

1 Supplementary Tables

2 Table S1. Full model parameters for the interactive effects of eugenol and thymol on four strains
 3 of *C. bombi*. Model parameters were estimated using a Universal Response Surface Analysis as
 4 described by Greco *et al.* (Greco *et al.* 1990, 1995). The parameter “m” describes how rapidly
 5 growth decreased at the EC50 phytochemical concentration. Parameter “gmin” represents the
 6 lower limit of growth at very high phytochemical concentrations; “gmax” represents the
 7 maximum growth in the absence of phytochemicals. The EC50 is the concentration (in ppm
 8 phytochemical) that inhibited growth by 50%. The interaction parameter “f” indicates synergy ($f >$
 9 0), additivity ($f = 0$), or antagonism ($f < 0$) between the two compounds. SE: standard error. The
 10 parameter “s” is related to “f” by the equation

$$11 \quad s = 4(s^2 - s)$$

12 where $s > 1$ indicates synergy, $s = 1$ indicates additivity, and $s < 1$ indicates antagonism. Values of
 13 “NA” in the confidence interval indicate that the parameter was fixed to assist model
 14 convergence.

Strains tested in series					
				95% CI	
Round	Strain	Parameter	estimate	lower	upper
1	IL13.2	m(eugenol)	-2.10	-2.37	-1.84
1	IL13.2	m(thymol)	-1.13	-1.19	-1.07
1	IL13.2	gmin	0.50	NA	NA
1	IL13.2	gmax	19.24	NA	NA
1	IL13.2	EC50(eugenol)	171.60	158.98	184.22
1	IL13.2	EC50(thymol)	30.98	29.18	32.78
1	IL13.2	f	5.07	4.22	5.93
1	IL13.2	s	1.73	1.64	1.82

2	IL13.2	m(eugenol)	-1.73	-2.26	-1.21
2	IL13.2	m(thymol)	-0.69	-0.76	-0.61
2	IL13.2	gmin	0.53	-0.28	1.35
2	IL13.2	gmax	18.53	17.94	19.13
2	IL13.2	EC50(eugenol)	154.03	139.01	169.05
2	IL13.2	EC50(thymol)	28.81	25.11	32.51
2	IL13.2	f	6.14	3.78	8.50
2	IL13.2	s	1.84	1.59	2.04
3	IL13.2	m(eugenol)	-2.84	-3.05	-2.62
3	IL13.2	m(thymol)	-1.83	-1.93	-1.74
3	IL13.2	gmin	0.35	0.22	0.48
3	IL13.2	gmax	18.31	18.01	18.61
3	IL13.2	EC50(eugenol)	123.44	119.09	127.78
3	IL13.2	EC50(thymol)	22.24	21.34	23.14
3	IL13.2	f	1.12	0.94	1.31
3	IL13.2	s	1.23	1.20	1.26
4	VT1	m(eugenol)	-1.63	-1.71	-1.55
4	VT1	m(thymol)	-1.54	-1.62	-1.47
4	VT1	gmin	0.55	0.52	0.59
4	VT1	gmax	7.00	6.90	7.10
4	VT1	EC50(eugenol)	58.77	56.88	60.65
4	VT1	EC50(thymol)	14.88	14.34	15.43
4	VT1	f	0.69	0.57	0.81
4	VT1	s	1.15	1.13	1.17
5	C1.1	m(eugenol)	-1.93	-2.06	-1.79
5	C1.1	m(thymol)	-1.91	-2.04	-1.77
5	C1.1	gmin	0.49	0.43	0.54
5	C1.1	gmax	7.44	7.28	7.61
5	C1.1	EC50(eugenol)	56.53	53.85	59.20
5	C1.1	EC50(thymol)	13.46	12.83	14.09
5	C1.1	f	0.33	0.18	0.48
5	C1.1	s	1.08	1.04	1.11
6	S08	m(eugenol)	-1.59	-1.64	-1.54
6	S08	m(thymol)	-1.37	-1.43	-1.32
6	S08	gmin	0.46	0.44	0.49
6	S08	gmax	8.25	8.16	8.33
6	S08	EC50(eugenol)	43.99	42.87	45.11
6	S08	EC50(thymol)	8.47	8.23	8.71
6	S08	f	0.50	0.42	0.58
6	S08	s	1.11	1.10	1.13

Strains tested in parallel					
				95% CI	
Round	Strain	Parameter	estimate	lower	upper
Together	IL13.2	m(eugenol)	-1.61	-1.82	-1.39
Together	IL13.2	m(thymol)	-0.70	-0.80	-0.60
Together	IL13.2	gmin	0.50	NA	NA
Together	IL13.2	gmax	23.41	NA	NA
Together	IL13.2	EC50(eugenol)	184.99	176.48	193.51
Together	IL13.2	EC50(thymol)	49.81	49.49	50.12
Together	IL13.2	f	6.00	5.76	6.25
Together	IL13.2	s	1.82	1.80	1.85
Together	C1.1	m(eugenol)	-2.20	-2.41	-1.99
Together	C1.1	m(thymol)	-1.61	-1.74	-1.47
Together	C1.1	gmin	0.50	NA	NA
Together	C1.1	gmax	11.37	NA	NA
Together	C1.1	EC50(eugenol)	87.17	81.63	92.72
Together	C1.1	EC50(thymol)	22.82	21.39	24.25
Together	C1.1	f	1.34	0.86	1.82
Together	C1.1	s	1.27	1.18	1.34
Together	VT1	m(eugenol)	-2.46	-2.88	-2.03
Together	VT1	m(thymol)	-1.33	-1.49	-1.17
Together	VT1	gmin	0.50	NA	NA
Together	VT1	gmax	10.66	10.13	11.18
Together	VT1	EC50(eugenol)	100.60	92.43	108.76
Together	VT1	EC50(thymol)	26.60	23.25	29.95
Together	VT1	f	2.12	1.68	2.57
Together	VT1	s	1.38	1.32	1.44
Together	S08	m(eugenol)	-2.26	-2.54	-1.98
Together	S08	m(thymol)	-1.17	-1.29	-1.05
Together	S08	gmin	0.50	NA	NA
Together	S08	gmax	13.61	13.07	14.15
Together	S08	EC50(eugenol)	102.07	90.86	113.27
Together	S08	EC50(thymol)	21.29	18.30	24.28
Together	S08	f	2.96	1.95	3.98
Together	S08	s	1.50	1.36	1.62

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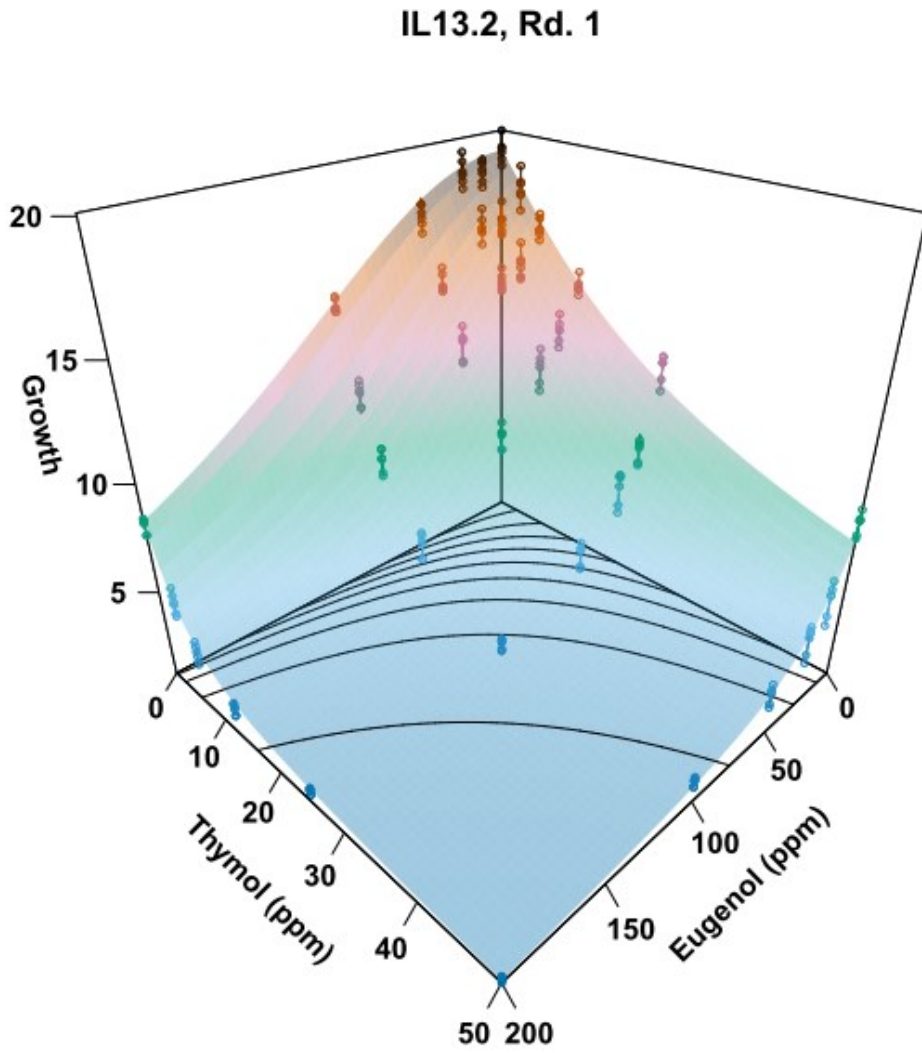
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17 **Supplementary Figures**

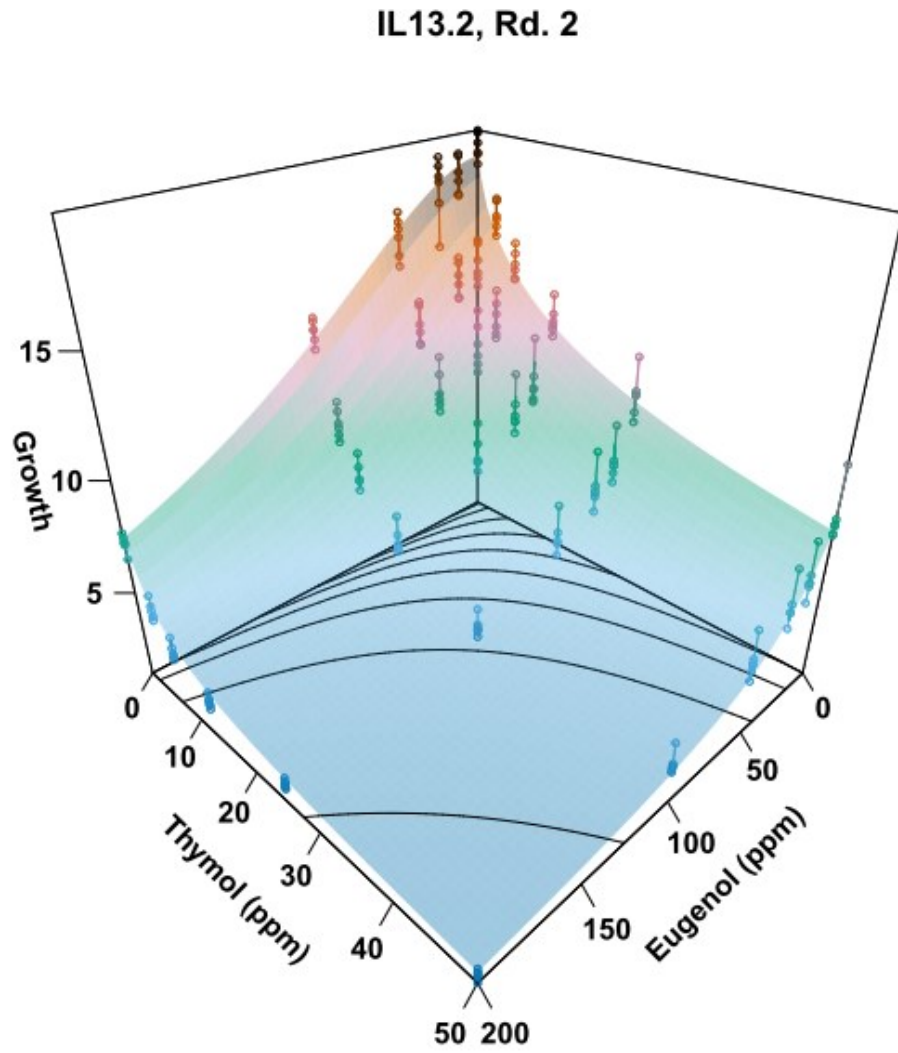
18 **Supplementary Figures S1-S6: Response surface plots showing combinatorial effects of**
19 **eugenol and thymol against *C. bombi* for a series of 6 experiments on 4 strains.** Each graph
20 shows the effects of the two compounds for a given strain and week. Contour lines on the basal
21 x-y plane show isoclines of equal growth. The concave isoclines in panels indicate synergistic
22 effects. The response surface shows model-predicted growth, points show observed growth, and
23 drop-lines indicate the deviation between observed and predicted growth; drop-lines are not
24 visible in some cases due to the orientation of the graph and the good fit of the model. Surfaces
25 and points are color-coded according the z-axis, which shows the integral of growth over five
26 days; z-axes are scaled according to each strain's maximum growth. Each experiment included n
27 = 216 replicates (6 replicate wells at each of 36 combinations of eugenol and thymol). ppm: parts
28 per million.

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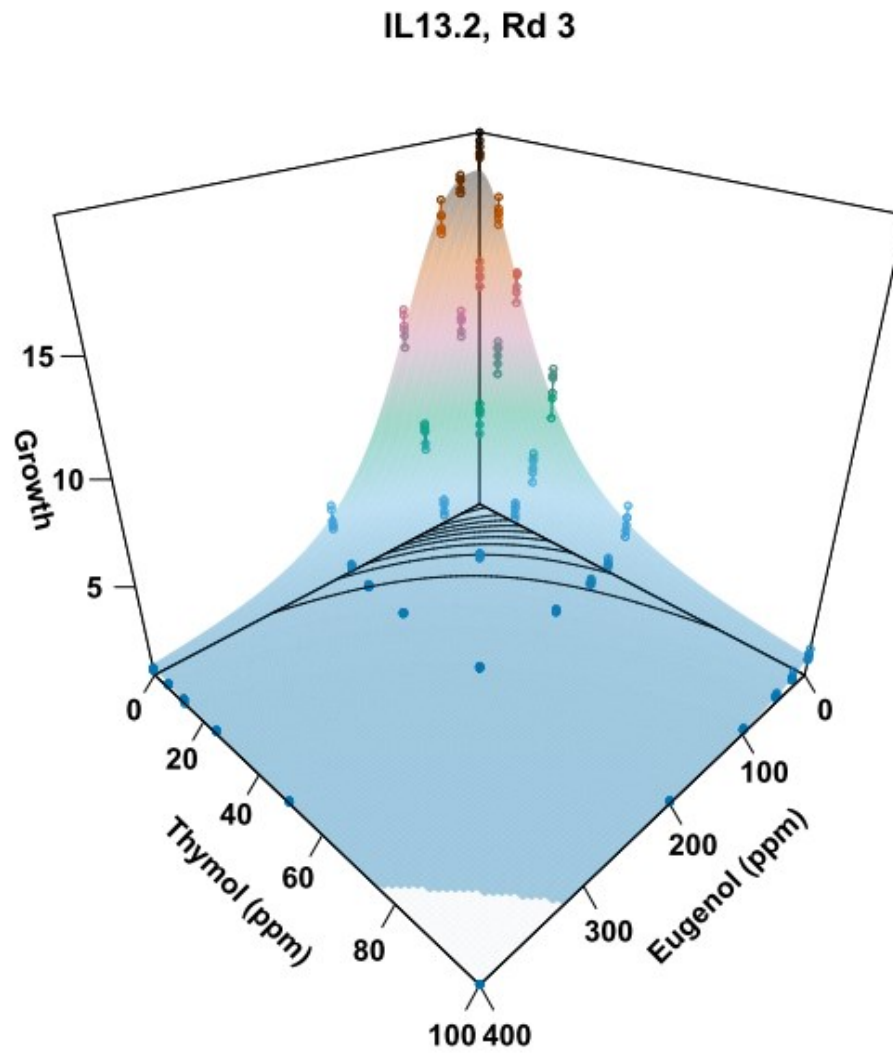
30 Figure S1. Strain IL13.2, Round 1



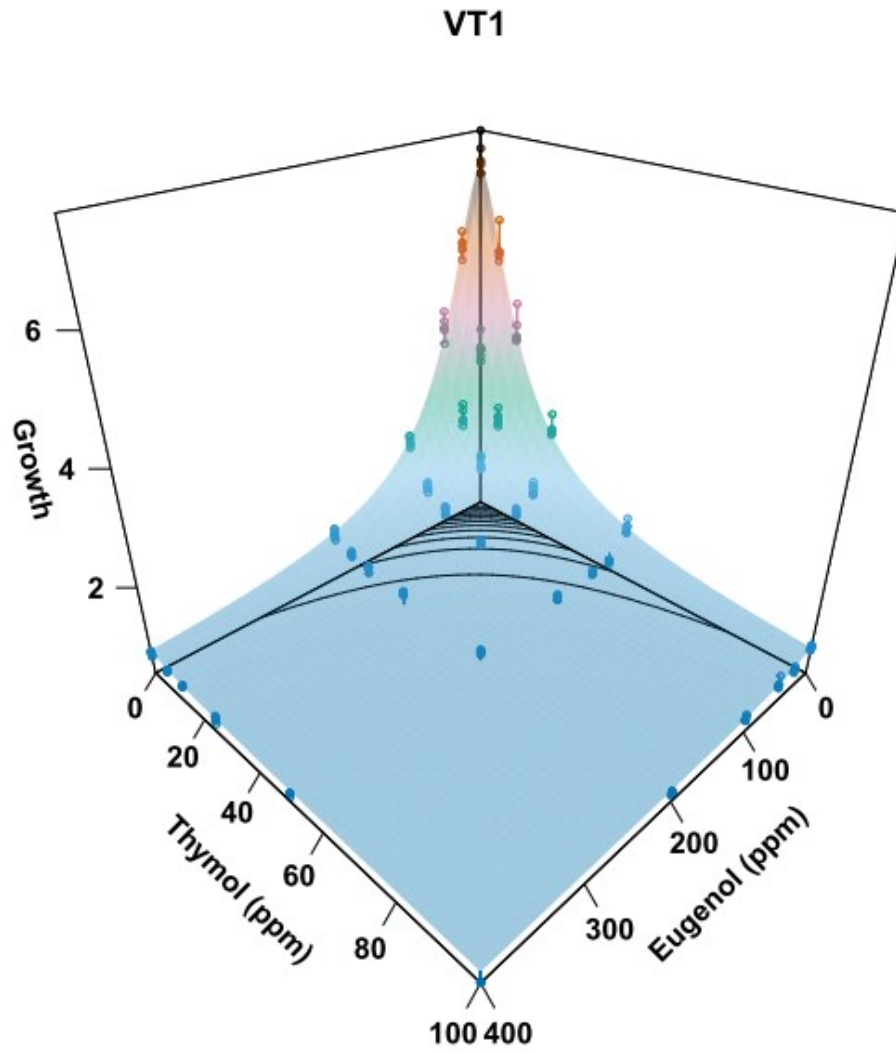
32 **Figure S2. Strain IL13.2, Round 2**



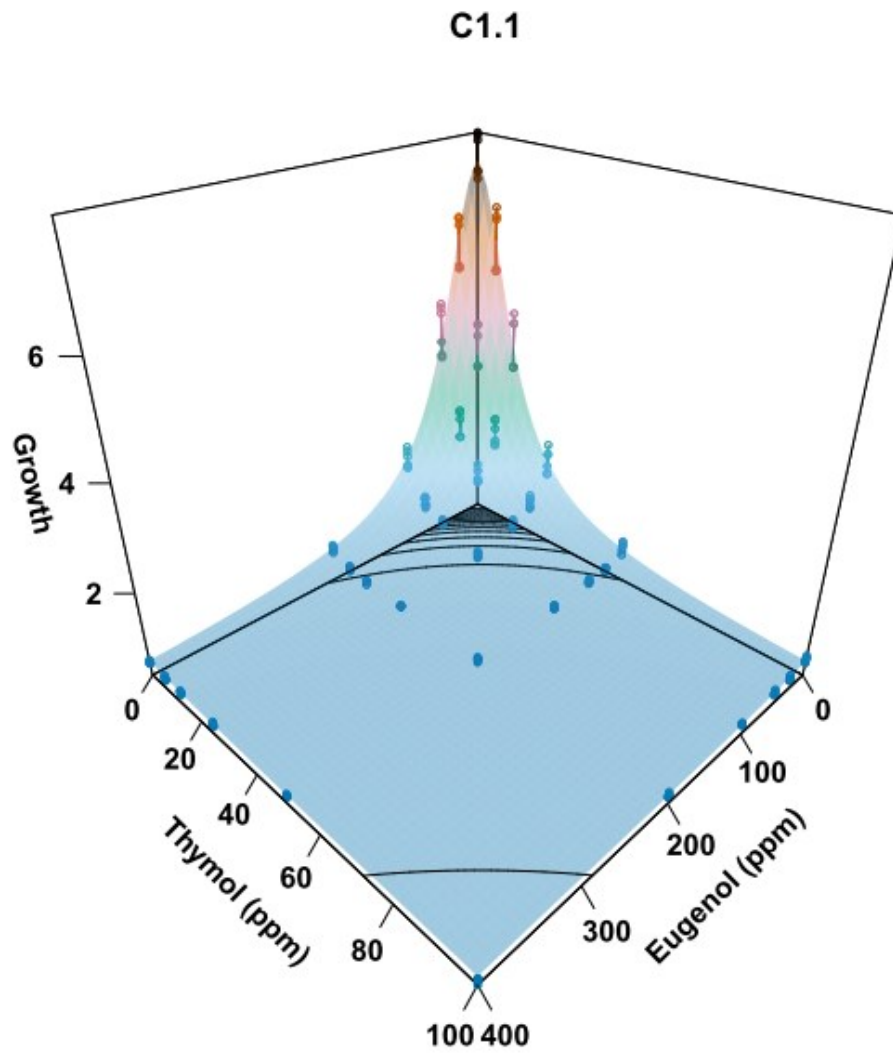
34 **Figure S3. Strain IL13.2, Round 3**



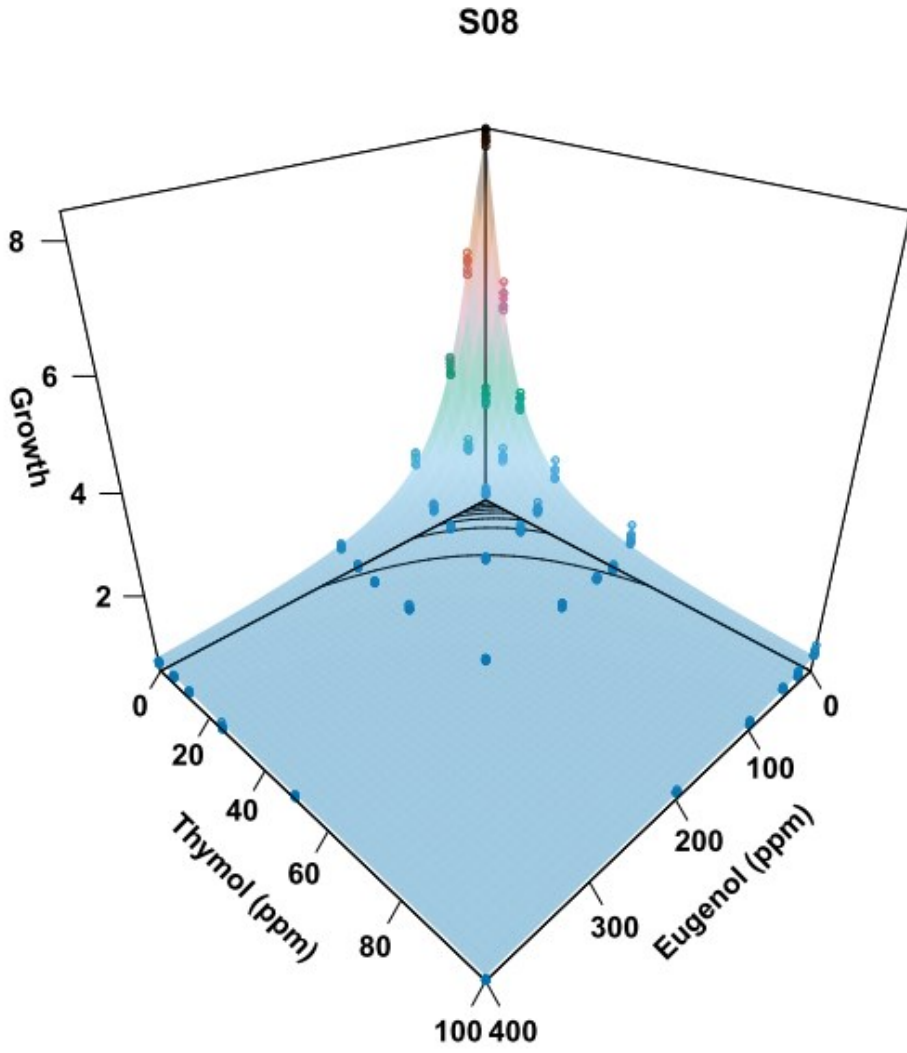
36 **Figure S4. Strain VT1**



38 **Figure S5. Strain C1.1**



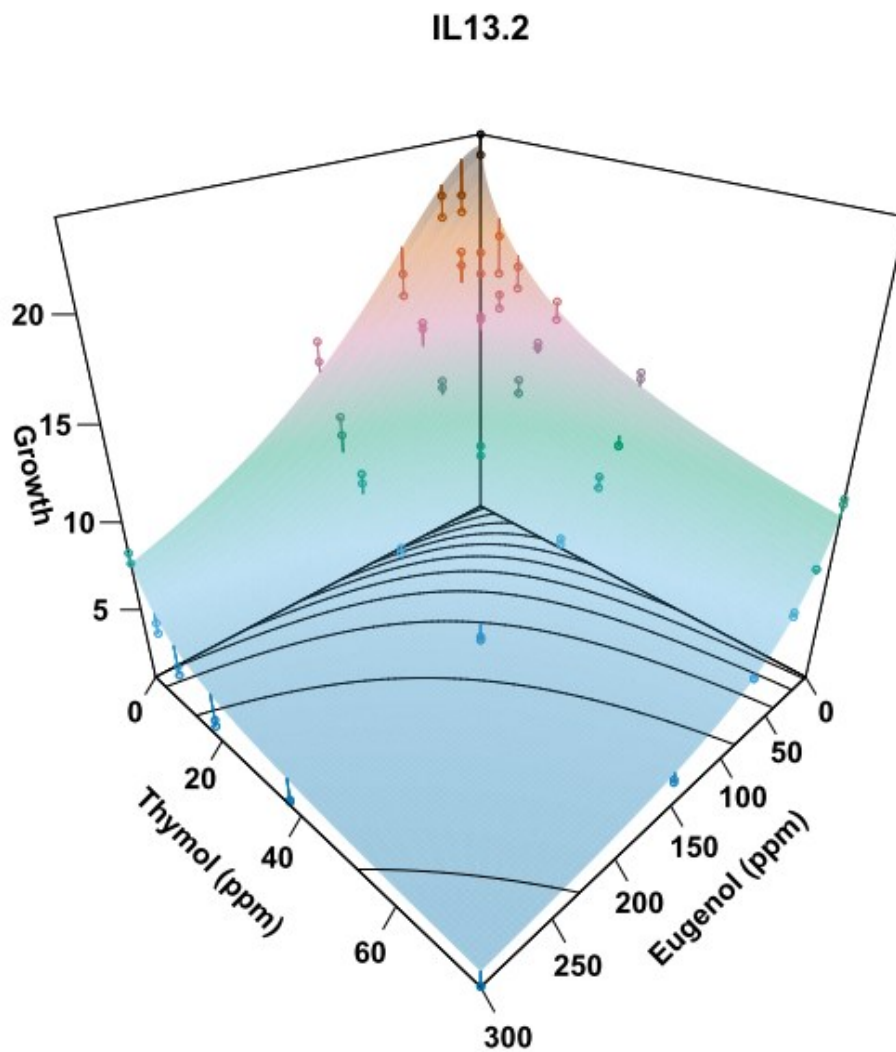
40 **Figure S6, Strain S08**



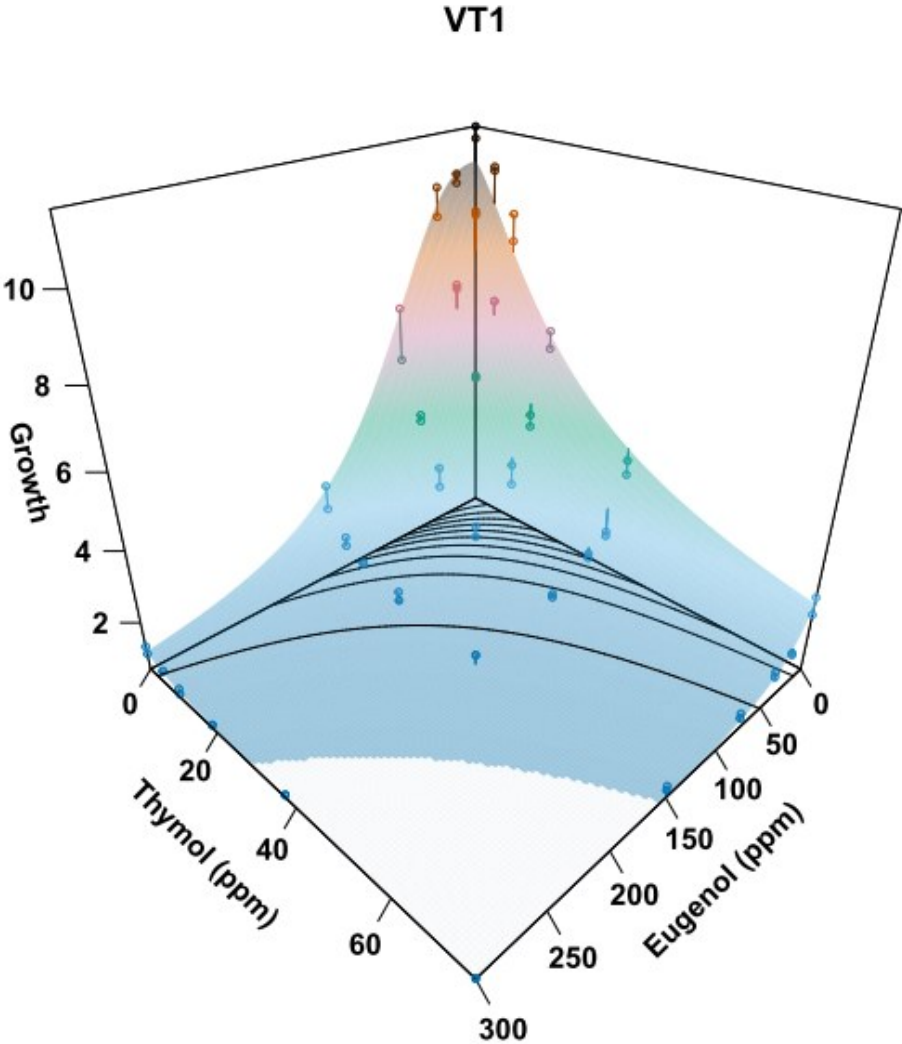
42 **Supplementary Figures S7-S10: Response surface plots for experiments with strains tested**
43 **in parallel (i.e., concurrently).** Each graph shows the effects of the two compounds for a given
44 strain and week. Contour lines on the basal x-y plane show isoclines of equal growth. The
45 concave isoclines in panels indicate synergistic effects. The response surface shows model-
46 predicted growth, points show observed growth, and drop-lines indicate the deviation between
47 observed and predicted growth; drop-lines are not visible in some cases due to the orientation of
48 the graph and the good fit of the model. Surfaces and points are color-coded according the z-axis,
49 which shows the integral of growth over five days; z-axes are scaled according to each strain's
50 maximum growth. Tests of each strain included $n = 72$ samples (2 replicate wells at each of 36
51 combinations of eugenol and thymol). ppm: parts per million.

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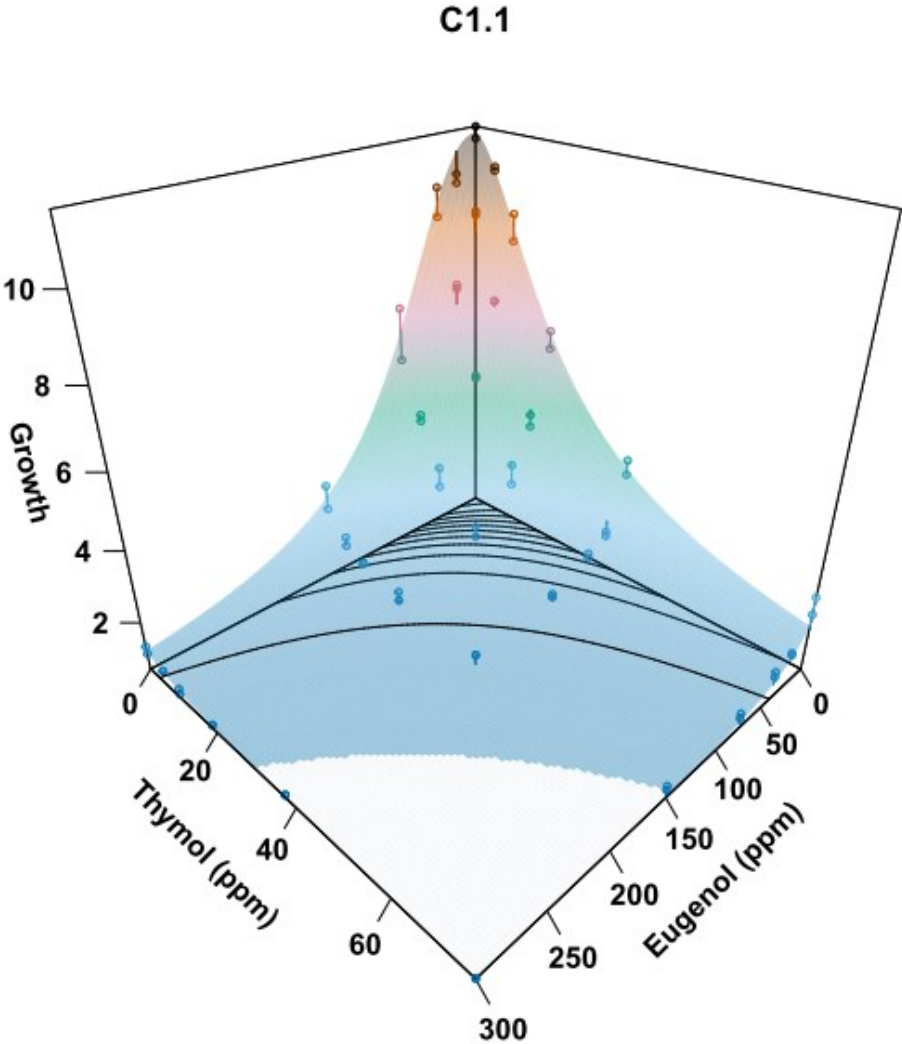
53 **Figure S7. Strain IL13.2**



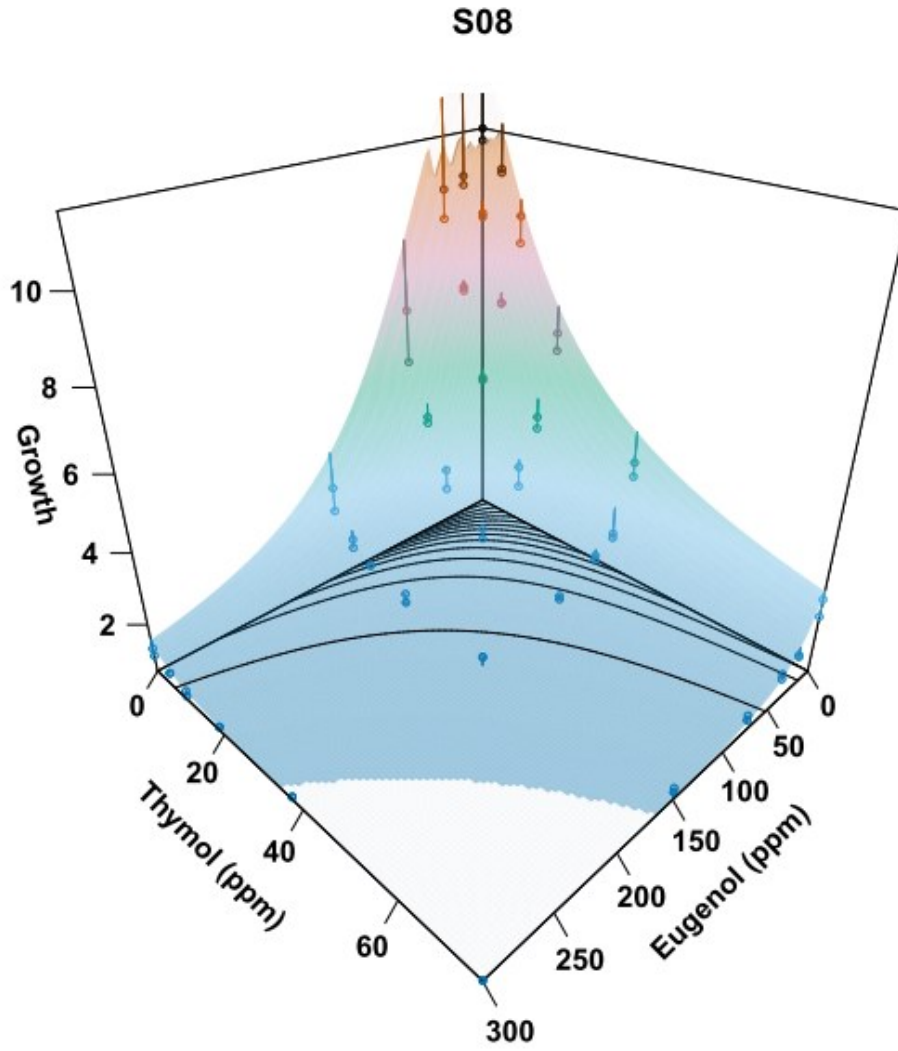
55 **Figure S8. Strain VT1**



57 **Figure S9. Strain C1.1**



59 **Figure S10. Strain S08**



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