Minimizing inbreeding in a synthetic population by considering genetic distance and dose of parental components

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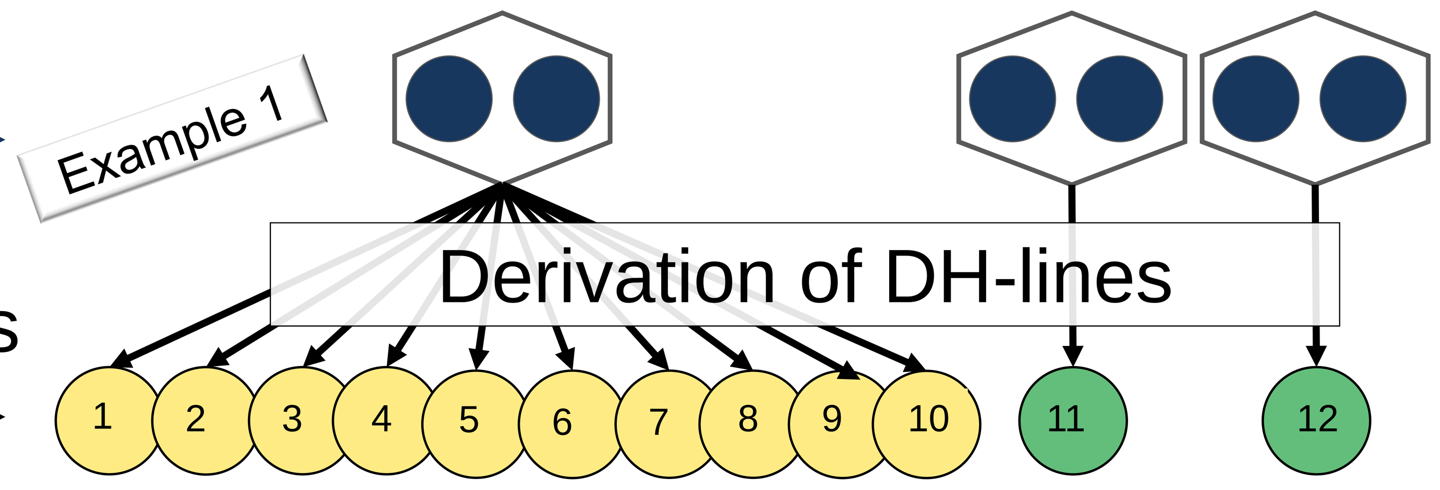
Imagine, you create a synthetic population, and some of your selected components are genetically related to each other (the other components are unrelated).

You would not create the initial mixture (Syn-0) as usual, with equal seed dose of each component! You would see that this might not be the best solution.

Find the optimum seed dose of the related components relative to the non-related ones! Lower dose for the related components, sure – but how low exactly?



Mutual distance among 12 homozygous components and resulting naïv and optimized mean distance

►► Components ▼	1	2	3	4	5	6	7	8	9	10	**11**	**12**	Mean distance	Optimized mean distance
Optimum "relative dose" per component; relative to **[11]** and to **[12]**	**0.1818**	0.1818	0.1818	0.1818	0.1818	0.1818	0.1818	0.1818	0.1818	0.1818	**1**	**1**		
Optimum dose per component (∑ = 1) ▼	**0.0476**	0.0476	0.0476	0.0476	0.0476	0.0476	0.0476	0.0476	0.0476	0.0476	**0.2619**	**0.2619**		
1	0.0	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	1.0	1.0	**0.542**	**0.738**
2	0.5	0.0	0.5	0.5	0.5	0.5	0.5	0.5	[illegible]	[illegible]	[illegible]	[illegible]	**0.542**	**0.738**
3	0.5	0.5	0.0	0.5	0.5	0.5	0.5	0.5	[illegible]	[illegible]	[illegible]	[illegible]	**0.542**	**0.738**
4	0.5	0.5	0.5	0.0	0.5	0.5	0.5	0.5	[illegible]	0.5	1.0	1.0	**0.542**	**0.738**
5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	0.5	0.5	0.5	1.0	1.0	**0.542**	**0.738**
6	0.5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	0.5	0.5	1.0	1.0	**0.542**	**0.738**
7	0.5	0.5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	0.5	1.0	1.0	**0.542**	**0.738**
8	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	1.0	1.0	**0.542**	**0.738**
9	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.0	0.5	1.0	1.0	**0.542**	**0.738**
10	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.0	1.0	1.0	**0.542**	**0.738**
11	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	1.0	**0.917**	**0.738**
12	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	**0.917**	**0.738**
Average ►►													**0.604**	**0.738**

Components [1-10] are mutually related, with genetic distances of d=0,5; each of [1-10] should enter with a dose of 4.76%, compared to 26.19% for [11] & [12]. The optimum "relative dose" of each member of [1-10] to [11] or [12] is 2/11 (i.e., 0.1818; cf. box at bottom); with this, each component's average distance is the same and maximum. The naïv mean distance is 22% smaller than the optimized mean distance (0.604<0.738); in maize, this might result in a heterotic yield gain of ~10%. As approximation, one could enter [1-10] with a relative dose of 2/10 each (they represent 2 ancestors). That mean distance then would be 0.717 (only 3% lower than optimum).

Mutual distance among 12 homozygous components and resulting mean and optimized mean distance (Example 2)

►► Components ▼	1	2	3	4	5	6	7	8	9	10	11	12	Mean distance	Optimized mean distance
Optimum "relative dose" per component; relative to [11] and to [12]	0.2222	0.2222	0.2222	0.2222	0.2222	0.2222	0.2222	0.2222	0.5333	0.5333	1	1		
Optimum dose per component (∑ = 1) ▼	0.0459	0.0459	0.0459	0.0459	0.0459	0.0459	0.0459	0.0459	0.1101	0.1101	0.2064	0.2064		
1	0.0	0.5	0.5	0.5	0.5	0.5	0.5	0.5	1.0	1.0	1.0	1.0	**0.625**	**0.794**
2	0.5	0.0	0.5	0.5	0.5	0.5	0.5	0.5	1.0	[illegible]	[illegible]	[illegible]	**0.625**	**0.794**
3	0.5	0.5	0.0	0.5	0.5	0.5	0.5	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**0.625**	**0.794**
4	0.5	0.5	0.5	0.0	0.5	0.5	0.5	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**0.625**	**0.794**
5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	0.5	[illegible]	1.0	1.0	1.0	**0.625**	**0.794**
6	0.5	0.5	0.5	0.5	0.5	0.0	0.5	0.5	1.0	1.0	1.0	1.0	**0.625**	**0.794**
7	0.5	0.5	0.5	0.5	0.5	0.5	0.0	0.5	1.0	1.0	1.0	1.0	**0.625**	**0.794**
8	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.0	1.0	1.0	1.0	1.0	**0.625**	**0.794**
9	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	0.125	1.0	1.0	**0.844**	**0.794**
10	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.125	0.0	1.0	1.0	**0.844**	**0.794**
11	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	1.0	**0.917**	**0.794**
12	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	0.0	**0.917**	**0.794**
Average ►►													**0.710**	**0.794**

Mutual distance among 12 non-homozygous components and resulting mean and optimized mean distance (Example 3)

►► Components ▼	1	2	3	4	5	6	7	8	9	10	11	12	Mean distance	Optimized mean distance
Optimum "relative dose" per component; relative to [11] and to [12]	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.4444	0.5333	0.5333	1	1		
Optimum dose per component (∑ = 1) ▼	0.0671	0.0671	0.0671	0.0671	0.0671	0.0671	0.0671	0.0671	0.0805	0.0805	0.1510	0.1510		
1	0.50	0.75	0.75	0.75	0.75	0.75	0.75	0.75	1.00	[illegible]	[illegible]	[illegible]	**0.813**	**0.849**
2	0.75	0.50	0.75	0.75	0.75	0.75	0.75	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**0.813**	**0.849**
3	0.75	0.75	0.50	0.75	0.75	0.75	0.75	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**0.813**	**0.849**
4	0.75	0.75	0.75	0.50	0.75	0.75	0.75	[illegible]	[illegible]	1.00	1.00	1.00	**0.813**	**0.849**
5	0.75	0.75	0.75	0.75	0.50	0.75	0.75	0.75	1.00	1.00	1.00	1.00	**0.813**	**0.849**
6	0.75	0.75	0.75	0.75	0.75	0.50	0.75	0.75	1.00	1.00	1.00	1.00	**0.813**	**0.849**
7	0.75	0.75	0.75	0.75	0.75	0.75	0.50	0.75	1.00	1.00	1.00	1.00	**0.813**	**0.849**
8	0.75	0.75	0.75	0.75	0.75	0.75	0.75	0.50	1.00	1.00	1.00	1.00	**0.813**	**0.849**
9	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	0.125	1.00	1.00	**0.844**	**0.849**
10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.125	0.00	1.00	1.00	**0.844**	**0.849**
11	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	1.00	**0.917**	**0.849**
12	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	0.00	**0.917**	**0.849**
Average ►►													**0.835**	**0.849**

Mutual distance among 12 homozygous components and resulting mean and optimized mean distance (Example 4)

Components	1	2	3	4	5	6	7	8	9	10	11	12	Mean distance	Optimized mean distance
Optimum dose per component (∑ = 1)	0.3333	0.1667	0	0	0	0	0	0	0	0	0.1667	0.3333		
1	0.0	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	1.0	**0.542**	**0.517**
2	0.1	0.0	0.1	0.2	0.3	0.4	0.5	0.6	[illegible]	[illegible]	[illegible]	[illegible]	**0.467**	**0.517**
3	0.2	0.1	0.0	0.1	0.2	0.3	0.4	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	**0.400**	**0.517**
4	0.3	0.2	0.1	0.0	0.1	0.2	0.3	[illegible]	[illegible]	[illegible]	[illegible]	0.8	**0.350**	**0.517**
5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	[illegible]	0.4	0.5	0.6	0.7	**0.317**	**0.517**
6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	0.3	0.4	0.5	0.6	**0.300**	**0.517**
7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	0.3	0.4	0.5	**0.300**	**0.517**
8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	0.3	0.4	**0.317**	**0.517**
9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	0.3	**0.350**	**0.517**
10	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	0.2	**0.400**	**0.517**
11	1.0	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	0.1	**0.467**	**0.517**
12	1.0	1.0	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1	0.0	**0.542**	**0.517**
Average ►►													**0.396**	**0.517**

Mutual distance among 12 homozygous components and resulting mean and optimized mean distance (Example 5)

► Components ▼	1	2	3	4	5	6	7	8	9	10	11	12	Mean dist.	Appr. optimized mean dist.	Optimized mean dist.
Optimum dose per component (∑ = 1)	0.0633	0.0548	0.0563	0.0722	0.0349	0.0725	0.0909	0.1231	0.1268	0.1194	0.1368	0.0489			
Approximate optimum dose per component (∑ = 1)	0.0627	0.0627	0.0659	0.0659	0.0506	0.0506	0.1182	0.1182	0.1182	0.1182	0.1182	0.0506			
1	0.0000	0.1165	0.9357	0.9484	0.9203	0.9436	0.9151	0.9304	0.9987	0.9452	0.9655	0.9216	0.795	**0.834**	**0.843**
2	0.1165	0.0000	0.9297	0.9469	0.9094	0.9334	0.9163	[illegible]	[illegible]	[illegible]	[illegible]	0.9165	0.793	**0.833**	**0.843**
3	0.9357	0.9297	0.0000	0.2068	0.9277	0.9221	0.9404	[illegible]	[illegible]	[illegible]	[illegible]	0.9158	0.803	**0.837**	**0.843**
4	0.9484	0.9469	0.2068	0.0000	0.9286	0.9285	0.9430	[illegible]	[illegible]	[illegible]	1.0000	0.9074	0.806	**0.840**	**0.843**
5	0.9203	0.9094	0.9277	0.9286	0.0000	0.2739	0.8948	0.9668	0.9678	0.9432	0.9768	0.5295	0.770	**0.839**	**0.843**
6	0.9436	0.9334	0.9221	0.9285	0.2739	0.0000	0.8900	0.9620	0.9849	0.9612	1.0000	0.5581	0.780	**0.849**	**0.843**
7	0.9151	0.9163	0.9404	0.9430	0.8948	0.8900	0.0000	0.9216	0.9582	0.9736	0.8963	0.8943	0.845	**0.818**	**0.843**
8	0.9304	0.9397	0.9755	0.9678	0.9668	0.9620	0.9216	0.0000	0.9505	1.0000	0.9847	0.9272	0.877	**0.846**	**0.843**
9	0.9987	1.0000	0.9465	0.9443	0.9678	0.9849	0.9582	0.9505	0.0000	0.9309	1.0000	0.9339	0.885	**0.850**	**0.843**
10	0.9452	0.9447	0.9334	0.9494	0.9432	0.9612	0.9736	1.0000	0.9309	0.0000	0.9712	0.9126	0.872	**0.843**	**0.843**
11	0.9655	0.9616	0.9960	1.0000	0.9768	1.0000	0.8963	0.9847	1.0000	0.9712	0.0000	0.9870	0.895	**0.858**	**0.843**
12	0.9216	0.9165	0.9158	0.9074	0.5295	0.5581	0.8943	0.9272	0.9339	0.9126	0.9870	0.0000	0.784	**0.841**	**0.843**
Average ►►													0.825	**0.841**	**0.843**

In example 2, eight homozygous components show mutual distances of d=0.5, and two further ones have d=0.125. Optimization leads to a gain in mean distance, since 0.794 > 0.710. The optimized "relative doses" of [1-8] : [9+10] : [11] : [12] are **16/9** : 16/15 : 1 : 1. Looking at the single components, this corresponds to [**8 · 0.2222**] : [2 · 0.5333] : [1] : [1]. Components 9 and 10 get - together - a dose which is barely higher than 1, obviously because they are nearly identical (d=0.125).

In example 3, again eight components compose one group, yet they are non-inbred components (diagonal d=0.5). Distances are d=0.75; the rest is as in example 2. Optimization increases mean distance (0.849 > 0.835). Optimized "relative doses" of [1-8] : [9+10] : [11] : [12] are **32/9** : 16/15 : 1 : 1. Components 1 to 8 get double dose compared to example 2 (0.444 *vs*. 0.222). Why? Crossing within this non-inbred group of eight leads to inbreeding effects which are half as large as in example 2.

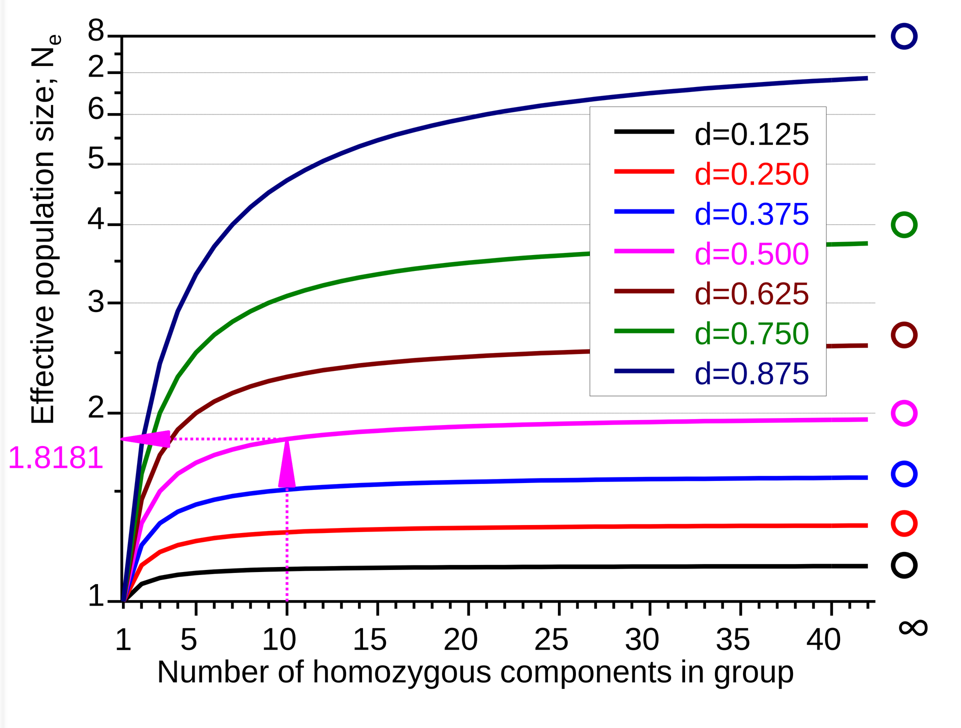
In example 4, the distances among the homozygous components [1] to [11] gradually increase from 0.1 to 1.0. Components [1] & [12] are the only ones with d=1 to two other components. This is an example where optimized doses of components are found as zero (components 3-10 are kicked out). This shows that this approach is focussed on maximizing inbreeding and heterozygosity, not diversity. Optimization leads to a gain in mean distance of 31%.

In example 5, we employ marker-based distance estimates from homozygous lines of *Vicia faba* (cf. Ali et al., 2016). For an approximate optimized distance, groups were identified as [1+2]; [3+4]; [5+6+12]. For the latter, the average within-group distance of d=0.444 was applied; all other distances were considered 1. The approximate optimization worked, in this example, fairly well. Optimization yielded a gain in mean distance of about 2%.

The result presented here were generated by maximizing the quadratic form: $Q(\mathbf{p}) = \sum_i \sum_j p_i p_j d_{ij}$, where $\mathbf{p} = (p_1, p_2, \ldots p_n)$ is the vector of parental contributions (doses), p_i is the dose of component i in Syn-0, and d_{ij} is the genetic distance of component i and component j, with $0 \le p_i$, $d \le 1$ and $\sum_i p_i = 1$. Marchais (1996) presented the calculatory tools to iteratively find those doses p_i which maximize the mean genetic distance in a synthetic.
The diagram shows the reasoning in simple cases such as in examples 1-3. Given there are groups of components with constant intragroup d and d <1; and the reminder distances are d=1. Then an effective size N_e can be deduced for each such group as:

$N_e = \frac{N}{N-(N-1)(d)}$. Example 1: $N_e = \frac{10}{10-(9)(0.5)} = \frac{20}{11} = 1.818$;

i.e., [1-10] are genetically as ‚narrow' as **1.818** unrelated components (**"relative dose"** of [1-10]; value is indicated in diagram).



●Ali, M.B.M, G.C. Welna, A. Sallam, R. Martsch, C. Balko, B. Gebser, O. Sass, and W. Link, 2016. Association analyses to genetically improve drought and freezing tolerance of faba bean (*Vicia faba* L.). Crop Science (First Look). ●Brünjes, L., 2013: Experimental and theoretical contribution to optimize the composition of synthetic populations of faba bean (*Vicia faba* L.), a partially allogamous grain legume. MSc thesis, Univ. Kassel, 94 pages. ●Castellanos, J.S., 2011: Inbreeding and yield of synthetic varieties derived from single and double cross hybrids. Maydica 56, 265-271. ●Marchais, L., 1996: Parental proportions maximizing the mean value of a parameter in a panmictic population can be useful in plant breeding. Agronomie 16, 257-264.