightarrow{d=145\mu m} = \frac{4}{3}\pi R^3 = 1.6*10^6\,\mu m^3 + 0.13*10^6\,\mu m^3 = 1.73*10^6\,\mu m^3$$

$$R = 76\mu m\,,\ \Delta r = 76 - \frac{145}{2} = 3.5\mu m$$

Thus the pore walls measure 7 μm in the case of large NaCl particles, and 3.5 μm in the case of small NaCl particles.

At 20wt% glass, f_{comp} = 9.3%.

At large NaCl particle sizes, the volume of composite for each volume of NaCl is:

$$Vol_{comp} \xrightarrow{r=440\mu m} 45*10^6\,\frac{0.093}{(1-0.093)} = 4.7*10^6\,\mu m^3$$

At small NaCl particle sizes;

$$Vol_{comp} \xrightarrow{r=145\mu m} 1.6*10^6\,\frac{0.093}{(1-0.093)} = 0.16*10^6\,\mu m^3$$

The total volume of the NaCl particle plus the composite coating for large NaCl particles at 20wt% of glass would be:

$$Vol_{Total}\,(NaCl + composite) \xrightarrow{d=440\mu m} = 4\pi R^3 = 45*10^6\,\mu m^3 + 4.7*10^6\,\mu m^3 = 49.7*10^6\,\mu m^3$$

Taking: $Vol_{Total} = \frac{4}{3}\pi R^3$:

$$R = 228\mu m, \qquad \Delta r = 227 - \frac{440}{2} = 8\mu m$$

And the total volume of the NaCl particle plus the composite coating for small NaCl particles would be:

$$Vol_{Total}(NaCl + composite) \xrightarrow{d=145\mu m} = \frac{4}{3}\pi R^3 = 1.6*10^6\ \mu m^3 + 0.16*10^6\ \mu m^3 = 1.76*10^6\ \mu m^3$$

$$R = 74\mu m, \ \Delta r = 74 - \frac{145}{2} = 1.5\mu m$$

Thus the pore walls measure 8 μm in the case of large NaCl particles, and 1.5 μm in the case of small NaCl particles.

Appendix Chapter 3

Composition nº	Porosity (%)	s.d.
1F	**95,11**	0,13
2F	**88,46**	2,43
3F	**96,13**	0,36
4F	**89,01**	0,91
5E	**94,86**	0,03
5F	**96,03**	0,05
6E	**82,60**	5,19
7E	**95,22**	0,17
7F	**95,78**	0,69
8E	**85,74**	0,50
8F	**87,25**	1,94
9E	**93,87**	0,54
9F	**95,85**	0,28
10E	**83,78**	1,73
10F	**88,28**	0,14
11E	**92,94**	0,47
11F	**96,21**	0,14
12E	**82,46**	1,81
12F	**87,73**	0,32

Table App3. 1: Porosity results for compositions 1-12. Porosity was measured by mercury pycnometry

Composition nº	Porosity (%)	s.d.
J1	**95,14**	0,69
J2	**95,41**	0,20
J3	**87,58**	1,52
J4	**88,46**	1,38
J5	**95,33**	0,48
J6	**95,66**	1,01
J7	**86,69**	0,38
J8	**86,79**	0,49
J9	**94,76**	0,24
J10	**95,74**	0,41
J11	**87,21**	0,54
J12	**87,52**	0,50
J13	**94,88**	0,37
J14	**94,91**	1,11
J15	**86,95**	0,56
J16	**86,57**	0,83

Table App3. 2: Porosity results for compositions J1-J16

Composition nº	Stiffness (MPa)	s.d.
J1	**0,29**	0,07
J2	**0,53**	0,22
J3	**6,35**	0,76
J4	**7,23**	3,00
J5	**0,22**	0,05
J6	**0,43**	0,08
J7	**4,78**	1,28
J8	**6,23**	1,83
J9	**0,23**	0,04
J10	**0,74**	0,17
J11	**8,82**	3,71
J12	**10,16**	2,27
J13	**0,22**	0,05
J14	**0,43**	0,09
J15	**4,55**	1,27
J16	**7,08**	1,28

Table App3. 3: Compression tests results for compositions nº J1-J16

Compositions nº	Crystallinity (%)
J1	21,2
J2	31,5
J3	30,0
J4	28,3
J5	21,0
J6	56,5
J7	27,0
J8	39,4
J9	24,7
J10	24,4
J11	17,3
J12	23,8
J13	24,9
J14	46,6
J15	28,1
J16	30,4
Unprocessed PLA	31,8

Table App3. 4: Crystallinity results for compositions nº J1-J16

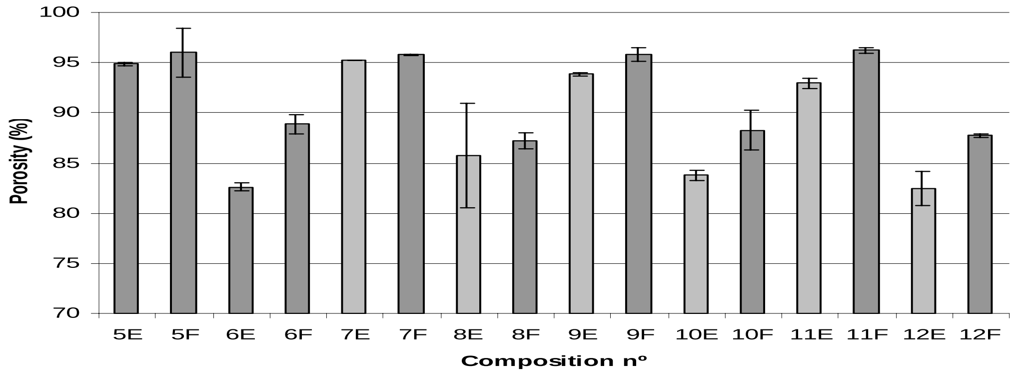
Composition nº	Tg (°C)
J1	48,52
J2	47,23
J3	58,72
J4	55,81
J5	53,0
J6	52
J7	53,31
J8	57,28
J9	61,53
J10	60,53
J11	61,19
J12	61,06
J13	61,2
J14	60,9
J15	60,47
J16	60,56
Unprocessed PLA	61,9

Table App3. 5: Tg results for compositions J1-J16

Table App3. 6: Experiment Design Calculations for the factors influencing the porosity of the phase-separated scaffolds. Preliminary study, without glass particles

Composition nº	w/v% PLA	v/v% H_2O	Quenching Temp.	Solvent removal method	Porosity (%)
5F	-1	-1	1	1	96,0285483
6F	1	-1	1	1	88,85411649
7F	-1	1	1	1	95,78376248
8F	1	1	1	1	87,24554746
9F	-1	-1	-1	1	95,84554535
10F	1	-1	-1	1	88,28261668
11F	-1	1	-1	1	96,20947201
12F	1	1	-1	1	87,72769388
5E	-1	-1	1	-1	94,86207562
6E	1	-1	1	-1	82,59932691
7E	-1	1	1	-1	95,2203058
8E	1	1	1	-1	85,74265553
9E	-1	-1	-1	-1	93,86985173
10E	1	-1	-1	-1	83,77863423
11E	-1	1	-1	-1	92,94222436
12E	1	1	-1	-1	82,45983793

Freeze-extraction =-1
Freeze-drying =+1



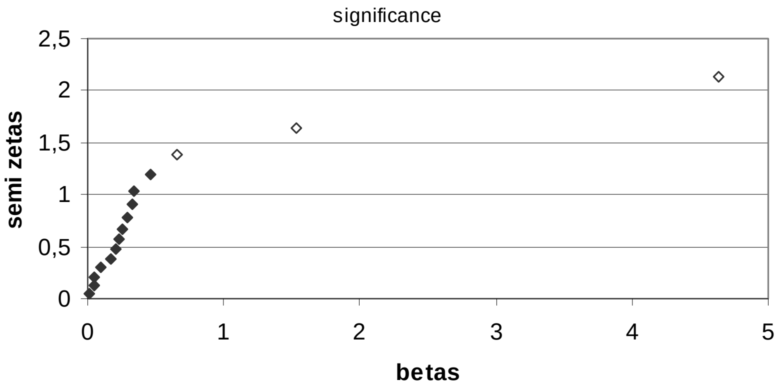
Porosity (%)	w/v% PLA = **X1**	v/v % H_2O= **X2**	Quenching T.= **X3**	Solvent removal method = **X4**	**X1X2**	**X1X3**	**X1X4**	**X2X3**	**X2X4**	**X3X4**	**X1X2X3**	**X1X2X4**	**X2X3X4**	**X1X3X4**	**X1X2X3X4**
96,029	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
88,854	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	-1	1	-1
95,784	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	1	-1	-1
87,246	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
95,846	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
88,283	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	1	-1	1
96,209	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	-1	1	1
87,728	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
94,862	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
82,599	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	1	-1	1
95,22	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	-1	1	1
85,743	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
93,87	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
83,779	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	-1	1	-1
92,942	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	1	-1	-1
82,46	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1

Calculation of the value of the βs (SUMPRODUCT of the response vector and the factor vector)

Factors	**X1**	**X2**	**X3**	**X4**	**X1X2**	**X1X3**	**X1X4**	**X2X3**	**X2X4**	**X3X4**	**X1X2X3**	**X1X2X4**	**X2X3X4**	**X1X3X4**	**X1X2X3X4**
Coeficients (βs)	-4,62946	-0,04933	0,326278901	1,531399	0,006956	-0,0522	0,65979	0,255351	-0,20622	-0,34545	0,170708	-0,29229	-0,46315	0,093678	-0,22633

Coefficients (βs)	β abs ord	i	corrected accumulated frequencies	probability	semi z
-4,62945938	0,006957	1	0,033333333	0,51666667	0,041789
-0,04932687	0,049327	2	0,1	0,55	0,125661
0,326280625	0,052171	3	0,166666667	0,58333333	0,210429
1,531399375	0,093679	4	0,233333333	0,61666667	0,296739
0,006956875	0,170708	5	0,3	0,65	0,385321
-0,05217063	0,206219	6	0,366666667	0,68333333	0,47704
0,659790625	0,226324	7	0,433333333	0,71666667	0,572968
0,255351875	0,255352	8	0,5	0,75	0,67449
-0,20621938	0,292286	9	0,566666667	0,78333333	0,7835
-0,34544938	0,326281	10	0,633333333	0,81666667	0,902735
0,170708125	0,345449	11	0,7	0,85	1,036433
-0,29228563	0,463146	12	0,766666667	0,88333333	1,191815
-0,46314563	0,659791	13	0,833333333	0,91666667	1,382996
0,093679375	1,531399	14	0,9	0,95	1,644853
-0,22632438	4,629459	15	0,966666667	0,98333333	2,128045

non significant βs	significant βs
0,006957	
0,049327	
0,052171	
0,093679	
0,170708	
0,206219	
0,226324	
0,255352	
0,292286	
0,326281	
0,345449	
0,463146	
	0,659791
	1,531399
	4,629459



SCR = 8*(Σ of non significant β)^2	11,64485
SCEx= 8*(Σ of significant β)^2	387,3984
SCT= (Σ of all β)	399,0433
R^2=SCEx/SCT	0,970818
average	90,46576

Error calculations
linear model = porosity = 90,47 - 4,63X1 + 1,53X4 +0,66 X1X4

β	Porosity (%)	w/v% PLA = **X1**	Solvent removal method = **X4**	**X1X4**	**Y^**	**e**
-4,62946	96,02855	-1	1	-1	95,96707	0,061480171
1,531399	88,85412	1	1	1	88,02773	0,826385864
0,659791	95,78376	-1	1	-1	95,96707	-0,18330564
	87,24555	1	1	1	88,02773	-0,782183165
	95,84555	-1	1	-1	95,96707	-0,121522779
	88,28262	1	1	1	88,02773	0,254886058
	96,20947	-1	1	-1	95,96707	0,242403886
	87,72769	1	1	1	88,02773	-0,30003675
	94,86208	-1	-1	1	94,22385	0,638224997
	82,59933	1	-1	-1	83,64535	-1,046023719
	95,22031	-1	-1	1	94,22385	0,996455174
	85,74266	1	-1	-1	83,64535	2,097304904
	93,86985	-1	-1	1	94,22385	-0,353998892
	83,77863	1	-1	-1	83,64535	0,133283608
	92,94222	-1	-1	1	94,22385	-1,281626266
	82,45984	1	-1	-1	83,64535	-1,1855127

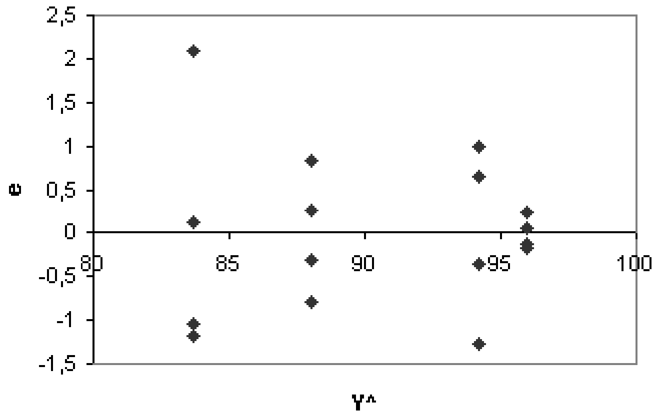
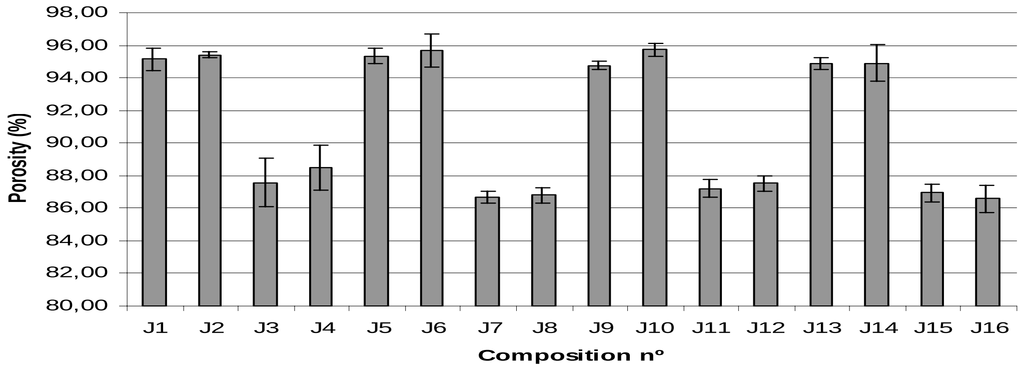


Table App3. 7: Experiment Design Calculations for the factors influencing the porosity of the phase-separated scaffolds. Optimisation study, with glass particles.

Composition nº	Temperature	w/v% PLA	v/v% H_20	Solvent removal method (E/F)	Porosity (%)
J1	-1	-1	-1	-1	95,1
J2	1	-1	-1	-1	95,4
J3	-1	1	-1	-1	87,6
J4	1	1	-1	-1	88,5
J5	-1	-1	1	-1	95,3
J6	1	-1	1	-1	95,7
J7	-1	1	1	-1	86,7
J8	1	1	1	-1	86,8
J9	-1	-1	-1	1	94,8
J10	1	-1	-1	1	95,7
J11	-1	1	-1	1	87,2
J12	1	1	-1	1	87,5
J13	-1	-1	1	1	94,9
J14	1	-1	1	1	94,9
J15	-1	1	1	1	86,9
J16	1	1	1	1	86,6



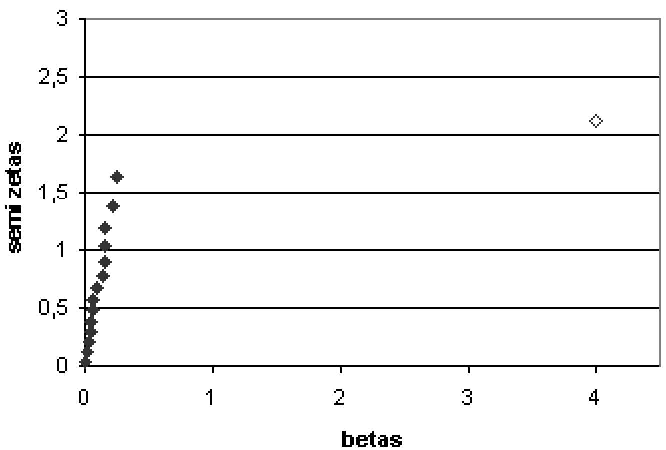
Porosity (%)	Temperature = X1	w/v% PLA = X2	v/v% H2O = X3	E/F = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
95,1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
95,4	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
87,6	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1
88,5	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1
95,3	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
95,7	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1
86,7	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1
86,8	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
94,8	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
95,7	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1
87,2	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1
87,5	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
94,9	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
94,9	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1
86,9	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1
86,6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Factors	X1	X2	X3	X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
Coefficients (βs)	0,157	-4,005	-0,253	-0,158	-0,043	- 0,148	-0,040	-0,219	-0,001	0,014	-0,036	-0,091	-0,058	0,155	0,068

Coefficients βs	β abs ord	i	corrected accumulated frequencies	probability	semi z
0,157	0,001	1	0,03333333	0,51666667	0,041789
-4,005	0,014	2	0,1	0,55	0,125661
-0,253	0,036	3	0,16666667	0,58333333	0,210429
-0,158	0,040	4	0,23333333	0,61666667	0,296739
-0,043	0,043	5	0,3	0,65	0,385321
-0,148	0,058	6	0,36666667	0,68333333	0,47704
-0,040	0,068	7	0,43333333	0,71666667	0,572968
-0,219	0,091	8	0,5	0,75	0,67449
-0,001	0,148	9	0,56666667	0,78333333	0,7835
0,014	0,155	10	0,63333333	0,81666667	0,902735
-0,036	0,157	11	0,7	0,85	1,036433
-0,091	0,158	12	0,76666667	0,88333333	1,191815
-0,058	0,219	13	0,83333333	0,91666667	1,382996
0,155	0,253	14	0,9	0,95	1,644853
0,068	4,005	15	0,96666667	0,98333333	2,128045

non significant βs	significant βs
0,001	
0,014	
0,036	
0,040	
0,043	
0,058	
0,068	
0,091	
0,148	
0,155	
0,157	
0,158	
0,219	
0,253	
	4,005

semi z



SCR = 8*(Σ of non significant β)^2 3,6595137
SCEx= 8*(Σ of significant β)^2 256,59738
SCT= (Σ of all β) 260,25689

R^2=SCEx/SCT 0,9859388
average 91,2

linear model = porosity = 91,2 -4,005 * X2

Error Calcultations
linear model = porosity = 91,2 -4,005 * X2

β	**Porosity (%)**	**X2**	**Y^**	**e**
-4,005	95,1	-1	4,005	91,13957
	95,4	-1	4,005	91,41021
	87,6	1	-4,005	91,5865
	88,5	1	-4,005	92,46467
	95,3	-1	4,005	91,32554
	95,7	-1	4,005	91,65207
	86,7	1	-4,005	90,69273
	86,8	1	-4,005	90,79326
	94,8	-1	4,005	90,75498
	95,7	-1	4,005	91,73159
	87,2	1	-4,005	91,21015
	87,5	1	-4,005	91,52532
	94,9	-1	4,005	90,87928
	94,9	-1	4,005	90,90557
	86,9	1	-4,005	90,95282
	86,6	1	-4,005	90,57336

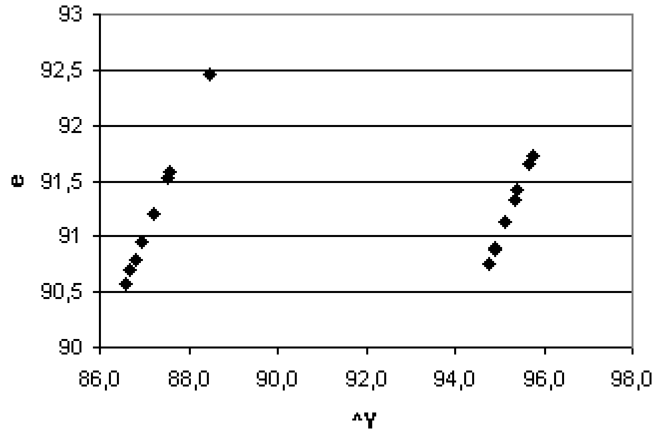
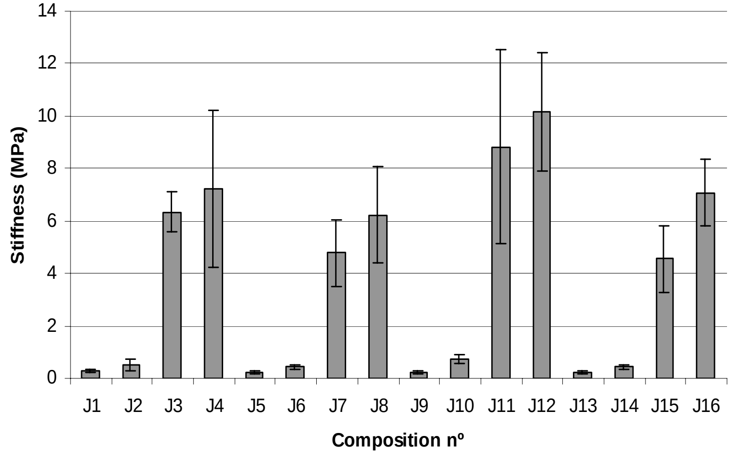


Table App3. 8: Experiment Design Calculations for the factors influencing the stiffness of the phase-separated scaffolds. Optimisation study, with glass particles.

omposition nº	Temperature	w/v% PLA	v/v% H_20	Solvent removal method (E/F)	Stiffness (MPa)
J1	-1	-1	-1	-1	0,29
J2	1	-1	-1	-1	0,53
J3	-1	1	-1	-1	6,35
J4	1	1	-1	-1	7,23
J5	-1	-1	1	-1	0,22
J6	1	-1	1	-1	0,43
J7	-1	1	1	-1	4,78
J8	1	1	1	-1	6,23
J9	-1	-1	-1	1	0,23
J10	1	-1	-1	1	0,74
J11	-1	1	-1	1	8,82
J12	1	1	-1	1	10,16
J13	-1	-1	1	1	0,22
J14	1	-1	1	1	0,43
J15	-1	1	1	1	4,55
J16	1	1	1	1	7,08

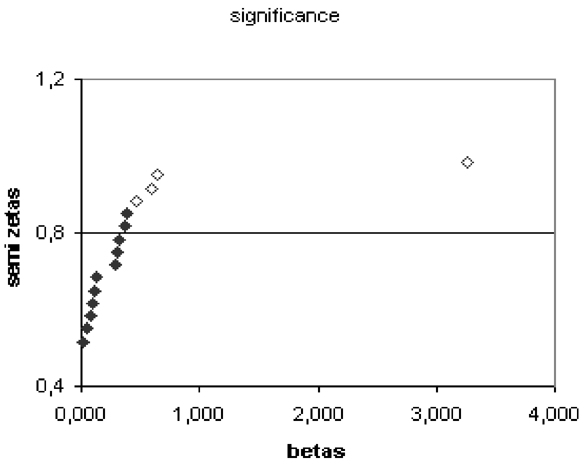


Stiffness (MPa)	Temperature = X1	w/v% PLA = X2	v/v% H2O = X3	E/F = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
0,29	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
0,53	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
6,35	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1
7,23	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1
0,22	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
0,43	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1
4,78	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1
6,23	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
0,23	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
0,74	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1
8,82	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1
10,16	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
0,22	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
0,43	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1
4,55	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1
7,08	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Factors	X1	X2	X3	X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
Coefficients (βs)	0,460	3,257	-0,650	0,387	0,314	0,090	0,112	-0,589	0,367	-0,308	0,131	0,079	0,022	-0,288	0,055

estimated βs	β abs ord	i	corrected accumulated frequencies	probability	semi z
0,460	0,022	1	0,033333333	0,51666667	0,022
3,257	0,055	2	0,1	0,55	0,055
-0,650	0,079	3	0,166666667	0,58333333	0,079
0,387	0,090	4	0,233333333	0,61666667	0,090
0,314	0,112	5	0,3	0,65	0,112
0,090	0,131	6	0,366666667	0,68333333	0,131
0,112	0,288	7	0,433333333	0,71666667	0,288
-0,589	0,308	8	0,5	0,75	0,308
0,367	0,314	9	0,566666667	0,78333333	0,314
-0,308	0,367	10	0,633333333	0,81666667	0,367
0,131	0,387	11	0,7	0,85	0,387
0,079	0,460	12	0,766666667	0,88333333	0,460
0,022	0,589	13	0,833333333	0,91666667	0,589
-0,288	0,650	14	0,9	0,95	0,650
0,055	3,257	15	0,966666667	0,98333333	3,257

non significant βs	significant βs
0,022	
0,055	
0,079	
0,090	
0,112	
0,131	
0,288	
0,308	
0,314	
0,367	
0,387	
	0,460
	0,589
	0,650
	3,257



SCR = 8*(Σ of non significant β)^2 9,73496306
SCEx= 8*(Σ of significant β)^2 185,368534
SCT= (Σ of all β) 195,103497

R^2=SCEx/SCT 0,9501036
average 3,64

linear model = stiffness = 3,64 +3,527*X2 - 0,650*X3 +0,460 *X1 -0,589* X2X3

Error calculations
linear model = stiffness = 3,64 +3,527*X2 - 0,650*X3 +0,460 *X1 -0,589* X2X3

βs	Stiffness (MPa)	X2	X3	X1	X2X3	Y^	e
3,527	0,3	-1	-1	-1	1	0,892	-0,604448
-0,65	0,5	-1	-1	1	1	1,812	-1,28219
0,46	6,3	1	-1	-1	-1	6,768	-0,4180633
0,589	7,2	1	-1	1	-1	7,688	-0,461418
	0,2	-1	1	-1	-1	-1,586	1,806234
	0,4	-1	1	1	-1	-0,666	1,096642
	4,8	1	1	-1	1	6,646	-1,868538
	6,2	1	1	1	1	7,566	-1,33606
	0,2	-1	-1	-1	1	0,892	-0,6594725
	0,7	-1	-1	1	1	1,812	-1,0702075
	8,8	1	-1	-1	-1	6,768	2,05242
	10,2	1	-1	1	-1	7,688	2,467795
	0,2	-1	1	-1	-1	-1,586	1,8070575
	0,4	-1	1	1	-1	-0,666	1,095182
	4,6	1	1	-1	1	6,646	-2,0913625
	7,1	1	1	1	1	7,566	-0,483638

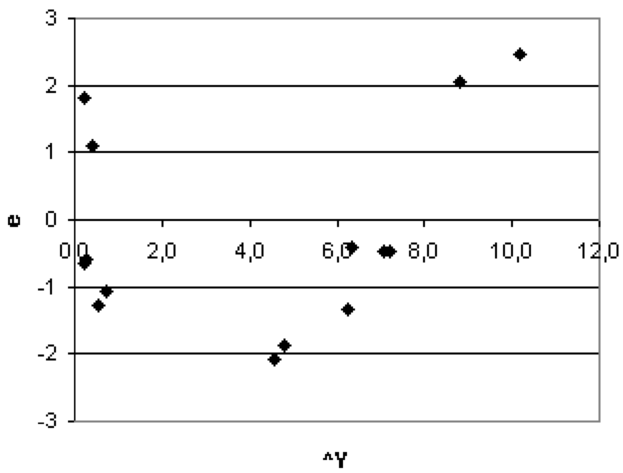
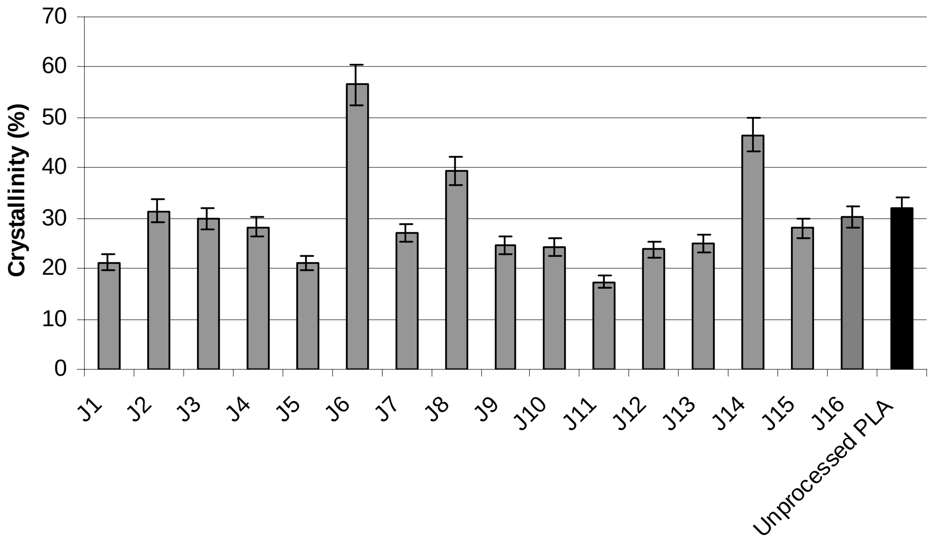


Table App3. 9: Experiment Design Calculations for the factors influencing the crystallinity of the phase-separated scaffolds. Optimisation study, with glass particles.

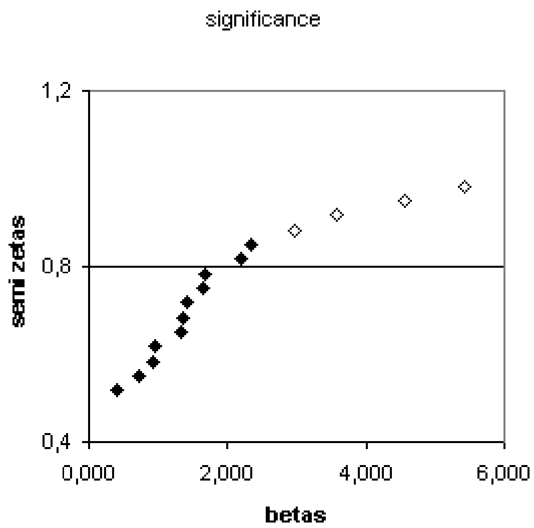
Composition nº	Temperature	w/v% PLA	v/v% H_20	Solvent removal method (E/F)	Cristallinity (%)
J1	-1	-1	-1	-1	21,2
J2	1	-1	-1	-1	31,5
J3	-1	1	-1	-1	30,0
J4	1	1	-1	-1	28,3
J5	-1	-1	1	-1	21,0
J6	1	-1	1	-1	56,5
J7	-1	1	1	-1	27,0
J8	1	1	1	-1	39,4
J9	-1	-1	-1	1	24,7
J10	1	-1	-1	1	24,4
J11	-1	1	-1	1	17,3
J12	1	1	-1	1	23,8
J13	-1	-1	1	1	24,9
J14	1	-1	1	1	46,6
J15	-1	1	1	1	28,1
J16	1	1	1	1	30,4



Cristallinity (%)	Temperature = X1	w/v% PLA = X2	v/v% H2O = X3	E/F = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
21,2	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
31,5	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
30,0	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1
28,3	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1
21,0	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
56,5	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1
27,0	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1
39,4	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
24,7	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
24,4	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1
17,3	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1
23,8	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
24,9	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
46,6	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1
28,1	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1
30,4	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Factors	X1	X2	X3	X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
Coefficients (βs)	5,411	-1,660	4,546	-2,181	-2,978	3,571	-1,640	-1,356	-0,962	0,417	-2,337	1,410	-1,338	0,733	-0,929

β estimada	β abs ord	i	corrected accumulated frequencies	probability	semi z	non significant βs	significant βs
5,411	0,417	1	0,033333333	0,5166667	0,417	0,417	
-1,660	0,733	2	0,1	0,55	0,733	0,733	
4,546	0,929	3	0,166666667	0,5833333	0,929	0,929	
-2,181	0,962	4	0,233333333	0,6166667	0,962	0,962	
-2,978	1,338	5	0,3	0,65	1,338	1,338	
3,571	1,356	6	0,366666667	0,6833333	1,356	1,356	
-1,640	1,410	7	0,433333333	0,7166667	1,410	1,410	
-1,356	1,640	8	0,5	0,75	1,640	1,640	
-0,962	1,660	9	0,566666667	0,7833333	1,660	1,660	
0,417	2,181	10	0,633333333	0,8166667	2,181	2,181	
-2,337	2,337	11	0,7	0,85	2,337	2,337	
1,410	2,978	12	0,766666667	0,8833333	2,978		2,978
-1,338	3,571	13	0,833333333	0,9166667	3,571		3,571
0,733	4,546	14	0,9	0,95	4,546		4,546
-0,929	5,411	15	0,966666667	0,9833333	5,411		5,411



SCR = $8*(\Sigma \text{ of non significant } \beta)^2$ 380,419148
SCEx= $8*(\Sigma \text{ of significant } \beta)^2$ 1145,118
SCT= (Σ of all β) 1525,53715

R^2=SCEx/SCT 0,75063266
average 29,688

linear model = crystallinity= 29,688 +5,411X1 +4,546X3 + 3,571X1X3 -2,978X1X2

Error calculations

linear model = crystallinity= 29,688 +5,411X1 +4,546X3 + 3,571X1X3 -2,978X1X2

βs	Cristallinity (%)	X1	X3	X1X3	X1X2	Y^	e
5,411	21,2	-1	-1	1	1	20,324	0,902638
4,546	31,5	1	-1	-1	-1	29,960	1,511536
3,571	30,0	-1	-1	1	-1	26,280	3,6877766
-2,978	28,3	1	-1	-1	1	24,004	4,288159
	21,0	-1	1	-1	1	22,274	-1,244999
	56,5	1	1	1	-1	46,194	10,347353
	27,0	-1	1	-1	-1	28,230	-1,183813
	39,4	1	1	1	1	40,238	-0,860986
	24,7	-1	-1	1	1	20,324	4,3806187
	24,4	1	-1	-1	-1	29,960	-5,577615
	17,3	-1	-1	1	-1	26,280	-8,969581
	23,8	1	-1	-1	1	24,004	-0,223119
	24,9	-1	1	-1	1	22,274	2,6024769
	46,6	1	1	1	-1	46,194	0,3580945
	28,1	-1	1	-1	-1	28,230	-0,174146
	30,4	1	1	1	1	40,238	-9,840578

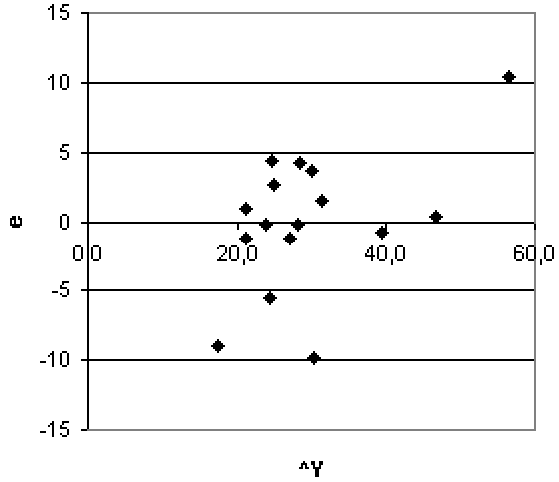
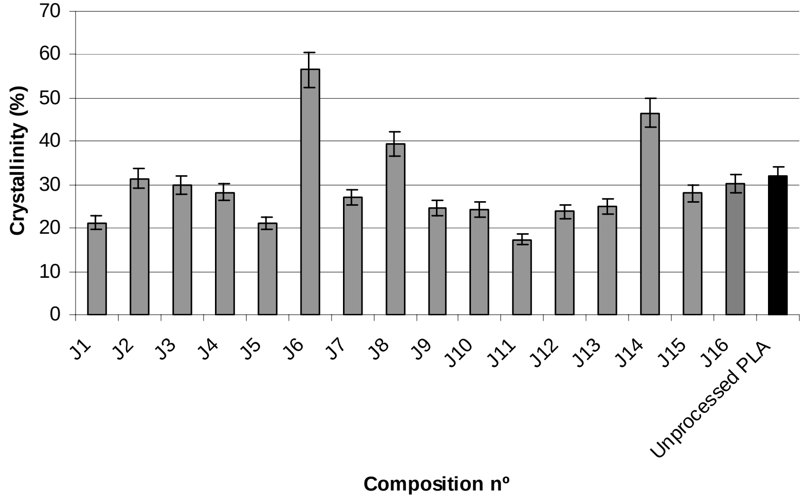


Table App3. 10: Experiment Design Calculations for the factors influencing the crystallinity of the phase-separated scaffolds. Optimisation study, with glass particles.

Composition nº	Temperature	w/v% PLA	v/v% H_20	Solvent removal method (E/F)	Tg
J1	-1	-1	-1	-1	48,52
J2	1	-1	-1	-1	47,23
J3	-1	1	-1	-1	58,72
J4	1	1	-1	-1	55,81
J5	-1	-1	1	-1	53,0
J6	1	-1	1	-1	52
J7	-1	1	1	-1	53,31
J8	1	1	1	-1	57,28
J9	-1	-1	-1	1	61,53
J10	1	-1	-1	1	60,53
J11	-1	1	-1	1	61,19
J12	1	1	-1	1	61,06
J13	-1	-1	1	1	61,2
J14	1	-1	1	1	60,9
J15	-1	1	1	1	60,47
J16	1	1	1	1	60,56

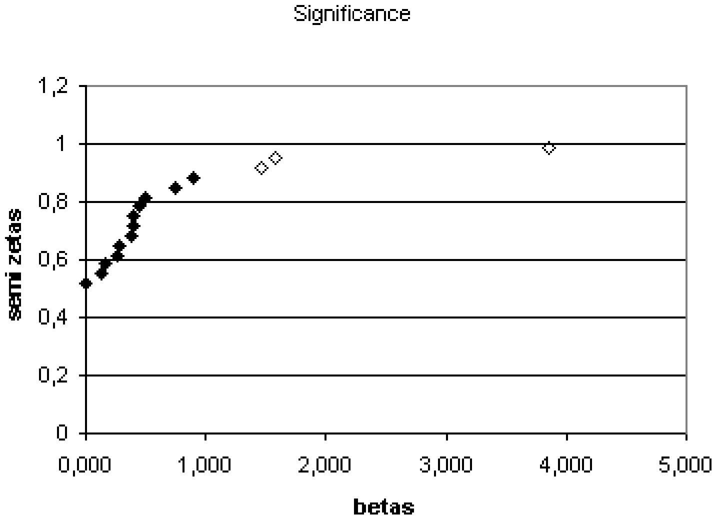


Tg	Temperature = X1	w/v% PLA = X2	v/v% H2O = X3	E/F = X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
48,52	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1	-1	-1	1
47,23	1	-1	-1	-1	-1	-1	-1	1	1	1	1	1	1	-1	-1
58,72	-1	1	-1	-1	-1	1	1	-1	-1	1	1	1	-1	1	-1
55,81	1	1	-1	-1	1	-1	-1	-1	-1	1	-1	-1	1	1	1
53,0	-1	-1	1	-1	1	-1	1	-1	1	-1	1	-1	1	1	-1
52	1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1	1	1
53,31	-1	1	1	-1	-1	-1	1	1	-1	-1	-1	1	1	-1	1
57,28	1	1	1	-1	1	1	-1	1	-1	-1	1	-1	-1	-1	-1
61,53	-1	-1	-1	1	1	1	-1	1	-1	-1	-1	1	1	1	-1
60,53	1	-1	-1	1	-1	-1	1	1	-1	-1	1	-1	-1	1	1
61,19	-1	1	-1	1	-1	1	-1	-1	1	-1	1	-1	1	-1	1
61,06	1	1	-1	1	1	-1	1	-1	1	-1	-1	1	-1	-1	-1
61,2	-1	-1	1	1	1	-1	-1	-1	-1	1	1	1	-1	-1	1
60,9	1	-1	1	1	-1	1	1	-1	-1	1	-1	-1	1	-1	-1
60,47	-1	1	1	1	-1	-1	-1	1	1	1	-1	-1	-1	1	-1
60,56	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1

Factor	X1	X2	X3	X4	X1X2	X1X3	X1X4	X2X3	X2X4	X3X4	X1X2X3	X1X2X4	X1X3X4	X2X3X4	X1X2X3X4
Coefficients	-0,161	1,468	0,258	3,848	0,288	0,506	-0,007	-0,903	-1,578	-0,406	0,382	-0,131	-0,391	0,746	-0,442

β estimada	β abs ord	i	corrected accumulated frequencies	probability	semi z
-0,161	0,007	1	0,033333333	0,516666667	0,007
1,468	0,131	2	0,1	0,55	0,131
0,258	0,161	3	0,166666667	0,583333333	0,161
3,848	0,258	4	0,233333333	0,616666667	0,258
0,288	0,288	5	0,3	0,65	0,288
0,506	0,382	6	0,366666667	0,683333333	0,382
-0,007	0,391	7	0,433333333	0,716666667	0,391
-0,903	0,406	8	0,5	0,75	0,406
-1,578	0,442	9	0,566666667	0,783333333	0,442
-0,406	0,506	10	0,633333333	0,816666667	0,506
0,382	0,746	11	0,7	0,85	0,746
-0,131	0,903	12	0,766666667	0,883333333	0,903
-0,391	1,468	13	0,833333333	0,916666667	1,468
0,746	1,578	14	0,9	0,95	1,578
-0,442	3,848	15	0,966666667	0,983333333	3,848

non significant βs	significant βs
0,007	
0,131	
0,161	
0,258	
0,288	
0,382	
0,391	
0,406	
0,442	
0,506	
0,746	
0,903	
	1,468
	1,578
	3,848



SCR = 8*(Σ of non significant β)^2 39,648075

SCEx= 8*(Σ of significant β)^2 311,26297

SCT= (Σ of all β) 350,91104

R^2=SCEx/SCT 0,8870139

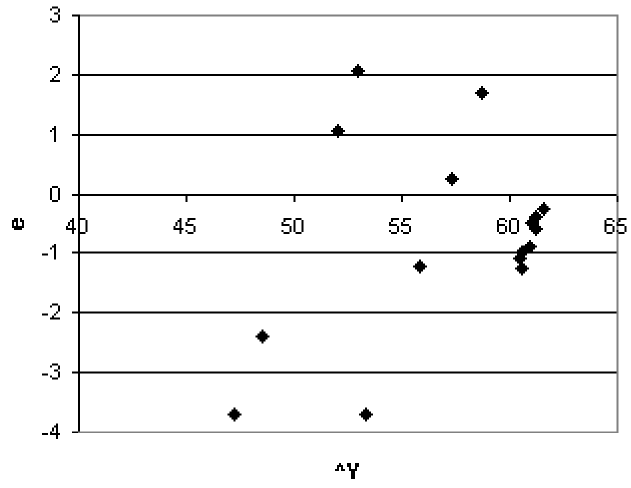
average 57,082

Linear model = Tg= 57,82 + 3,848X4 -1,578*X2*X4 +1,468X2

Error calculations

Linear model = Tg= 57,82 + 3,848X4 -1,578*X2*X4 +1,468X2

βs	Tg	X4	X2X4	X2	Y^	e
3,85	48,52	-1	1	-1	50,926	-2,406
-1,58	47,23	-1	1	-1	50,926	-3,696
1,468	58,72	-1	-1	1	57,018	1,702
	55,81	-1	-1	1	57,018	-1,208
	53,0	-1	1	-1	50,926	2,074
	52	-1	1	-1	50,926	1,074
	53,31	-1	-1	1	57,018	-3,708
	57,28	-1	-1	1	57,018	0,262
	61,53	1	-1	-1	61,778	-0,248
	60,53	1	-1	-1	61,778	-1,248
	61,19	1	1	1	61,558	-0,368
	61,06	1	1	1	61,558	-0,498
	61,2	1	-1	-1	61,778	-0,578
	60,9	1	-1	-1	61,778	-0,878
	60,47	1	1	1	61,558	-1,088
	60,56	1	1	1	61,558	-0,998



Appendix Chapter 4

Weeks in SBF	Porosity (%)	
	Solvent Casting	Phase Separation
0	**94,8** ± 0,09	**88,8** ± 0,55
2	**94,6** ± 0,25	**88,2** ± 0,70
4	**94,1** ± 0,42	**88,3** ± 0,86
6	**93,6** ± 0,39	**88,8** ± 0,65
8	**93,7** ± 0,53	**89,0** ± 0,48
10	**94,3** ±0,08	**89,1** ± 0,93

Table App4. 1: Porosity results for the solvent cast and phase-separated scaffolds during the ten weeks of degradation in SBF.

Weeks in SBF	Solvent Casting Stiffness (kPa)	Phase Separation Stiffness (MPa)
0	**78,81** ±19,8	**7,10** ± 1,4
2	**70,75** ± 16,2	**6,09** ± 1,9
4	**68,64** ± 15,1	**6,50** ± 1,2
6	**68,26** ± 10,0	**6,48** ± 2,1
8	**60,84** ± 6,5	**/**
10	**49,22** ± 6,7	**6,59** ± 2,3

Table App4. 2: Stiffness results for the solvent cast and phase-separated scaffolds during the ten weeks of degradation in SBF. Note, results for the solvent cast scaffolds are given in kPa.

Weeks in SBF	% weight loss	
	Solvent Casting	Phase Separation
0	**/**	**/**
2	**0,63%** ± 0,93%	**1,32%** ± 0,29%
4	**4,04%** ± 1,52%	**3,94%** ± 0,60%
6	**8,47%** ± 1,99%	**6,86%** ± 1,16%
8	**9,93%** ± 0,90%	**8,01%** ± 2,24%
10	**/**	**11,08%** ± 2,31%

Table App4. 3: % weight loss results for the solvent cast and phase separated scaffolds during the ten weeks of degradation in SBF.

Weeks in SBF	Glass particle content (%)	
	Solvent Casting	Phase Separation
0	**43,92%** ± 1,69%	**47,85%** ± 0,45%
2	**43,58%** ± 1,16%	**46,82%** ±0,18%
4	**42,01%** ± 1,28%	**47,52%** ± 1,47%
6	**40,65%** ± 0,41%	**45,18%** ± 0,42%
8	**39,63%** ± 0,89%	**41,79%** ± 0,21%
10	**37,49%** ± 0,73%	**43,04%** ± 0,25%

Table App4. 4: Glass particle content results for the solvent cast and phase separated scaffolds during the ten-week degradation in SBF.

Week	Tg (ºC) (2nd ramp)	Tm(ºC) (1st ramp)	Hf (J/g) (1st ramp)	Tc (ºC) (2nd ramp)	Hc (J/g) (2nd ramp)	% X_c 1st ramp)
0	63.05 ± 0.47	158.20 ± 0.90	8.07 ± 1.29	129.73 ± 0.98	2.85 ± 1.11	12.0% ± 6.3%
2	62.81 ± 0.54	158.11 ± 0.55	11.07 ± 1.04	125.94 ± 1.35	9.58 ± 1.70	21.1% ± 2.0%
4	61.97 ± 0.42	157.78 ± 0.26	12.85 ± 0.54	125.48 ± 0.43	13.37 ± 1.80	23.8% ± 1.0%
6	61.93 ± 0.17	159.15 ± 0.53	13.11 ± 0.09	123.87 ± 1.37	12.54 ± 1.58	23.7% ± 0.2%
8	61.70 ± 0.09	159.69 ± 0.45	13.85 ± 1.50	120.67 ± 0.53	17.31 ± 1.58	24.6% ± 2.7%
10	61.70 ± 0.45	159.25 ± 0.21	12.60 ± 0.26	123.49 ± 3.56	15.42 ± 3.18	21.6% ± 0.5%

Table App4. 5: Evolution of the thermal properties of the solvent cast scaffolds during the ten-week degradation in SBF.

Week	Tg (ºC) (2nd ramp)	Tm(ºC) (1st ramp)	Hf (J/g) (1st ramp)	Tc (ºC) (2nd ramp)	Hc (J/g) (2nd ramp)	% X_c 1st ramp)
0	59.35 ± 1.13	158.56 ± 1.56	13.16 ± 1.08	130.40 ± 2.10	2.05 ± 0.46	27.1% ± 2.2%
2	60.22 ± 1.05	160.63 ± 0.92	15.64 ± 0.45	126.44 ± 3.07	12.46 ± 3.43	31.6% ± 0.9%
4	61.36 ± 0.24	161.37 ± 0.64	15.77 ± 0.76	130.04 ± 0.61	7.31 ± 1.21	32.3% ± 1.6%
6	61.01 ± 0.70	162.57 ± 1.07	16.71 ± 0.12	125.28 ± 4.16	12.24 ± 3.61	32.7% ± 0.2%
8	60.20 ± 1.03	163.00 ± 0.98	17.81 ± 1.45	118.35 ± 4.16	16.33 ± 1.52	32.9% ± 2.7%
10	59.43 ± 0.39	163.46 ± 0.94	19.44 ± 1.46	115.31 ± 2.46	19.05 ± 1.05	36.7% ± 2.8%

Table App4. 6: Evolution of the thermal properties of the phase-separated scaffolds during the ten-week degradation in SBF.

Appendix Chapter 5

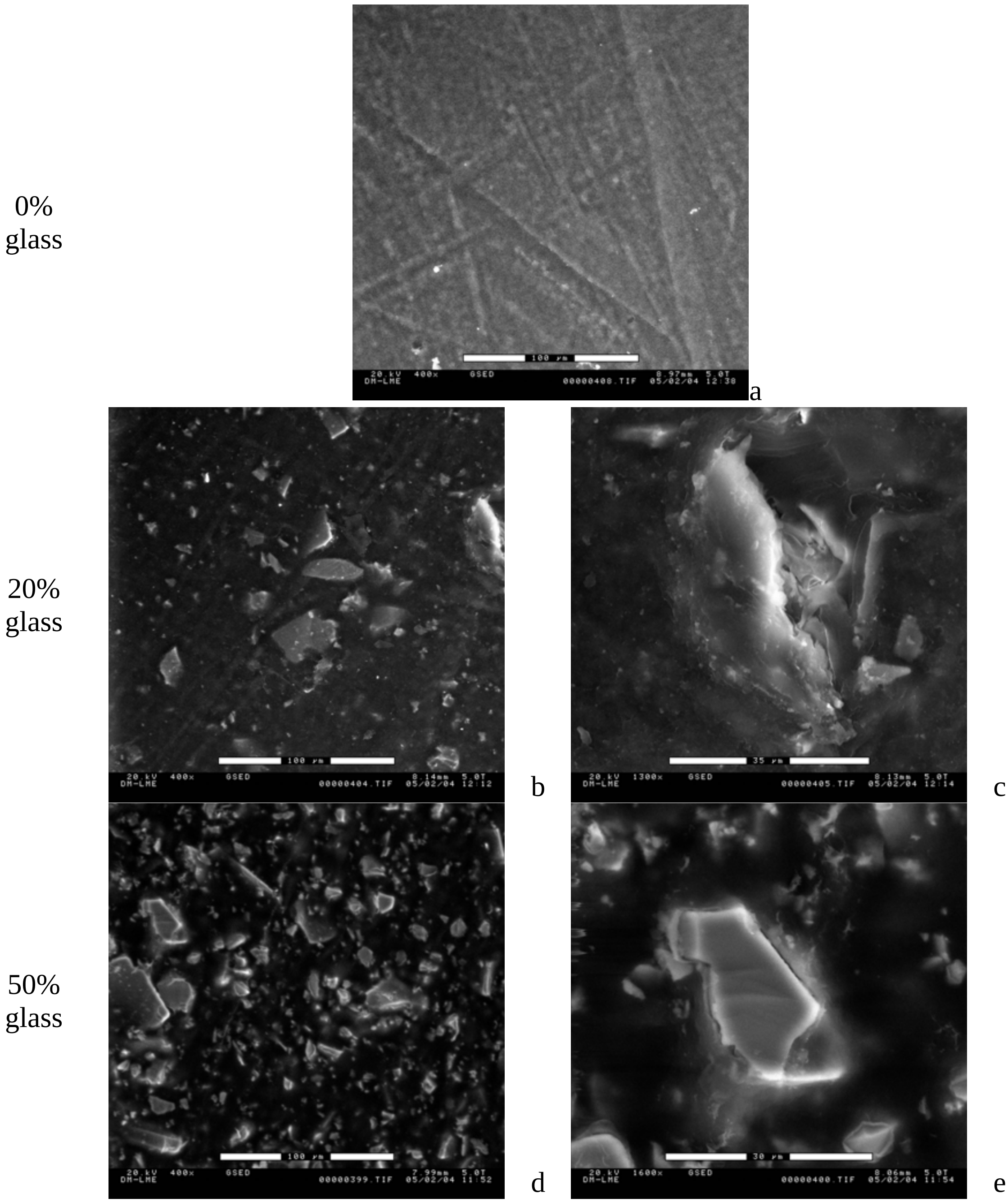
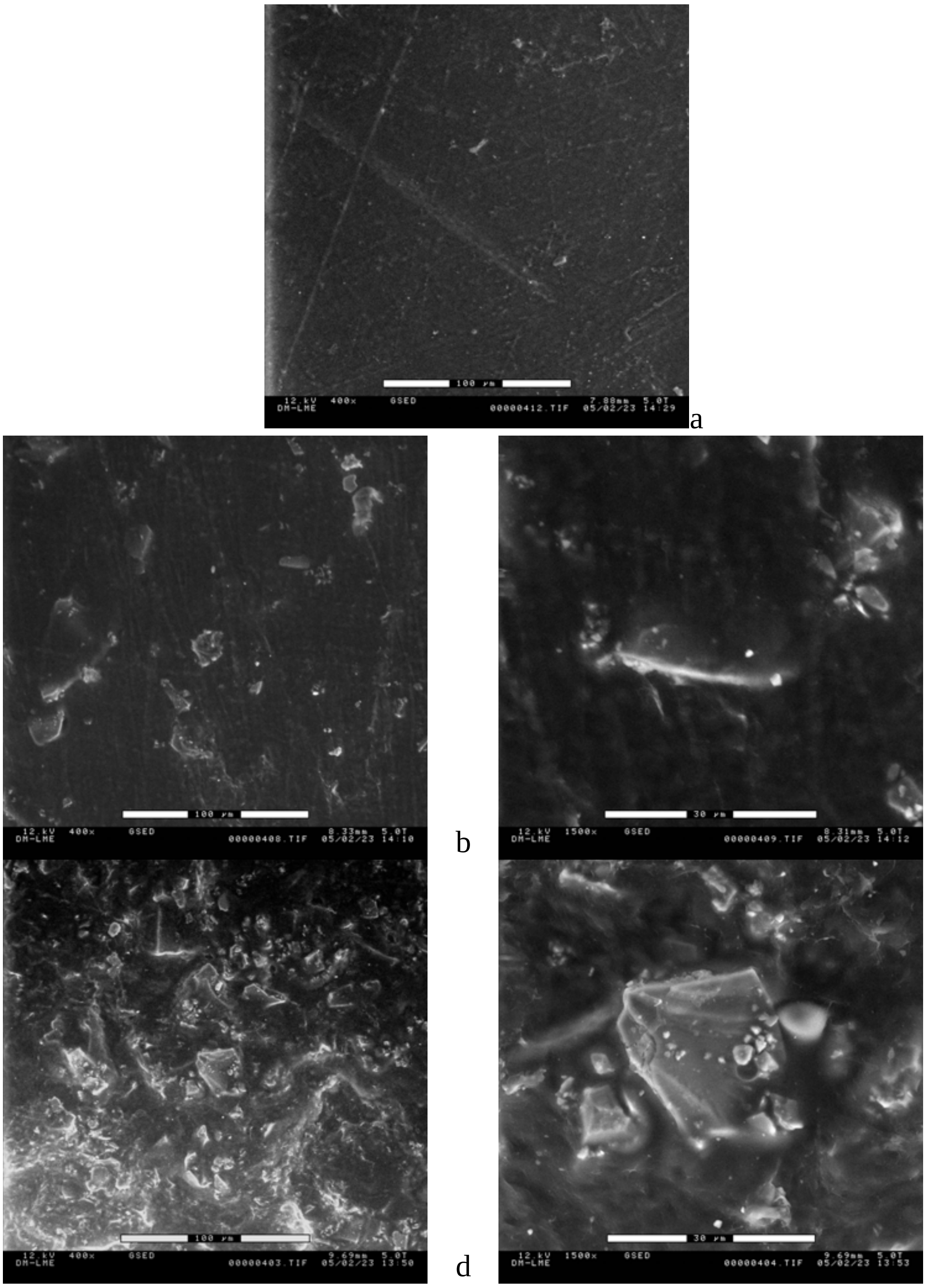


Figure App5. 1: ESEM images of the lower surface of the composite films made of PLA dissolved in chloroform with 0%, 20% and 50 wt% glass particles.



0% glass

a

20% glass

b c

50% glass

d e

Figure App5. 2: ESEM images of the lower surface of the composite films made of PLA dissolved in dioxane with 0%, 20% and 50 wt% glass particles.

Composition	Sa (nm)	Sku	Ssk	SAI
0%C lower face	497.20 ± 131.89	64.00 ± 66.43	-1.40 ± 3.09	1.06 ± 0.01
20%C lower face	890.00 ± 137.78	47.10 ± 40.79	-2.67 ± 2.91	1.12 ± 0.04
50%C lower face	2778.06 ± 429.00	7.91 ± 1.90	-1.39 ± 0.43	1.52 ± 0.10
0%D lower face	525.73 ±70.50	19.05 ± 7.24	0.86 ± 0.82	1.06 ± 0.01
20%D lower face	728.52 ± 77.00	51.58 ± 24.79	-3.10 ± 1.79	1.12 ± 0.03
50%D lower face	3106.99 ± 307.40	6.00 ± 0.98	-0.73 ± 0.40	1.43 ± 0.10

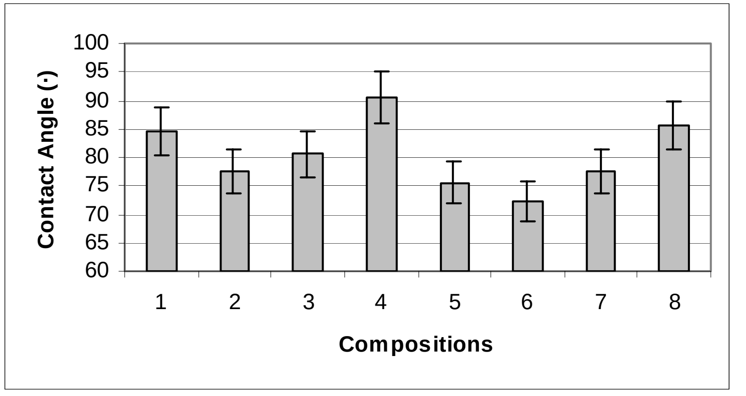
Table App5. 1: Roughness parameters of the lower faces of the composite films. Sa= spacing between local peaks, Sku = hurtosis of the surface, Ssk = skewdness of the surface plane, and SAI = surface area index.

Composition	Sa (nm)	Sku	Ssk	SAI
0%C sterilised	80.30 ± 25.13	90.67 ± 136.60	-3.74 ± 6.43	1.0 ± 0.001
20%C sterilised	1617.49 ± 186.60	9.80 ± 2.26	0.44 ± 0.47	1.11 ± 0.02
50%C sterilised	3759.11 ± 459.00	5.15 ± 1.29	-0.42 ± 0.31	1.54 ± 0.11
0%D sterilised	264.89 ± 46.60	15..32 ± 26.20	-0.90 ± 2.34	1.02 ± 0.02
20%D sterilised	1560.35 ± 145.71	14.62 ± 8.21	-1.06 ± 1.13	1.09 ± 0.02
50%D sterilised	4476.10 ± 207.70	3.58 ± 0.17	-0.022 ± 0.21	1.67 ± 0.03

Table App5. 2: Roughness parameters of the upper face of the sterilised composite films. Sa= spacing between local peaks, Sku = hurtosis of the surface, Ssk = skewdness of the surface plane, and SAI = surface area index.

Figure App5. 1: Experiment design calculation for the factors influecning the contact angle of the composite films.

0%-50%	X1	X2	X3	
Composition nº	**Glass wt% -1=0% +1=50%**	**Solvent -1=chloroform +1 =dioxane**	**Sterilisation -1=no +1=yes**	**Contact Angle (·)**
1	-	-	-	84,457
2	+	-	-	77,57
3	-	+	-	80,638
4	+	+	-	90,596
5	-	-	+	75,539
6	+	-	+	72,311
7	-	+	+	77,471
8	+	+	+	85,529

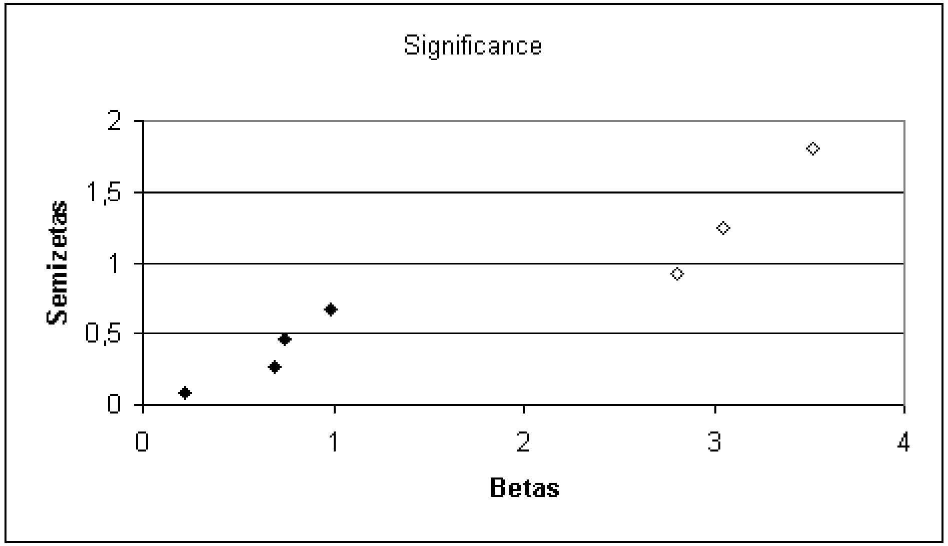


Contact Angle (·)	Glass wt% = **X1**	Solvent = **X2**	Sterilisation = **X3**	**X1X2**	**X1X3**	**X2X3**	**X1X2X3**
84,457	-1	-1	-1	1	1	1	-1
77,57	1	-1	-1	-1	-1	1	1
80,638	-1	1	-1	-1	1	-1	1
90,596	1	1	-1	1	-1	-1	-1
75,539	-1	-1	1	1	-1	-1	1
72,311	1	-1	1	-1	1	-1	-1
77,471	-1	1	1	-1	-1	1	-1
85,529	1	1	1	1	1	1	1

Term	**X1**	**X2**	**X3**	**X1X2**	**X1X3**	**X2X3**	**X1X2X3**
Coefficient	0,987625	3,044625	-2,801375	3,516375	0,219875	0,742875	-0,694875

stimated βs	β abs ord	i	frec corr.	prob	semi z	non significant βs	significant βs
0,987625	0,219875	1	0,071429	0,535714286	0,0896421	0,219875	
3,044625	0,694875	2	0,214286	0,607142857	0,2718798	0,694875	
-2,801375	0,742875	3	0,357143	0,678571429	0,4637081	0,742875	
3,516375	0,987625	4	0,500000	0,75	0,6744904	0,987625	
0,219875	2,801375	5	0,642857	0,821428571	0,9208225		2,801375
0,742875	3,044625	6	0,785714	0,892857143	1,2418673		3,044625
-0,694875	3,516375	7	0,928571	0,964285714	1,8027458		3,516375

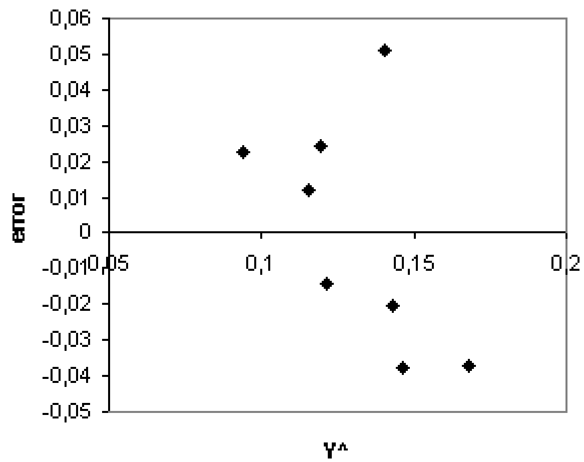
SCR = 8*(Σ of non significant β)^2	16,4677015
SCEx= 8*(Σ of significant β)^2	235,8586914
SCT= (Σ of all β)	252,3263929
R^2=SCEx/SCT	0,934736508
average	80,51



linear model: Contact Angle =Y= 80,51+3,52X1X2+3,04X2-2,80X3 = 80,51 +3,52*Glasswt%*SolventType + 3,042* Solvent Type - 2,80* Sterilisation

linear model: Contact Angle= Y= 80,51+3,52X1X2+3,04X2-2,80X3

betas
3,516375
3,044625
-2,801375



Contact Angle (·)	X1*X2	X2	X3	Y^	e
84,457	1	-1	-1	83,787	0,67
77,57	-1	-1	-1	76,75425	0,81575
80,638	-1	1	-1	82,8435	-2,2055
90,596	1	1	-1	89,87625	0,71975
75,539	1	-1	1	78,18425	-2,64525
72,311	-1	-1	1	71,1515	1,1595
77,471	-1	1	1	77,24075	0,23025
85,529	1	1	1	84,2735	1,2555