

The Hidden Interaction Problem: Why One-Factor-at-a-Time Experiments Mislead

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Abstract

One-factor-at-a-time experimentation asks how a response changes when one variable moves while the others are held fixed. That question is often useful, but it can be structurally incapable of revealing interactions: situations in which the effect of one factor depends on the level of another. In formulation, photochemistry, processing and materials testing, interactions can reverse apparent trends, move optima and make a locally successful setting fail when transferred. This methodological article develops the hidden interaction problem and explains why factorial, response-surface and mixture designs answer different questions from sequential one-factor exploration. The central proposition is that an interaction is not noise or a statistical complication; it is information about how the system behaves when variables operate together.

Keywords: interaction; factorial design; one-factor-at-a-time; DOE; response surface; mixture design; confounding; optimization

1. Purpose and evidence boundary

HEB-001 introduced factorial and mixture design and the limits of OFAT [1]. HEB-010 isolates the reasoning problem. It does not define a universal DOE recipe. The design must match factor geometry, measurement capability and scientific purpose.

2. The OFAT question is conditional

Changing factor A while B is fixed estimates the effect of A at that chosen level of B. It does not establish that the same effect exists at another level of B. The experimental statement is therefore conditional even when it is reported as a general trend.

3. Interaction means that effects depend on context

In a simple two-factor model, an AB term represents interaction. A positive main effect of A can coexist with a negative effect of A in part of the B range. The notion of a single 'effect of A' then becomes incomplete unless the state of B is specified.

4. Sequential optimisation can lock the experiment onto the wrong path

An OFAT workflow often chooses a preferred level of A, freezes it, then optimises B. If the best B depends on A, the first choice constrains what the second stage can discover. The final setting can be locally reasonable but globally poor within the investigated region.

5. Factorial designs expose combination effects

A factorial design deliberately samples combinations so that main effects and interactions can be estimated within the design assumptions. Czitrom's comparison of OFAT and designed experiments, cited in HEB-001, illustrates this structural advantage [2,3]. Factorial design does not guarantee a useful answer; it only makes certain interaction questions estimable [3].

6. Curvature requires more than a two-level comparison

When the response is curved, two levels per factor cannot identify pure quadratic terms. Centre points can reveal curvature; second-order response-surface designs can map it. Optimisation should therefore follow evidence that the fitted model adequately represents the region rather than assuming linearity because only linear contrasts were measured.

7. Mixture variables live on a constrained space

Formulation proportions satisfy a sum constraint. Increasing one component necessarily decreases one or more others, so conventional independent-factor intuition fails. HEB-001's photoinitiator-blend example used mixture design to balance reactivity and stability because the components interacted on a constrained composition space [1] [4].

8. Interaction can be physical, chemical or procedural

Temperature can alter viscosity and reaction kinetics simultaneously; exposure can alter both conversion and thermal state; washing time can interact with geometry through diffusion distance; operator technique can interact with fixture design. Statistical interaction is a pattern in response, not proof of one microscopic mechanism. Mechanistic attribution requires additional evidence.

9. Confounding can imitate interaction or hide it

Run order, batch, day or position can align with factor combinations and distort estimated effects. Randomisation, blocking and replication protect the design but do not rescue an invalid response measurement. The measurement method must be qualified before statistical sophistication becomes informative.

10. Practical design discipline

Start from the causal question, not from the software menu. Identify factors likely to act jointly, define feasible ranges, distinguish process factors from mixture proportions, specify the experimental unit, include replication at the relevant level and predefine how model adequacy will be judged. Use OFAT deliberately for screening only when interaction risk is acceptably low or when the claim is explicitly local.

11. A simple interaction can reverse the apparent effect

Consider a response measured at two temperatures and two concentrations. At low temperature, increasing concentration may raise the response; at high temperature, the same increase may lower it. Averaging across temperature could show little overall concentration effect even though concentration matters strongly at both temperatures. Alternatively, an OFAT experiment performed only at low temperature could conclude that more concentration is beneficial and transfer that rule into the high-temperature regime where it fails. This is the practical meaning of interaction: the direction or magnitude of an effect is conditional on another variable. A single main-effect statement compresses that conditional structure.

12. Interaction terms do not automatically identify mechanism

A statistically significant interaction says that the response pattern is non-additive on the chosen scale. It does not by itself reveal why. Temperature and concentration might interact because of viscosity, oxygen transport, radical kinetics, solubility, phase state or another variable correlated with them. Mechanistic interpretation requires targeted measurements or perturbations. This distinction keeps HEB-010 from turning DOE into a mechanistic oracle: designed experiments reveal structure in the response surface; additional science is needed to assign the physical cause.

13. Interaction risk should shape screening strategy

Not every study requires a large factorial design. Early screening can legitimately use simple one-factor changes when the objective is exploratory and resources are limited. The methodological requirement is to keep the inference local. If a factor is screened at one background condition, the result should be stated as conditional until interaction has been challenged. Factors suspected of strong coupling should be sampled together early because an OFAT screen can otherwise eliminate a component that would have been valuable in combination. Efficient design means matching complexity to the question, not maximising the number of model terms.

14. Competing responses create a second trade-off problem

An experimental setting can improve one response while degrading another. A formulation change may accelerate cure yet reduce storage stability; a post-cure condition may raise modulus while increasing distortion; a cleaning condition may remove residue faster while increasing swelling. Optimising one response sequentially can therefore create a false sense of progress. Multi-response design requires the objectives and trade-offs to be declared before the final setting is chosen. The useful region may be a Pareto-like compromise rather than the point that maximises one metric. This extends the interaction problem beyond factor-factor terms: experimental decisions themselves interact through competing outcomes. The author's 1999 mixture-design study provides a primary example of such reactivity-stability compromise [5]. HEB-013 owns the separate question of what a fitted optimum may claim.

15. Sparse designs still require scientific judgement

Large experimental spaces tempt aggressive reduction through fractional designs or screening arrays. These can be powerful when higher-order interactions are plausibly negligible or when alias structure is understood. But the assumption of sparsity is a scientific assumption, not a statistical fact. If a supposedly negligible interaction contains the mechanism of interest, the reduced design can hide it by construction. Efficient experimentation therefore requires a defensible hierarchy of likely interactions, followed by confirmation in the region where the provisional model will be used. The goal is not to estimate every possible term; it is to avoid making the design structurally blind to the combinations that could change the conclusion.

16. Conclusions

OFAT is not wrong; it answers a narrower question than it is often asked to support. When variables interact, isolated trends do not transfer automatically across the experimental space. Designed experiments expose combination effects, but they remain dependent on valid measurement, adequate replication and model checking. The hidden interaction problem is solved by treating context as part of the effect.

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Knowledge boundary

HEB-010 owns the inferential problem created when experimental design cannot estimate interactions. Mixture-design geometry and photoinitiator formulation optimisation are illustrated by the cited primary study [5]; model adequacy and optimum interpretation are owned by HEB-013. Application-specific engineering qualification remains with the relevant Engineering Reviews.

Limitations

This methodological article is a bounded synthesis of the controlled HEB and Engineering Review corpus. It does not report a new experimental dataset, does not establish universal numerical thresholds, and does not convert examples from one domain into application-wide specifications. Claims that require application-specific qualification remain with the corresponding technical review or primary study.