SNP Microarray Interpretation Guide

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Introduction

Single-nucleotide polymorphism (SNP) microarrays have found significant clinical utility over the past decade for the detection of both constitutional and somatic cytogenetic abnormalities. SNP arrays contain probes that identify the genotype of a SNPs throughout the genome. The advantage of having SNP probes in addition to copy-number probes is the ability to a) detect regions of homozygosity, b) corroborate copy-number probe data, and c) determine the haplotype of individuals. However, the pattern of SNP data can be non-intuitive for complex or mosaic situations. Therefore, an *in silico* model of a SNP array was developed to generate simulated SNP array data. The simulated array results can be used as a tool for learning SNP array analysis or as a reference for interpretation of SNP array data. This document contains simulated SNP array data which can be used as an educational resource for anyone interested in the analysis of SNP microarray data.

The *in silico* SNP array model used to generate this data is essentially a Monte Carlo simulation. The basic steps are as follows:

1) A large number of virtual cells are generated
2) In a subset of these cells, a specific abnormality is induced
3) For each simulated SNP, the number of times each allele is observed is counted
4) The allele difference and B-Allele Frequency (BAF) values are computed
5) The allele difference values or BAF values are plotted similar to how SNP array data is displayed

The following formulas are used to compute the allele difference and BAF values.

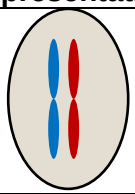
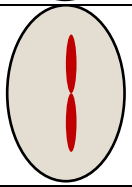
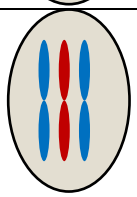
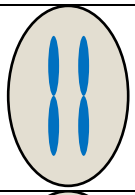
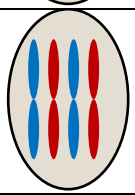
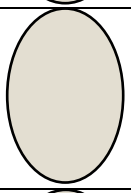
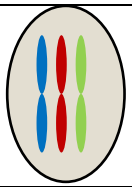
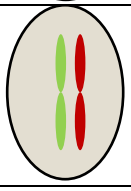
$$\text{Allele Difference} = \frac{(\text{Number of A Alleles}) - (\text{Number of B Alleles})}{2 \times \text{Number of Cells}}$$

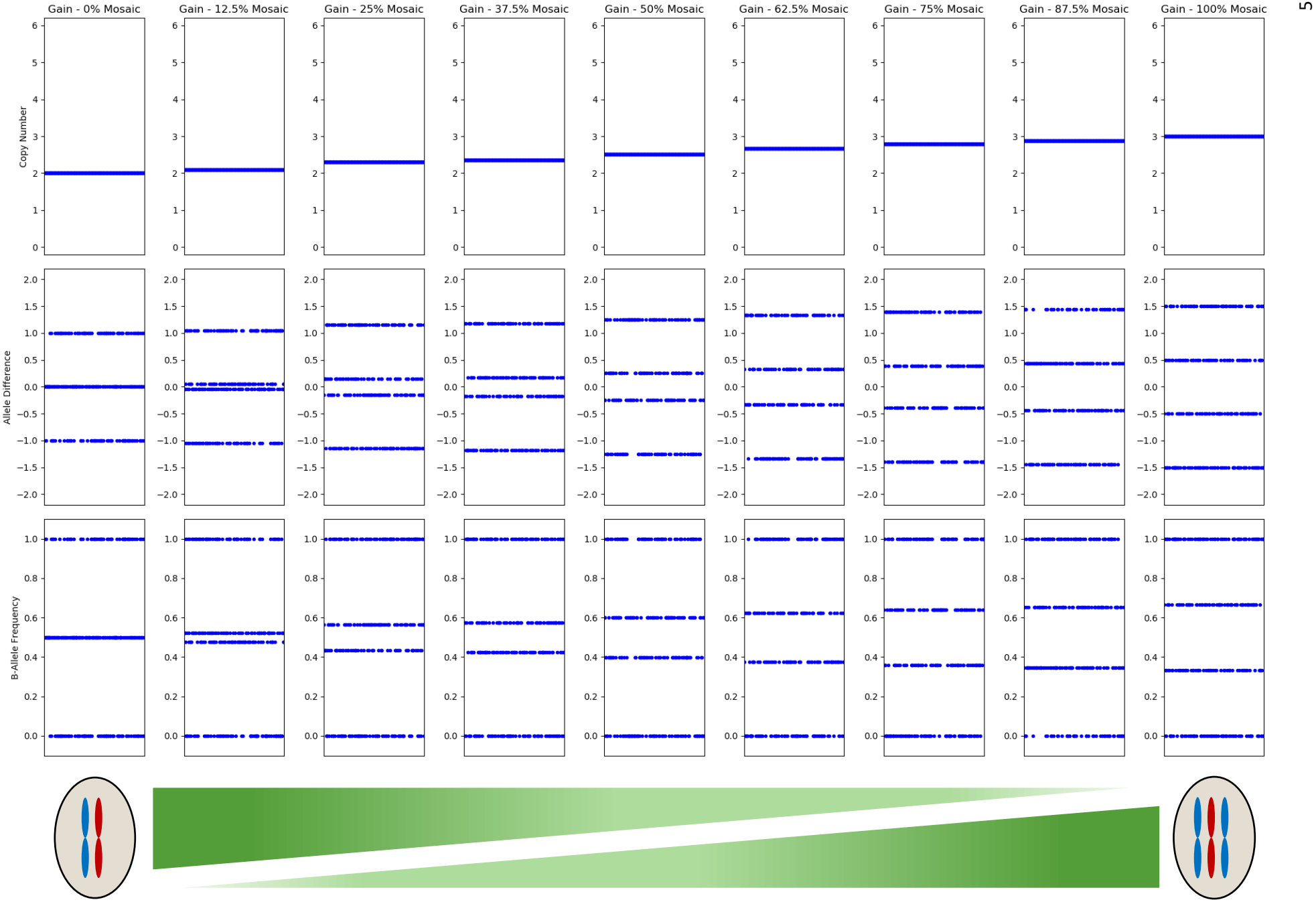
$$\text{BAF} = \frac{\text{Number of B Alleles}}{(\text{Number of A Alleles}) + (\text{Number of B Alleles})}$$

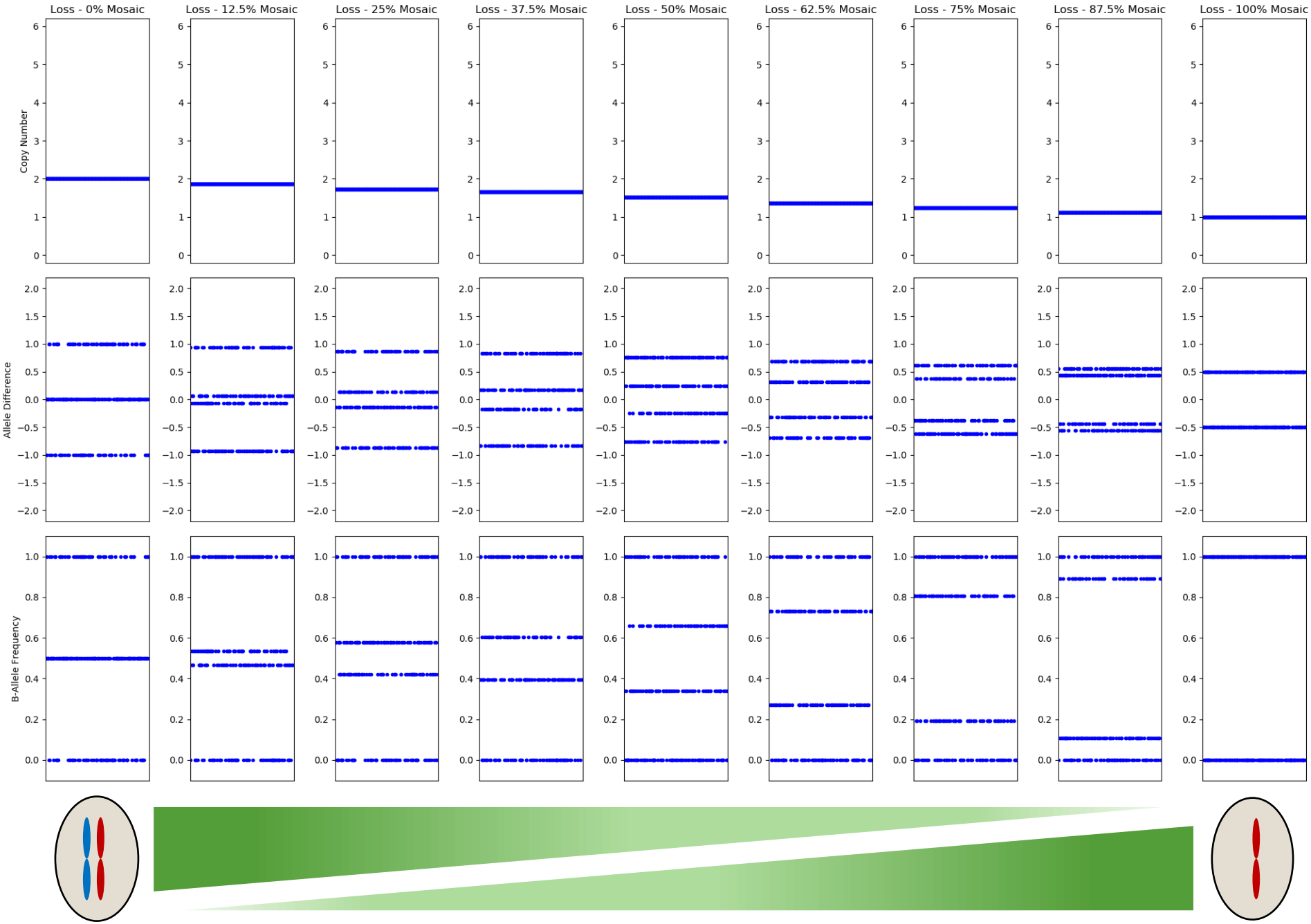
While this model could be used to simulate SNP array data from a large number of cases, 7 aberrations and the mosaic combinations thereof representing the most frequently occurring situations were selected for inclusion in this guide. The abnormalities included are described in detail in Table 1 below.

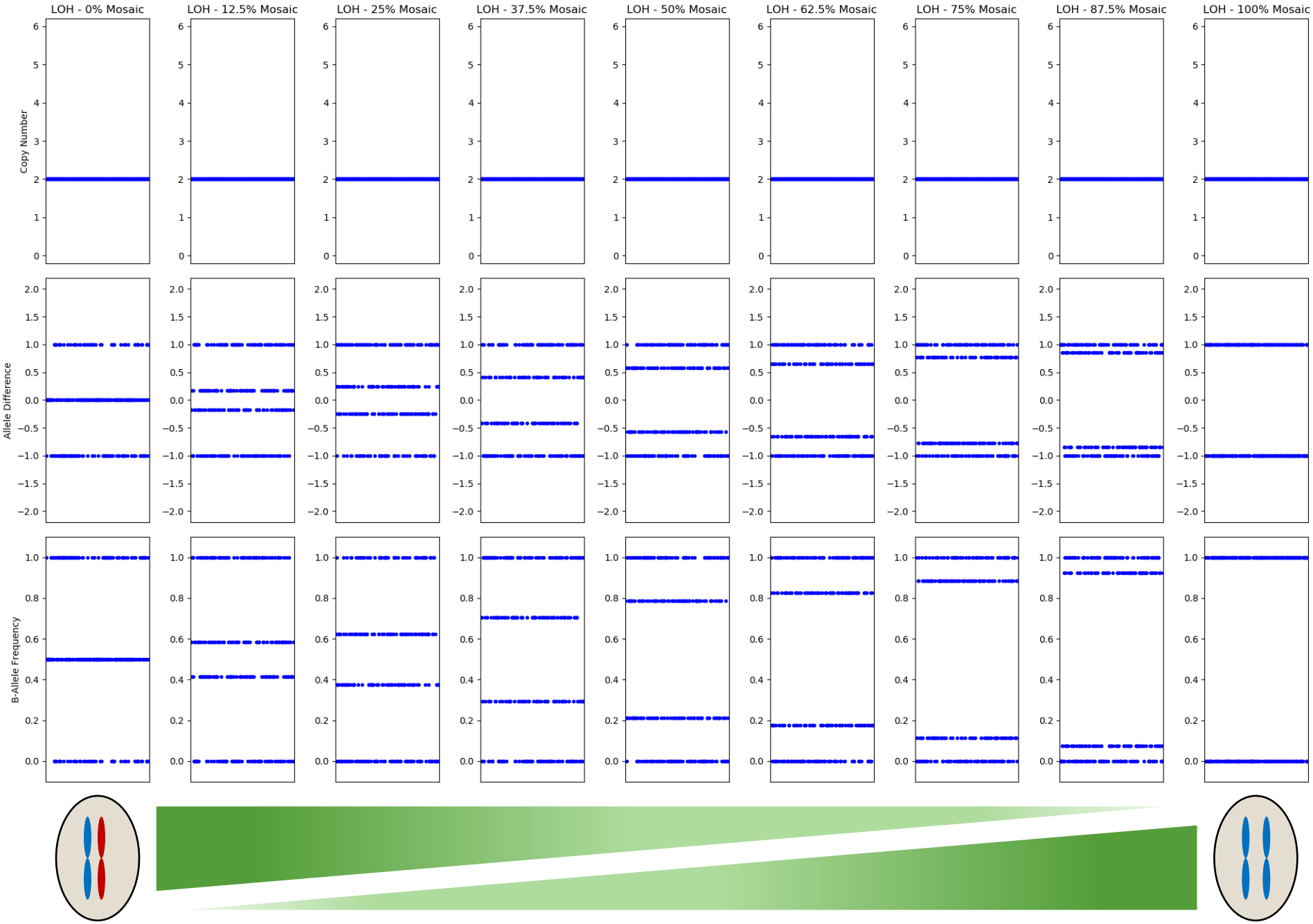
While this guide is a useful companion for the analysis of SNP array data, care should be taken when applying the results of this model as it represents the ideal case. Real-world data may not perfectly match the model output due to system noise, fluorescent dynamic range, variations in the input DNA, etc. Most microarray platforms cannot reliably detect mosaicism below 20%. This guide is not a substitute for proper training and experience in analysis with the specific microarray technology you may be using.

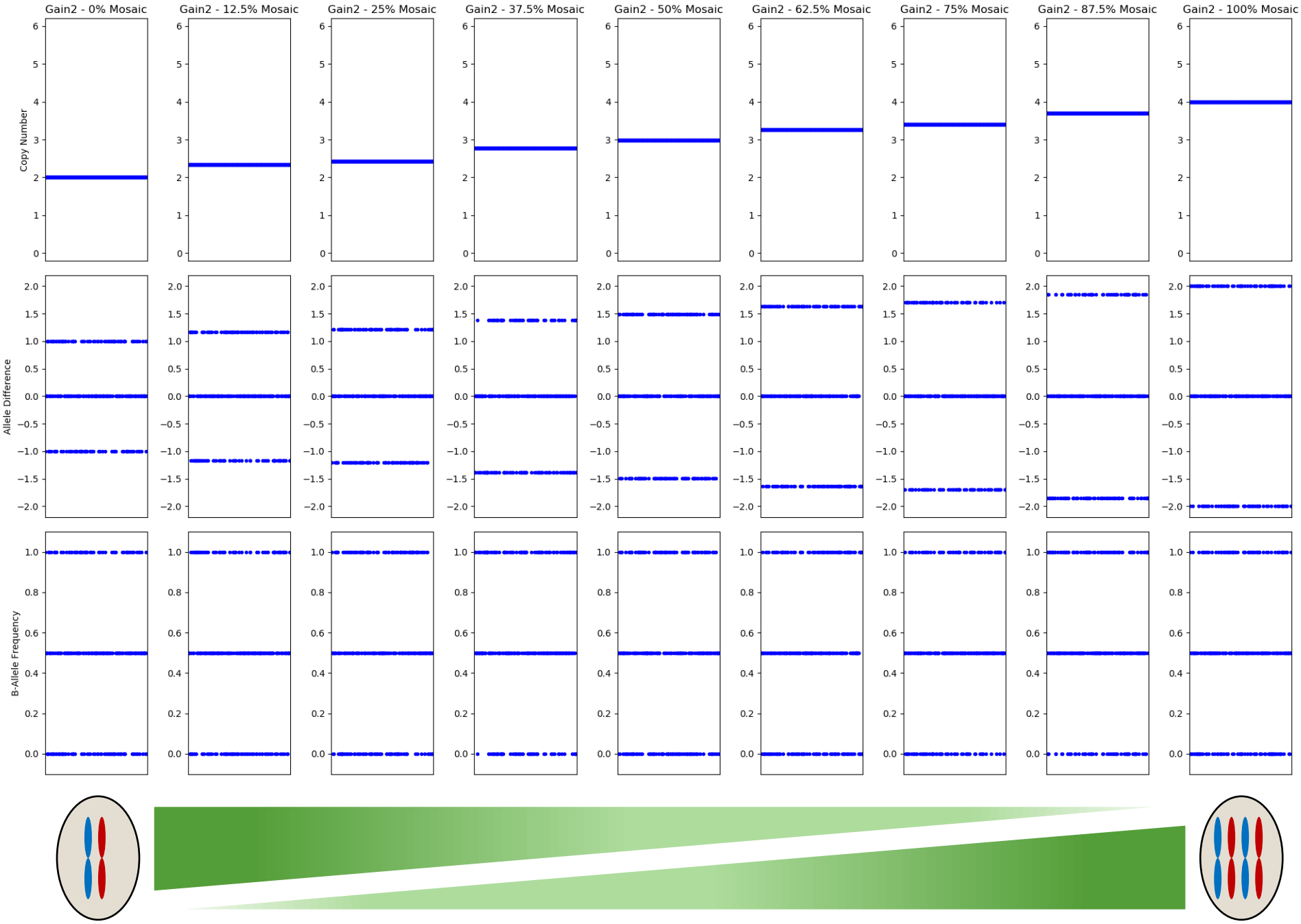
Table 1: The types of cell populations included in this interpretation guide.

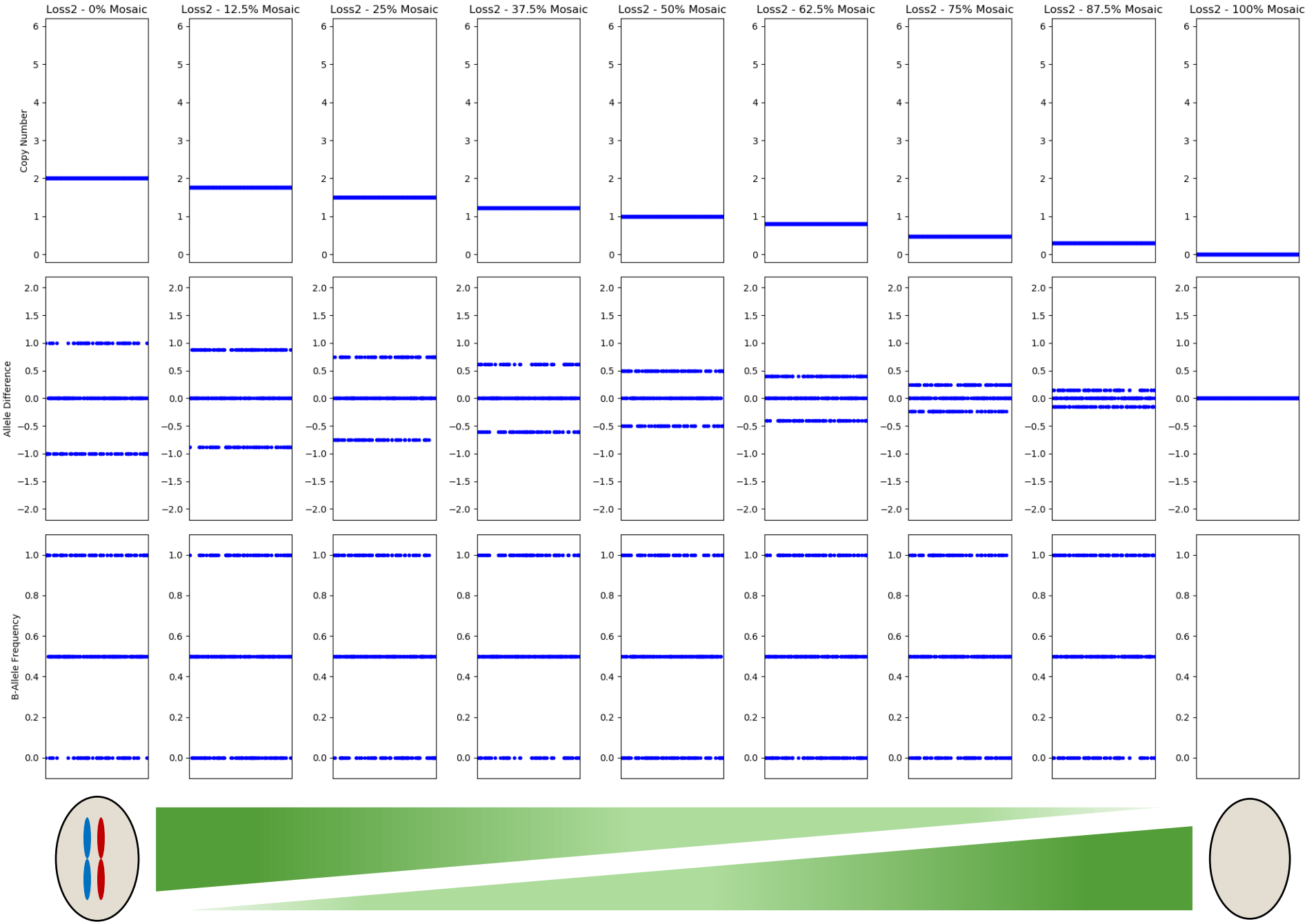
Cell Population	Pictoral Representation	Description
Normal Diploid		This represents the normal two-copy state of most cells. Each cell contains one allele from each parent.
One Copy Loss		This represents a loss of a single copy, leaving only one copy of an allele in the cell.
One Copy Gain		This represents a gain of a single copy, resulting in a two-haplotype state with three total copies.
Loss of Heterozygosity (LOH)		This represents a state where the copy-number is normal, but only a single haplotype is present. This could be due to uniparental disomy, meiotic or mitotic non-disjunction errors, or in cases with significant inbreeding.
Two Copy Gain		This represents a state where the entire diploid content of a cell is duplicated resulting in a tetrasomy state with four total copies and two haplotypes.
Two Copy Loss		This represents a state where both copies of an allele are lost; as in a homozygous deletion.
Three Haplotype State		This represents a single copy gain with three total copies, but also three unique haplotypes. The additional haplotype most likely originates from a parent.
Parental Cell Contamination		This represents a state where the haplotype of the cells matches one of the parents, rather than the offspring.

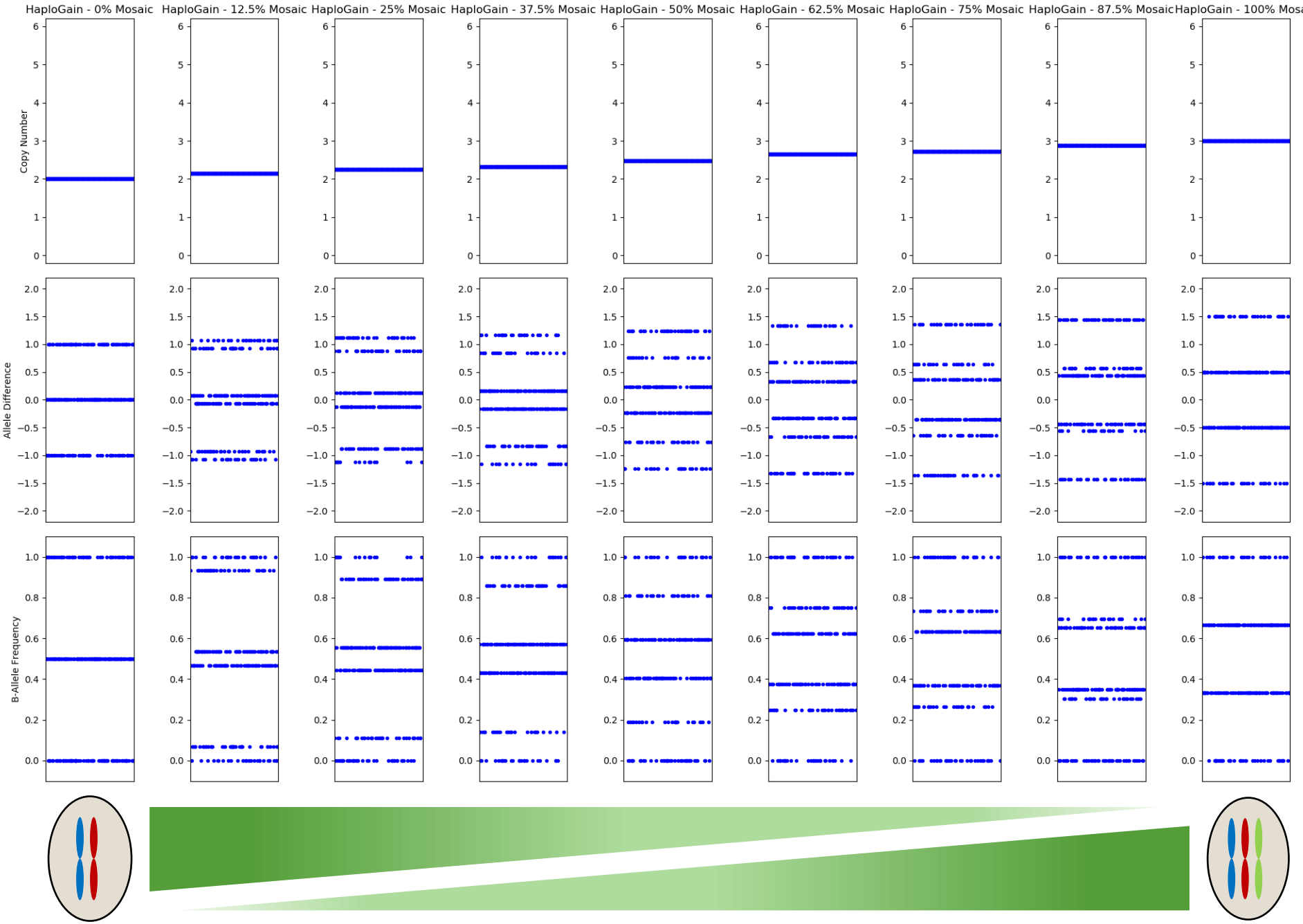

Gain - 0% Mosaic
Gain - 12.5% Mosaic
Gain - 25% Mosaic
Gain - 37.5% Mosaic
Gain - 50% Mosaic
Gain - 62.5% Mosaic
Gain - 75% Mosaic
Gain - 87.5% Mosaic
Gain - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency

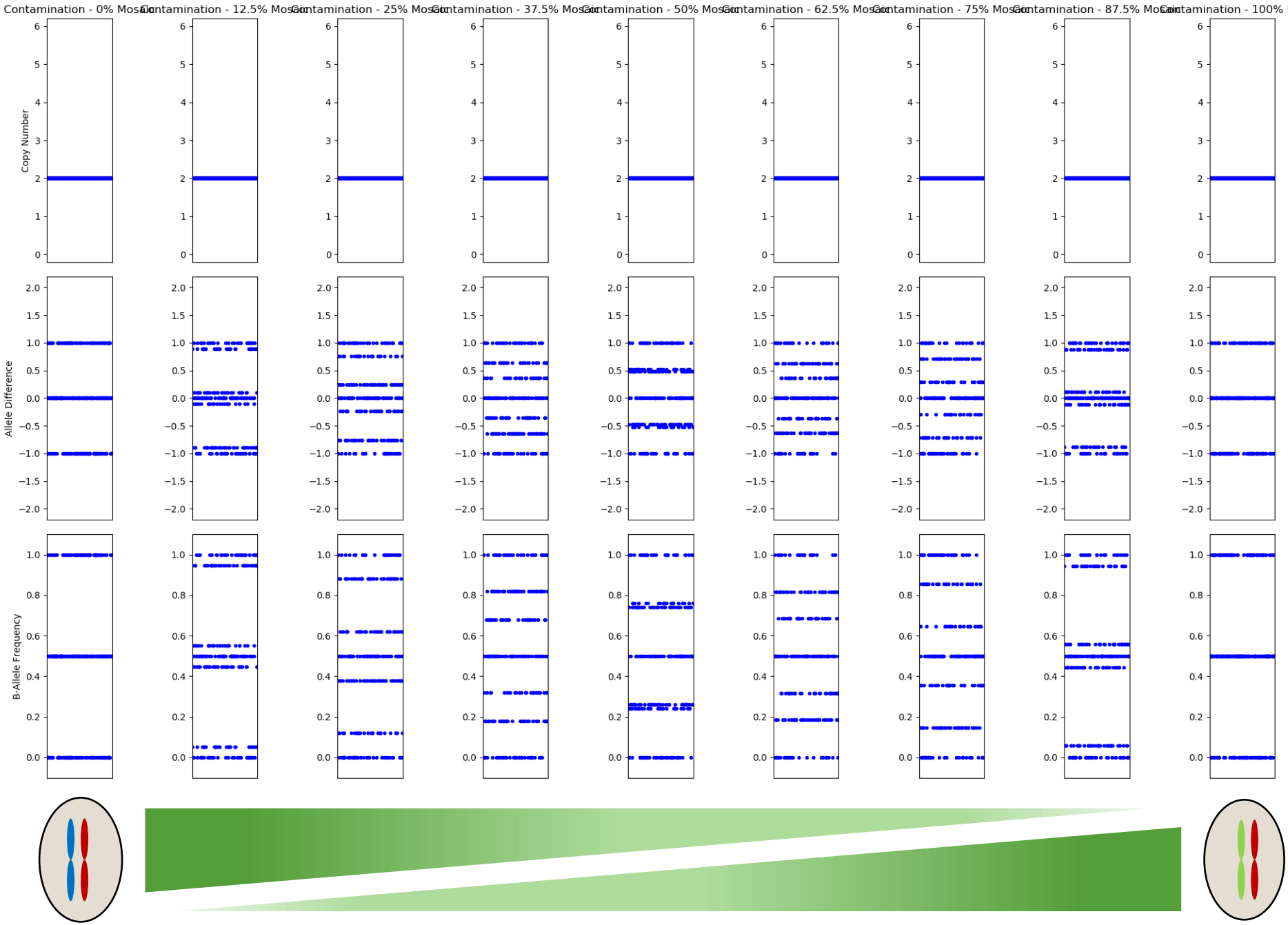

Loss - 0% Mosaic
Loss - 12.5% Mosaic
Loss - 25% Mosaic
Loss - 37.5% Mosaic
Loss - 50% Mosaic
Loss - 62.5% Mosaic
Loss - 75% Mosaic
Loss - 87.5% Mosaic
Loss - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency


LOH - 0% Mosaic
LOH - 12.5% Mosaic
LOH - 25% Mosaic
LOH - 37.5% Mosaic
LOH - 50% Mosaic
LOH - 62.5% Mosaic
LOH - 75% Mosaic
LOH - 87.5% Mosaic
LOH - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency


Gain2 - 0% Mosaic
Gain2 - 12.5% Mosaic
Gain2 - 25% Mosaic
Gain2 - 37.5% Mosaic
Gain2 - 50% Mosaic
Gain2 - 62.5% Mosaic
Gain2 - 75% Mosaic
Gain2 - 87.5% Mosaic
Gain2 - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency


Loss2 - 0% Mosaic
Loss2 - 12.5% Mosaic
Loss2 - 25% Mosaic
Loss2 - 37.5% Mosaic
Loss2 - 50% Mosaic
Loss2 - 62.5% Mosaic
Loss2 - 75% Mosaic
Loss2 - 87.5% Mosaic
Loss2 - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency


HaploGain - 0% Mosaic
HaploGain - 12.5% Mosaic
HaploGain - 25% Mosaic
HaploGain - 37.5% Mosaic
HaploGain - 50% Mosaic
HaploGain - 62.5% Mosaic
HaploGain - 75% Mosaic
HaploGain - 87.5% Mosaic
HaploGain - 100% Mosaic
Copy Number
Allele Difference
B-Allele Frequency


Contamination - 0% Mosaic
Contamination - 12.5% Mosaic
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Contamination - 37.5% Mosaic
Contamination - 50% Mosaic
Contamination - 62.5% Mosaic
Contamination - 75% Mosaic
Contamination - 87.5% Mosaic
Contamination - 100% Mosai
Copy Number
Allele Difference
B-Allele Frequency


Gain is 0, Loss is 0
Gain is 0, Loss is 10
Gain is 0, Loss is 20
Gain is 0, Loss is 30
Gain is 0, Loss is 40
Gain is 0, Loss is 50
Gain is 10, Loss is 0
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Gain is 10, Loss is 20
Gain is 10, Loss is 30
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Gain is 10, Loss is 50
Gain is 20, Loss is 0
Gain is 20, Loss is 10
Gain is 20, Loss is 20
Gain is 20, Loss is 30
Gain is 20, Loss is 40
Gain is 20, Loss is 50
Gain is 30, Loss is 0
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Gain is 40, Loss is 30
Gain is 40, Loss is 40
Gain is 40, Loss is 50
Gain is 50, Loss is 0
Gain is 50, Loss is 10
Gain is 50, Loss is 20
Gain is 50, Loss is 30
Gain is 50, Loss is 40
Gain is 50, Loss is 50
Allele Difference
2
1
0
−1
−2


Gain is 0, LOH is 0
Gain is 0, LOH is 10
Gain is 0, LOH is 20
Gain is 0, LOH is 30
Gain is 0, LOH is 40
Gain is 0, LOH is 50
Gain is 10, LOH is 0
Gain is 10, LOH is 10
Gain is 10, LOH is 20
Gain is 10, LOH is 30
Gain is 10, LOH is 40
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Gain is 30, LOH is 0
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Gain is 30, LOH is 20
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Gain is 30, LOH is 40
Gain is 30, LOH is 50
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Gain is 40, LOH is 40
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Gain is 50, LOH is 0
Gain is 50, LOH is 10
Gain is 50, LOH is 20
Gain is 50, LOH is 30
Gain is 50, LOH is 40
Gain is 50, LOH is 50
Allele Difference


Gain is 0, Gain+2 is 0
Gain is 0, Gain+2 is 10
Gain is 0, Gain+2 is 20
Gain is 0, Gain+2 is 30
Gain is 0, Gain+2 is 40
Gain is 0, Gain+2 is 50
Gain is 10, Gain+2 is 0
Gain is 10, Gain+2 is 10
Gain is 10, Gain+2 is 20
Gain is 10, Gain+2 is 30
Gain is 10, Gain+2 is 40
Gain is 10, Gain+2 is 50
Gain is 20, Gain+2 is 0
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Gain is 20, Gain+2 is 20
Gain is 20, Gain+2 is 30
Gain is 20, Gain+2 is 40
Gain is 20, Gain+2 is 50
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Gain is 30, Gain+2 is 40
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Gain is 40, Gain+2 is 30
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Gain is 40, Gain+2 is 50
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Gain is 50, Gain+2 is 20
Gain is 50, Gain+2 is 30
Gain is 50, Gain+2 is 40
Gain is 50, Gain+2 is 50
Allele Difference
2
1
0
−1
−2


Gain is 0, Loss-2 is 0
Gain is 0, Loss-2 is 10
Gain is 0, Loss-2 is 20
Gain is 0, Loss-2 is 30
Gain is 0, Loss-2 is 40
Gain is 0, Loss-2 is 50
Gain is 10, Loss-2 is 0
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Gain is 10, Loss-2 is 20
Gain is 10, Loss-2 is 30
Gain is 10, Loss-2 is 40
Gain is 10, Loss-2 is 50
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Gain is 20, Loss-2 is 30
Gain is 20, Loss-2 is 40
Gain is 20, Loss-2 is 50
Gain is 30, Loss-2 is 0
Gain is 30, Loss-2 is 10
Gain is 30, Loss-2 is 20
Gain is 30, Loss-2 is 30
Gain is 30, Loss-2 is 40
Gain is 30, Loss-2 is 50
Gain is 40, Loss-2 is 0
Gain is 40, Loss-2 is 10
Gain is 40, Loss-2 is 20
Gain is 40, Loss-2 is 30
Gain is 40, Loss-2 is 40
Gain is 40, Loss-2 is 50
Gain is 50, Loss-2 is 0
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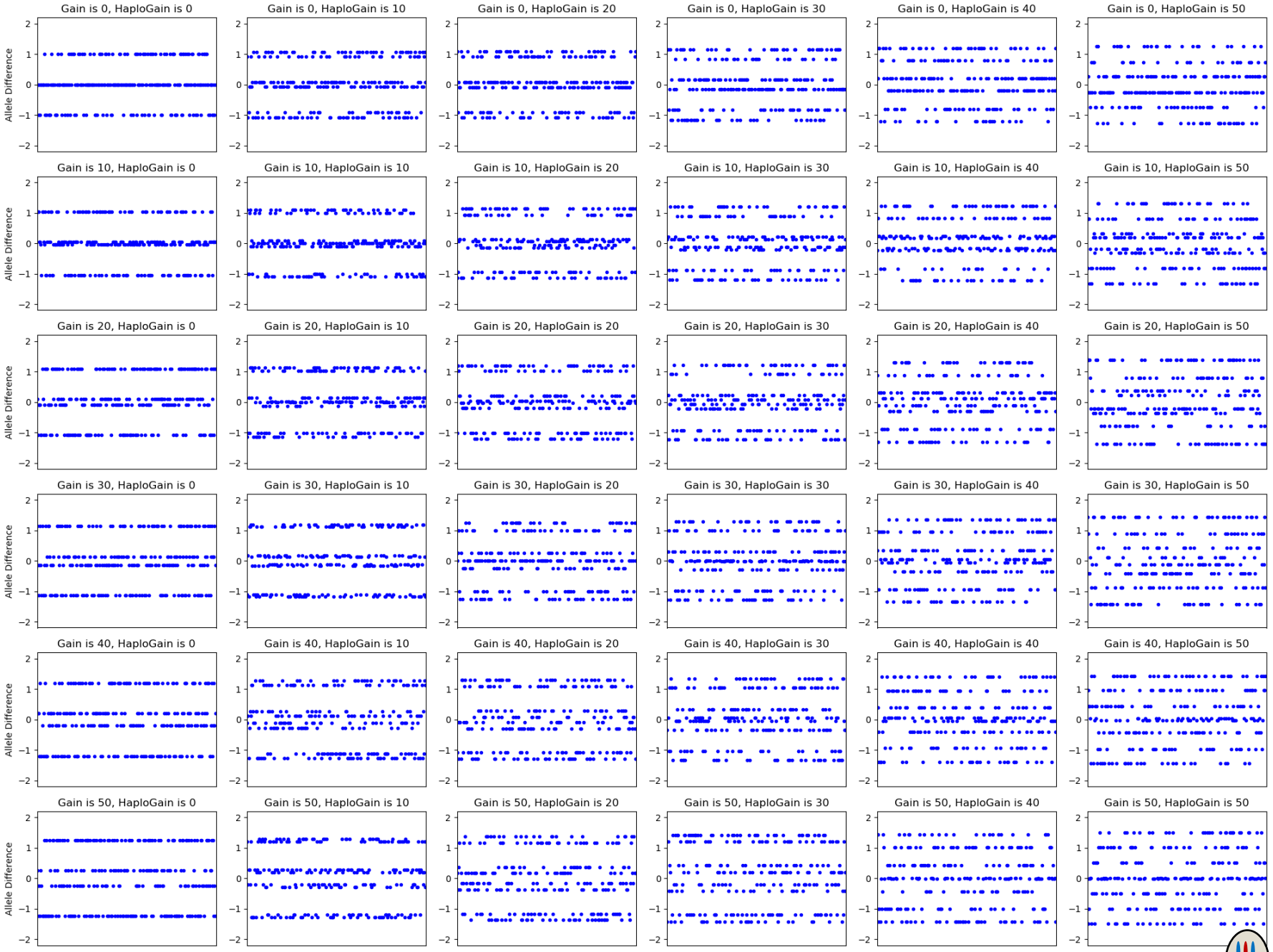
Gain is 50, Loss-2 is 50
Allele Difference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Gain is 0, HaploGain is 30
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Gain is 0, HaploGain is 50
Gain is 10, HaploGain is 0
Gain is 10, HaploGain is 10
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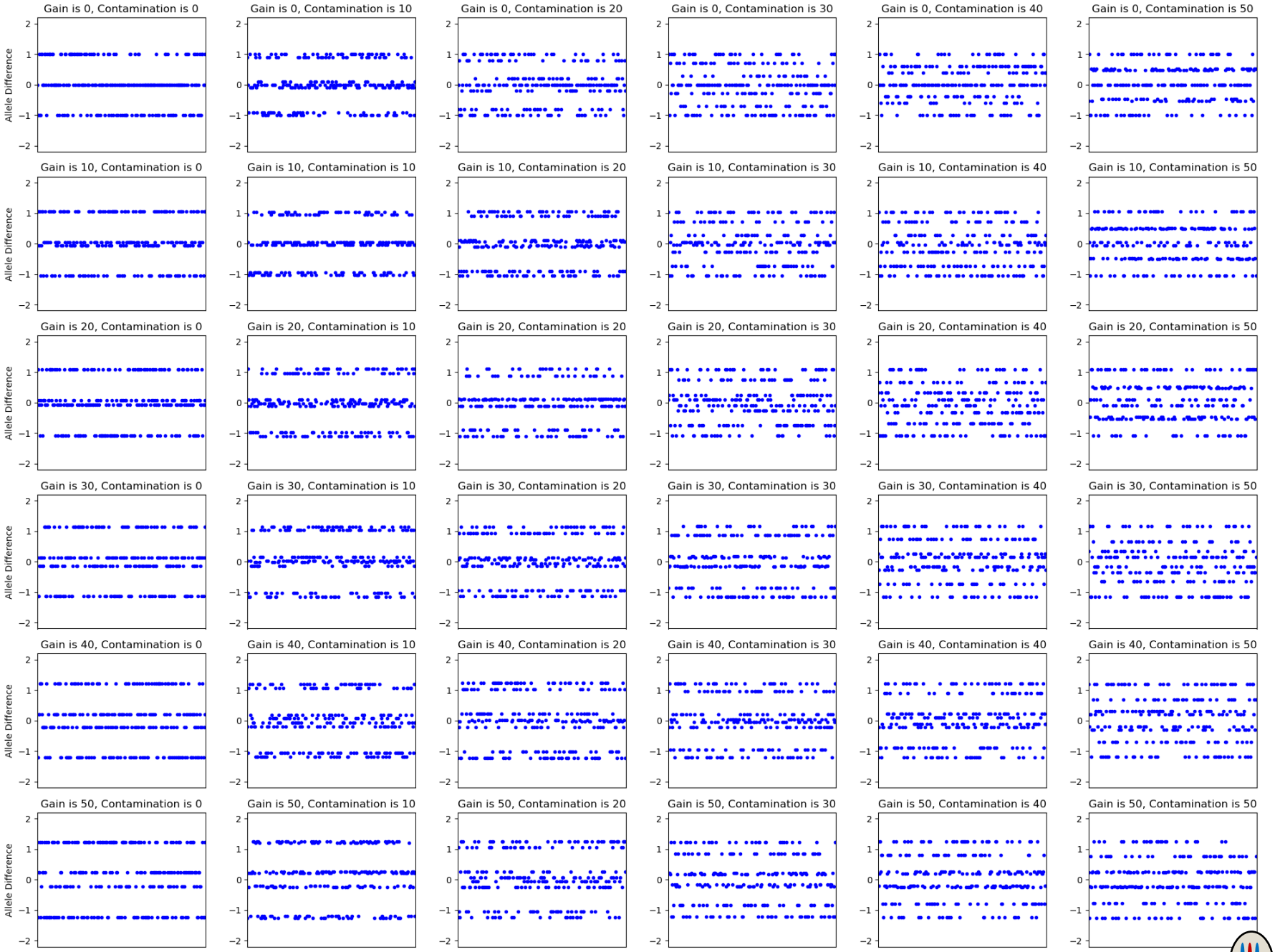
Allele Difference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Gain is 50, Contamination is 50
Allele Difference


Loss is 0, LOH is 0
Loss is 0, LOH is 10
Loss is 0, LOH is 20
Loss is 0, LOH is 30
Loss is 0, LOH is 40
Loss is 0, LOH is 50
Loss is 10, LOH is 0
Loss is 10, LOH is 10
Loss is 10, LOH is 20
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Loss is 40, LOH is 20
Loss is 40, LOH is 30
Loss is 40, LOH is 40
Loss is 40, LOH is 50
Loss is 50, LOH is 0
Loss is 50, LOH is 10
Loss is 50, LOH is 20
Loss is 50, LOH is 30
Loss is 50, LOH is 40
Loss is 50, LOH is 50
Allele Difference
2
1
0
−1
−2


Loss is 0, Gain+2 is 0
Loss is 0, Gain+2 is 10
Loss is 0, Gain+2 is 20
Loss is 0, Gain+2 is 30
Loss is 0, Gain+2 is 40
Loss is 0, Gain+2 is 50
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Loss is 10, Gain+2 is 30
Loss is 10, Gain+2 is 40
Loss is 10, Gain+2 is 50
Loss is 20, Gain+2 is 0
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Loss is 20, Gain+2 is 20
Loss is 20, Gain+2 is 30
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Loss is 30, Gain+2 is 0
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Loss is 50, Gain+2 is 30
Loss is 50, Gain+2 is 40
Loss is 50, Gain+2 is 50
Allele Difference
2
1
0
−1
−2


Loss is 0, Loss-2 is 0
Loss is 0, Loss-2 is 10
Loss is 0, Loss-2 is 20
Loss is 0, Loss-2 is 30
Loss is 0, Loss-2 is 40
Loss is 0, Loss-2 is 50
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Loss is 10, Loss-2 is 30
Loss is 10, Loss-2 is 40
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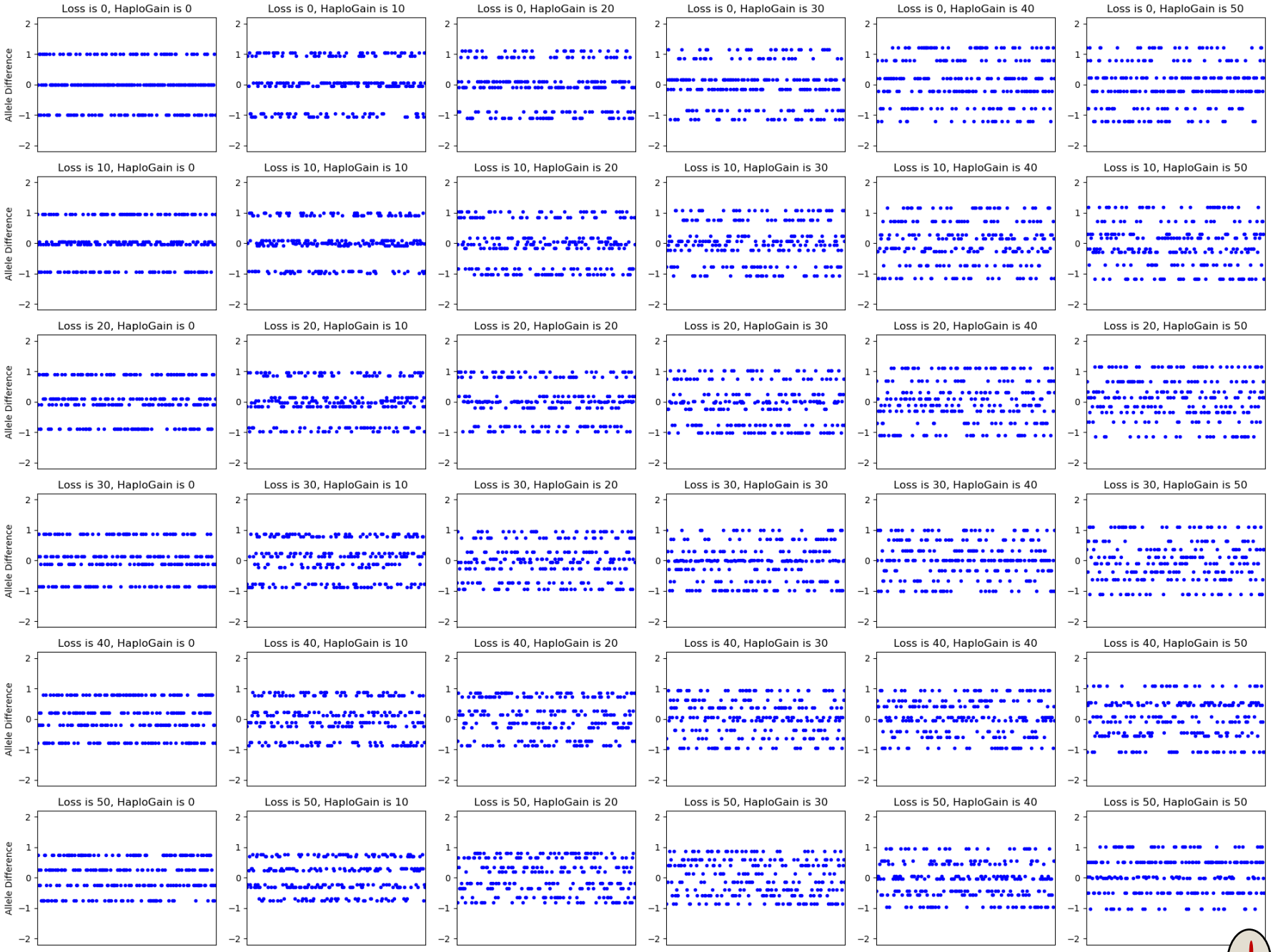
Loss is 20, Loss-2 is 0
Loss is 20, Loss-2 is 10
Loss is 20, Loss-2 is 20
Loss is 20, Loss-2 is 30
Loss is 20, Loss-2 is 40
Loss is 20, Loss-2 is 50
Loss is 30, Loss-2 is 0
Loss is 30, Loss-2 is 10
Loss is 30, Loss-2 is 20
Loss is 30, Loss-2 is 30
Loss is 30, Loss-2 is 40
Loss is 30, Loss-2 is 50
Loss is 40, Loss-2 is 0
Loss is 40, Loss-2 is 10
Loss is 40, Loss-2 is 20
Loss is 40, Loss-2 is 30
Loss is 40, Loss-2 is 40
Loss is 40, Loss-2 is 50
Loss is 50, Loss-2 is 0
Loss is 50, Loss-2 is 10
Loss is 50, Loss-2 is 20
Loss is 50, Loss-2 is 30
Loss is 50, Loss-2 is 40
Loss is 50, Loss-2 is 50
Allele Difference
2
1
0
−1
−2


Loss is 0, HaploGain is 0
Loss is 0, HaploGain is 10
Loss is 0, HaploGain is 20
Loss is 0, HaploGain is 30
Loss is 0, HaploGain is 40
Loss is 0, HaploGain is 50
Loss is 10, HaploGain is 0
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Loss is 30, HaploGain is 40
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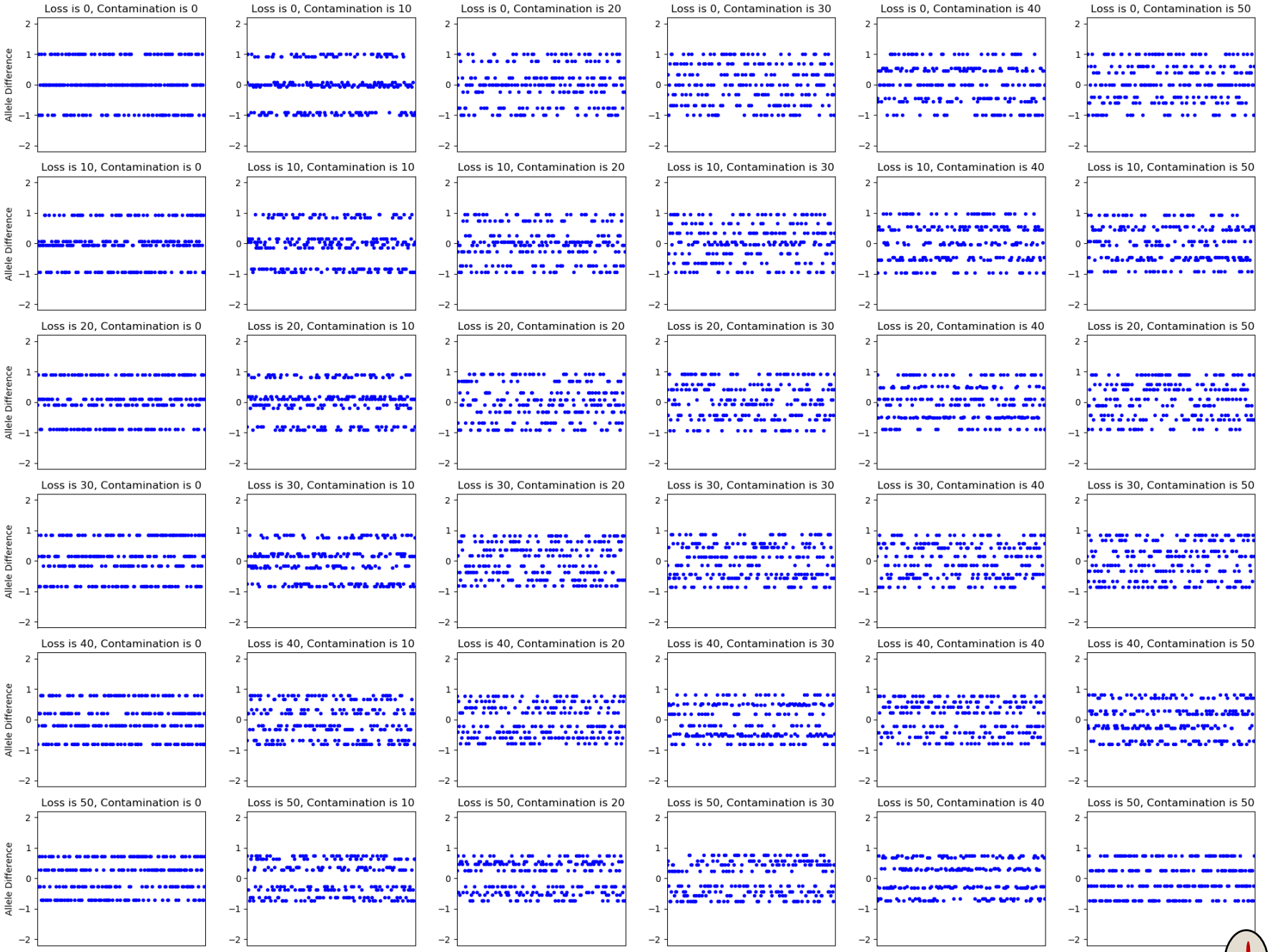
Allele Difference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Loss is 50, Contamination is 30
Loss is 50, Contamination is 40
Loss is 50, Contamination is 50
Allele Difference
2
1
0
−1
−2


LOH is 0, Gain+2 is 0
LOH is 0, Gain+2 is 10
LOH is 0, Gain+2 is 20
LOH is 0, Gain+2 is 30
LOH is 0, Gain+2 is 40
LOH is 0, Gain+2 is 50
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LOH is 50, Gain+2 is 40
LOH is 50, Gain+2 is 50
Allele Difference
2
1
0
−1
−2


LOH is 0, Loss-2 is 0
LOH is 0, Loss-2 is 10
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LOH is 50, Loss-2 is 50
Allele Difference
2
1
0
−1
−2


LOH is 0, HaploGain is 0
LOH is 0, HaploGain is 10
LOH is 0, HaploGain is 20
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Allele Difference
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0
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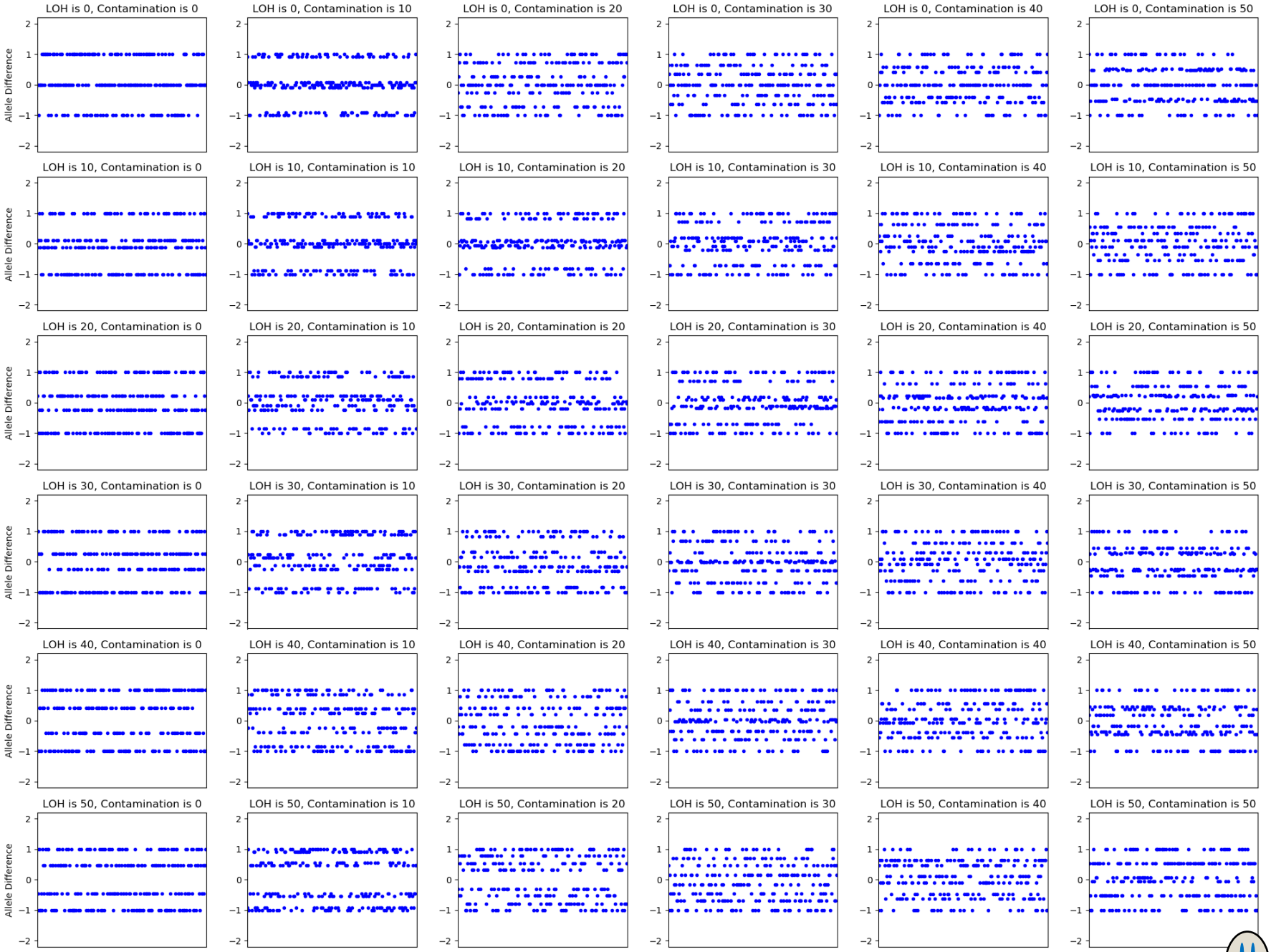
−2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LOH is 50, Contamination is 40
LOH is 50, Contamination is 50
Allele Difference


Gain+2 is 0, Loss-2 is 0
Gain+2 is 0, Loss-2 is 10
Gain+2 is 0, Loss-2 is 20
Gain+2 is 0, Loss-2 is 30
Gain+2 is 0, Loss-2 is 40
Gain+2 is 0, Loss-2 is 50
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Gain+2 is 50, Loss-2 is 20
Gain+2 is 50, Loss-2 is 30
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Allele Difference
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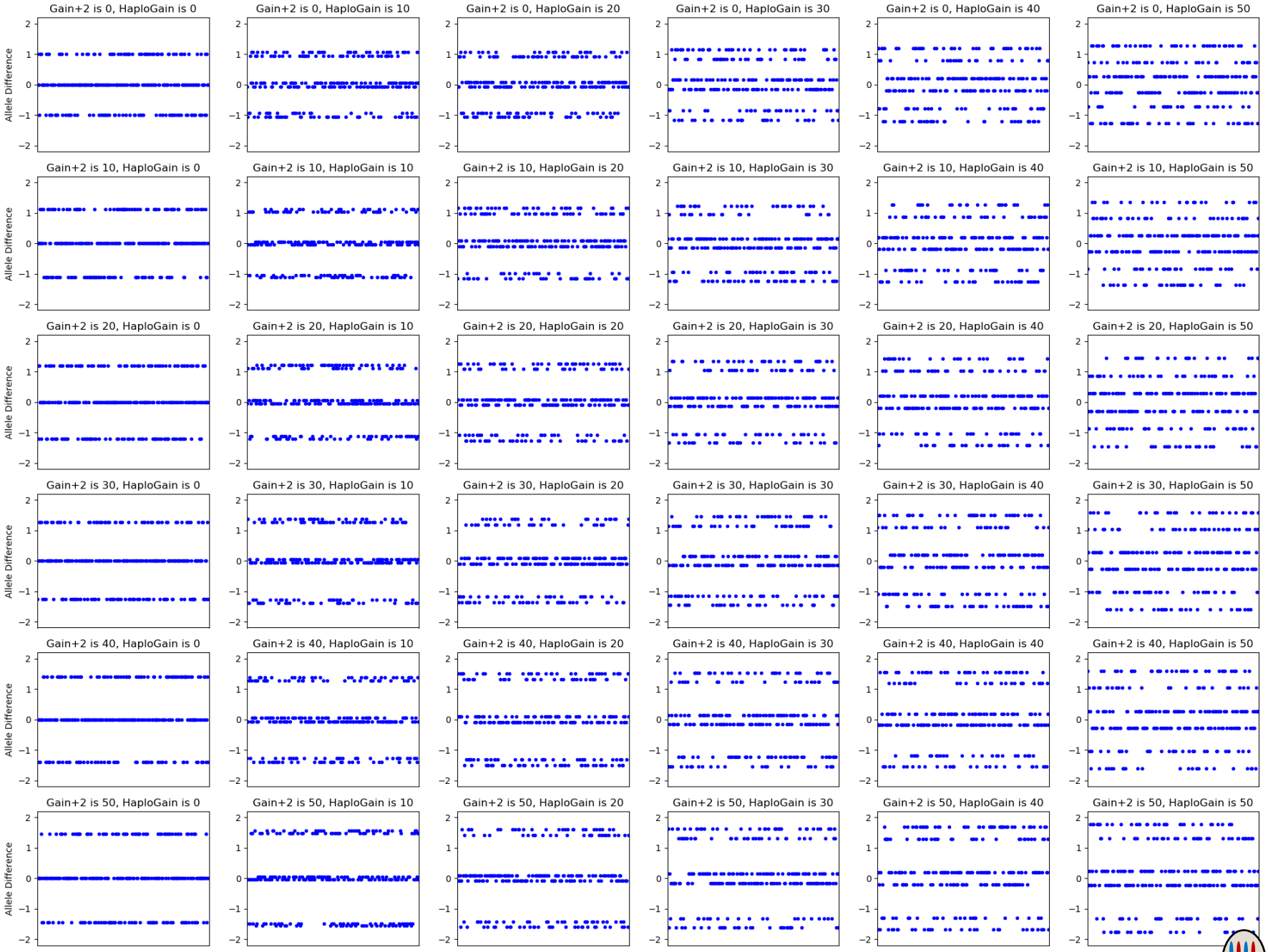
−1
−2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Gain+2 is 0, HaploGain is 40
Gain+2 is 0, HaploGain is 50
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Gain+2 is 20, HaploGain is 10
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Gain+2 is 40, HaploGain is 20
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Gain+2 is 50, HaploGain is 20
Gain+2 is 50, HaploGain is 30
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Allele Difference
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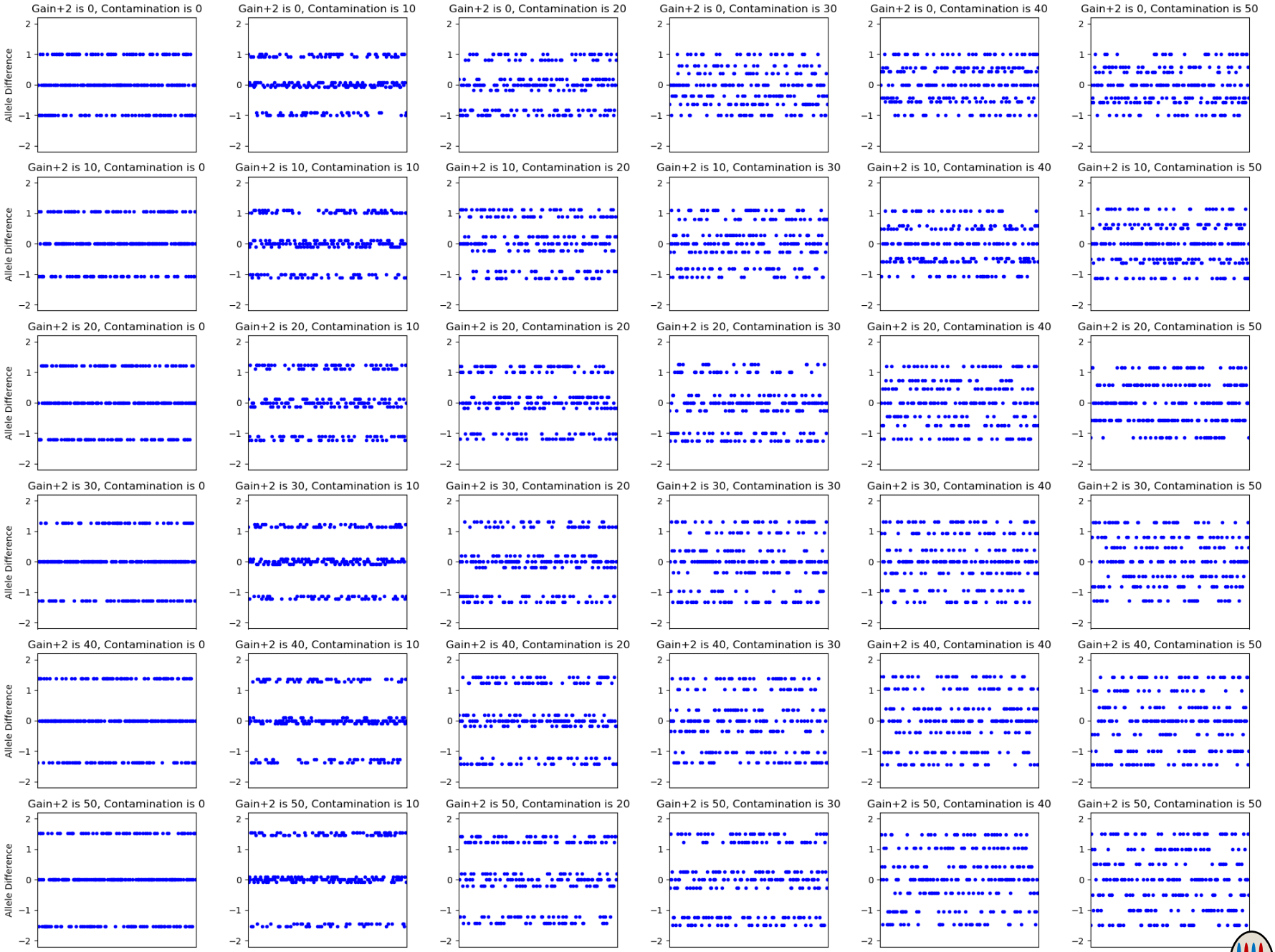
0
−1
−2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Gain+2 is 10, Contamination is 10
Gain+2 is 10, Contamination is 20
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Gain+2 is 20, Contamination is 40
Gain+2 is 20, Contamination is 50
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Gain+2 is 40, Contamination is 50
Gain+2 is 50, Contamination is 0
Gain+2 is 50, Contamination is 10
Gain+2 is 50, Contamination is 20
Gain+2 is 50, Contamination is 30
Gain+2 is 50, Contamination is 40
Gain+2 is 50, Contamination is 50
Allele Difference
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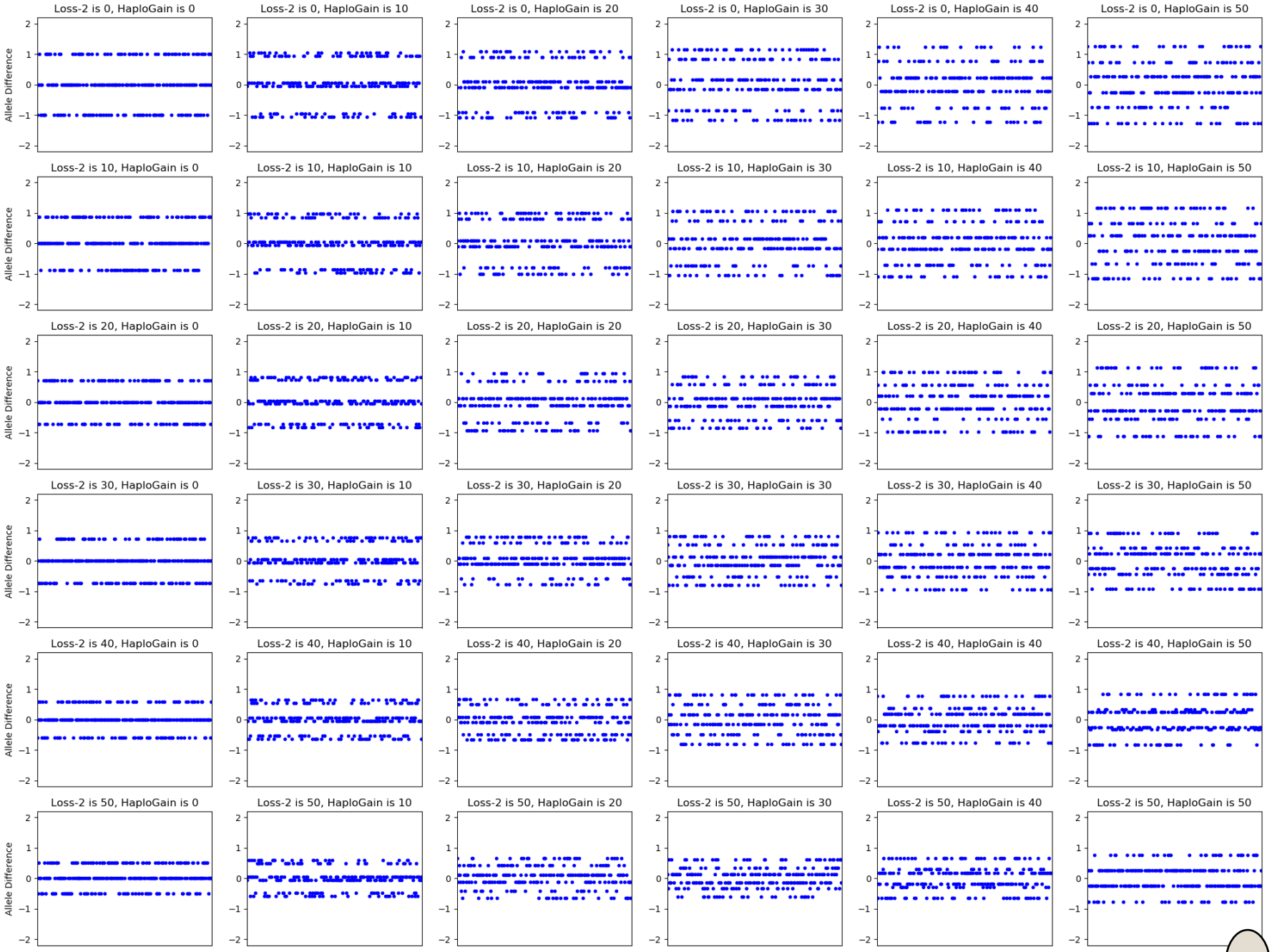
0
−1
−2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Loss-2 is 0, HaploGain is 30
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Loss-2 is 0, HaploGain is 50
Loss-2 is 10, HaploGain is 0
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Allele Difference
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0
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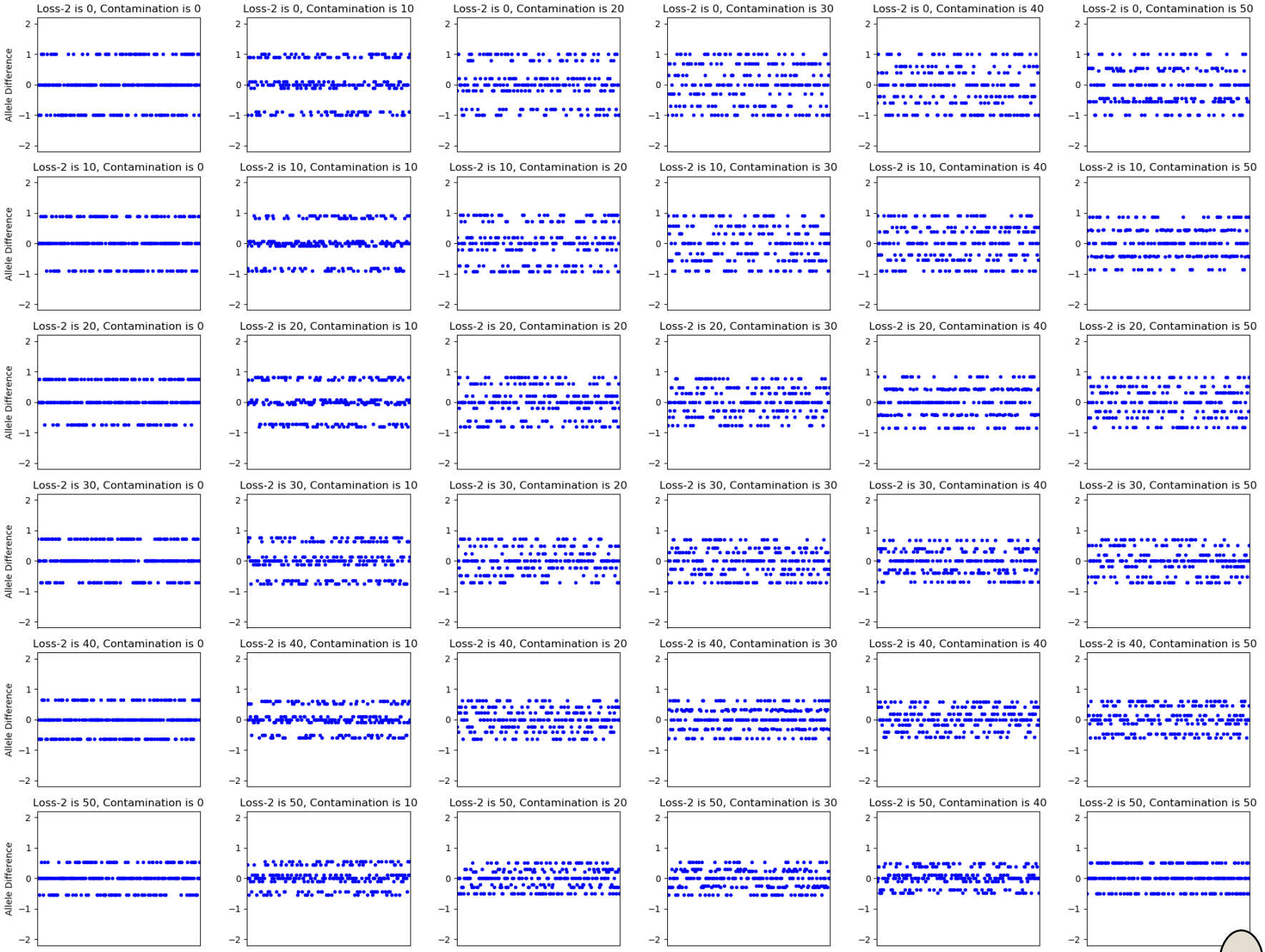
−2


Loss-2 is 0, Contamination is 0
Loss-2 is 0, Contamination is 10
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Loss-2 is 0, Contamination is 50
Loss-2 is 10, Contamination is 0
Loss-2 is 10, Contamination is 10
Loss-2 is 10, Contamination is 20
Loss-2 is 10, Contamination is 30
Loss-2 is 10, Contamination is 40
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Loss-2 is 50, Contamination is 20
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Allele Difference
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0
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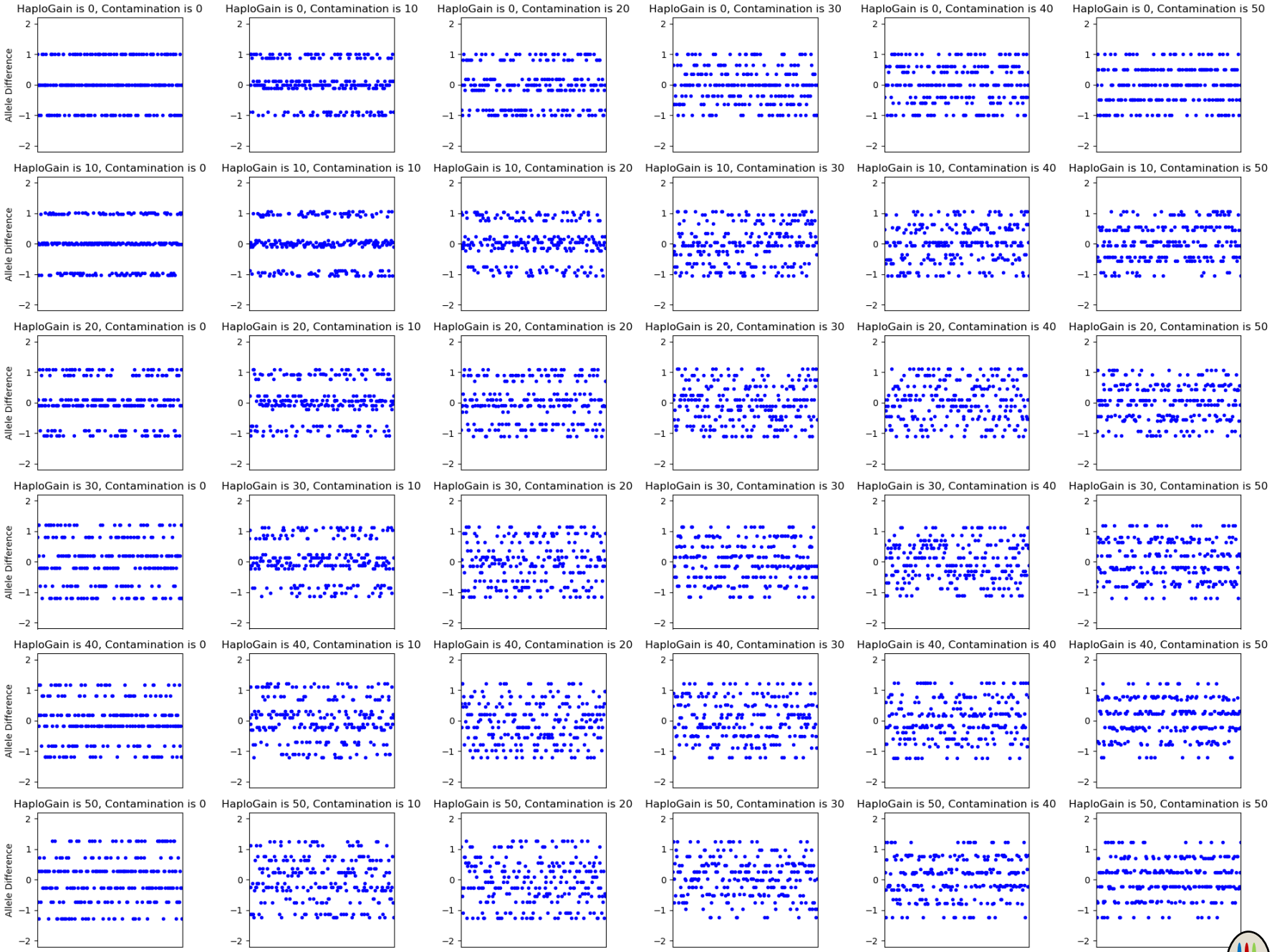
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HaploGain is 50, Contamination is 50
Allele Difference