## Gene interaction

A convenient way to see the general rule is via "inclusion-exclusion" on the lower-order terms. Concretely, label your fitness (or response) for a subset of genes  $S \subseteq \{1, ..., n\}$  by  $f_S$ . Then define the interaction  $\epsilon_S$  for that subset by recursively subtracting off all interactions belonging to strict sub-subsets of S. In symbols,

$$\epsilon_S = f_S - \sum_{\emptyset \neq T \subset S} \epsilon_T$$

Here are the small cases to see the pattern:

- $\begin{array}{l} \bullet \ \ {\rm Singles:} \ \epsilon_{\{i\}} = f_{\{i\}}. \\ \bullet \ \ {\rm Pairs:} \ \epsilon_{\{i,j\}} = f_{\{i,j\}} \epsilon_{\{i\}} \epsilon_{\{j\}} = f_{ij} f_i f_j. \end{array}$

$$\epsilon_{\{i,j,k\}} = f_{ijk} - \left(\epsilon_{\{i\}} + \epsilon_{\{j\}} + \epsilon_{\{k\}}\right) - \left(\epsilon_{\{i,j\}} + \epsilon_{\{i,k\}} + \epsilon_{\{j,k\}}\right)$$

and so forth. Equivalently, one may write this as an inclusion-exclusion formula

$$\epsilon_S = \sum_{T \subset S} (-1)^{|S| - |T|} f_T$$

provided you set  $f_{\emptyset} = 0$ . Either expression generalizes the notion that, to isolate a genuine k-way interaction, you must "peel off" all interactions from sub-collections off the same genes.

## 2025.01.27 - Derivation of Tau

The derivation for  $\tau_{ijk}$ , the triple interaction term, follows from the recursive definition of interactions. Let's walk through the steps systematically.

We start with the general recursive formula:

$$\tau_{ijk} = f_{ijk} - \sum_{S \subset \{i,j,k\}, |S| = 2} \tau_S - \sum_{T \subset \{i,j,k\}, |T| = 1} f_T$$

Here's the breakdown step by step:

1. Subtract contributions from single elements (  $f_i, f_j, f_k$  ):

The single fitness terms contribute:

$$\sum_{T\subset\{i,j,k\},|T|=1}f_T=f_i+f_j+f_k$$

These are the individual effects of the single genes i, j, k. 2. Subtract contributions from pairs  $(\tau_{ij}, \tau_{ik}, \tau_{jk})$ :

The pairwise interaction terms contribute:

$$\sum_{S\subset\{i,j,k\},|S|=2}\tau_S=\tau_{ij}+\tau_{ik}+\tau_{jk}$$

Each of these pairwise terms has already been recursively defined as:

$$\tau_{ij} = f_{ij} - f_i - f_j$$
  

$$\tau_{ik} = f_{ik} - f_i - f_k$$
  

$$\tau_{jk} = f_{jk} - f_j - f_k$$

3. Combine terms:

The triple interaction term  $au_{ijk}$  is then:

$$\tau_{ijk} = f_{ijk} - (f_{ij} - f_i - f_j) - (f_{ik} - f_i - f_k) - (f_{jk} - f_j - f_k) - f_i - f_j - f_k$$

Simplify step by step:

• Combine the single terms  $f_i, f_j, f_k$ :

$$\tau_{ijk} = f_{ijk} - f_{ij} - f_{ik} - f_{jk} + f_i + f_j + f_k$$

Final Form:

$$\tau_{ijk} = f_{ijk} - f_{ij} - f_{ik} - f_{jk} + f_i + f_j + f_k$$

This is the full expanded form of the triple interaction term  $\tau_{ijk}$ . It subtracts all pairwise and single contributions to isolate the unique interaction between i, j, k.

## 2025.02.02 - Gene Interaction Not Regressive Form

Digenic Interaction:

$$\epsilon_{ij} = f_{ij} - f_i f_j$$
, where  $f_i$  is fitness,

$$\epsilon_{ij} = \mathcal{F}(f_i, f_j, f_{ij}).$$

Trigenic Interaction:

$$\tau_{ijk} = f_{ijk} - f_i f_j f_k - \varepsilon_{ij} f_k - \varepsilon_{ik} f_j - \varepsilon_{jk} f_i.$$

Full Recursive Definition (subtracting out effects of digenic interactions):

$$\begin{split} \tau_{ijk} &= f_{ijk} - f_i f_j f_k \\ &- \left( f_{ij} - f_i f_j \right) f_k \\ &- \left( f_{ik} - f_i f_k \right) f_j \\ &- \left( f_{jk} - f_j f_k \right) f_i, \\ \tau_{ijk} &= \mathcal{F} \left( f_i, f_j, f_k, f_{ij}, f_{ik}, f_{jk}, f_{ijk} \right). \end{split}$$

**Fitness** 

$$f_i = \mathcal{F}(g_i, g_{wt})$$

Digenic Interaction:

$$\epsilon_{ij} = \mathcal{F}(f_i, f_j, f_{ij})$$

Trigenic Interaction:

$$\tau_{ijk} = \mathcal{F}\left(f_i, f_j, f_k, f_{ij}, f_{ik}, f_{jk}, f_{ijk}\right)$$