

Variant Sampling in vitro with a Scheduling Twist Alex Morehead¹, Elise Edman², Dr. Laurie Heyer², Dr. Jeff Poet¹

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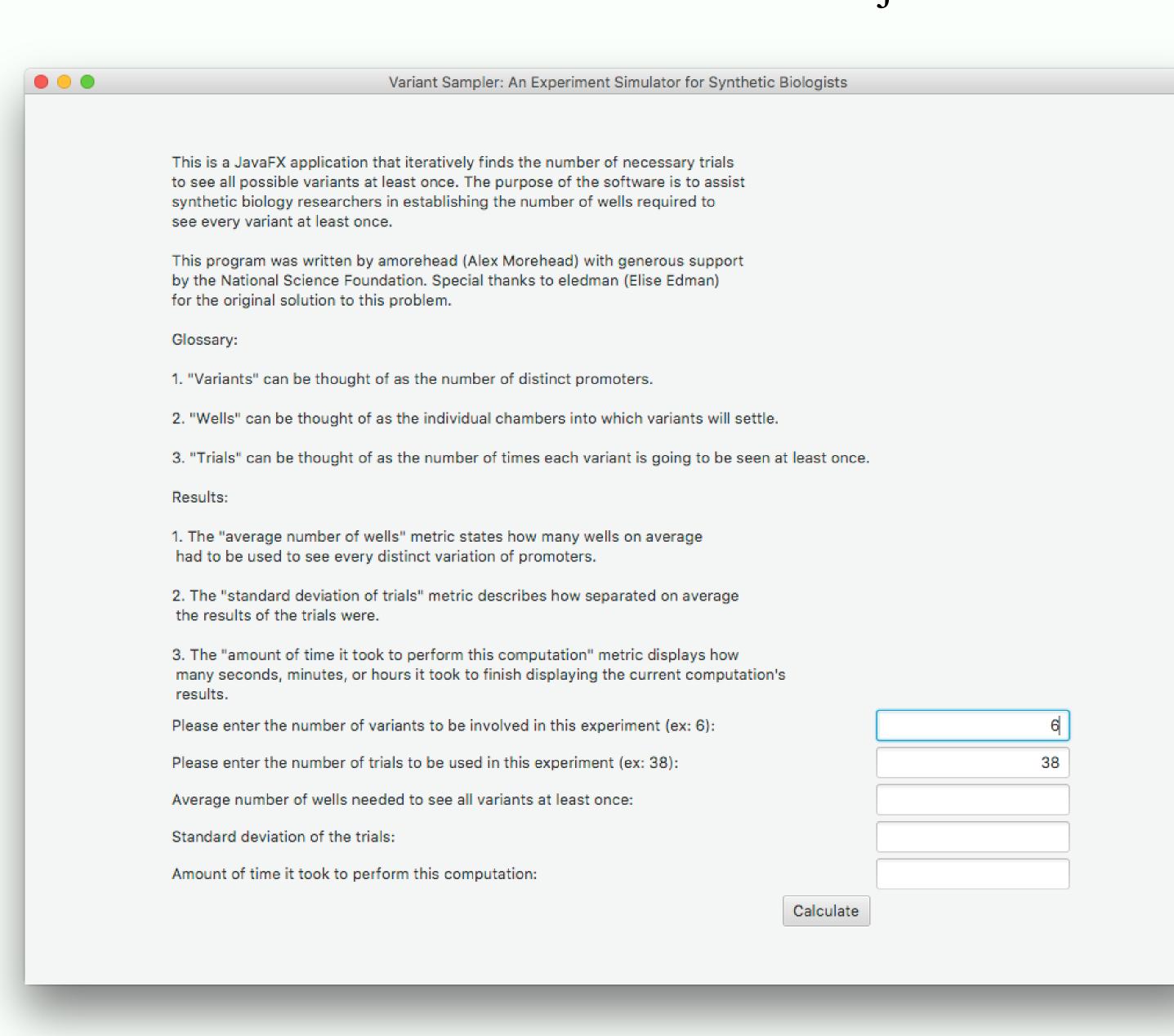


Abstract

The Coupon Problem and the Scheduling Problem are both found at the intersection of mathematics and synthetic biology. To solve the Coupon problem, we wrote a software called *Variant Sampler* that generates simulation data for a given number of variants and number of trials to be used in an experiment. The Scheduling Problem was approached with the help of Google's Optimization Tools (OR-Tools) software suite by treating it as a linear optimization problem. An executable version of Variant Sampler can be found at amorehead.github.io/assets/jar/Variant Sampler.jar

The Coupon Problem

Variant Sampler, which is designed for discovering the average number of wells needed to see each biological variant at least one time, was written in Java with the JavaFX library for making its graphical user interface. The purpose of the software is to assist synthetic biology researchers in modeling and establishing the necessary number of wells for trials performed in a laboratory setting. A small, purely mathematical illustration of the Coupon Problem is to ask, how many times must a standard 6-sided die be rolled in order to expect that each of the six sides has occurred face up at least once? In the biological setting, it could be thousands or millions of variants instead of just 6.



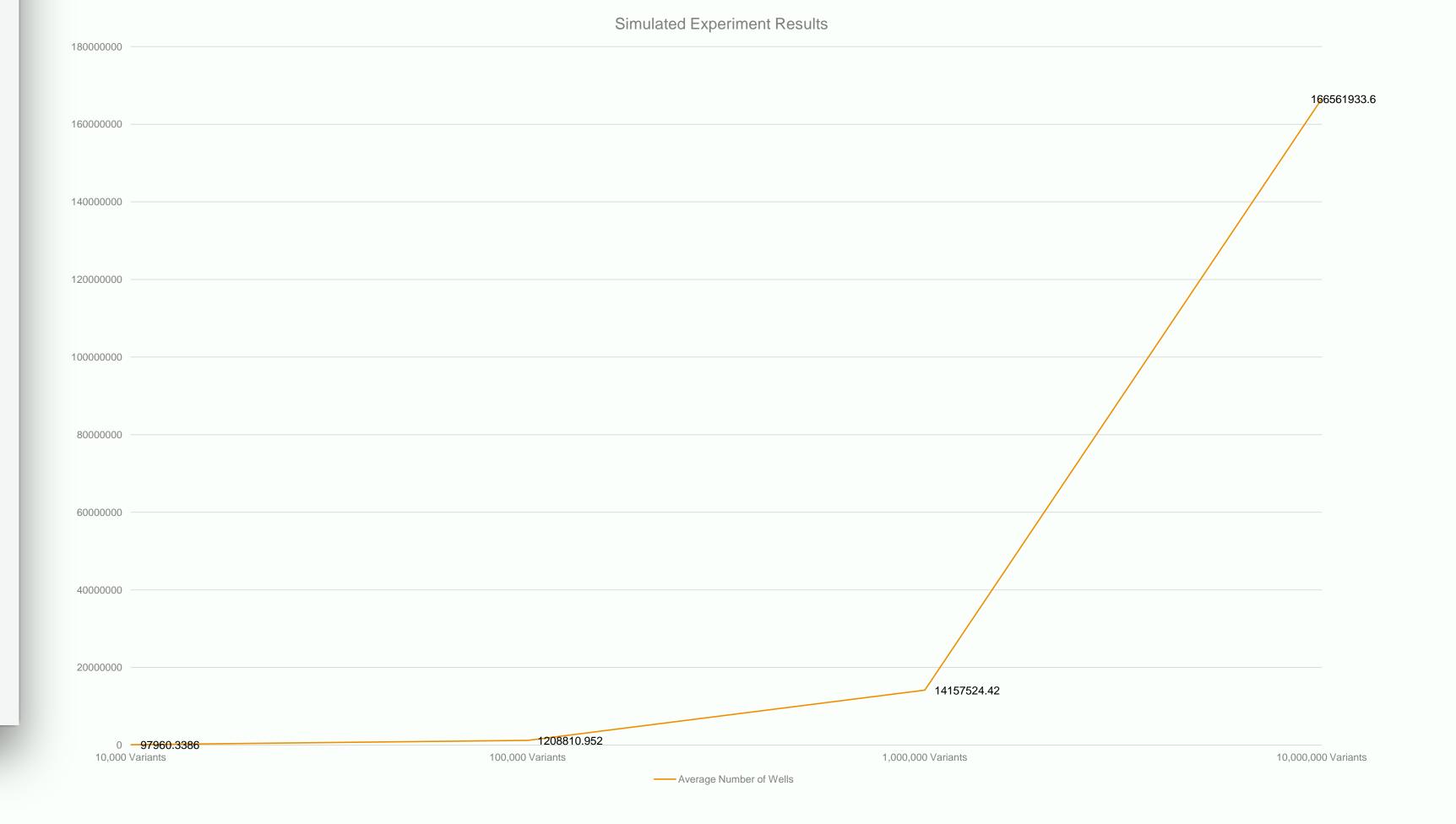
The Scheduling Problem

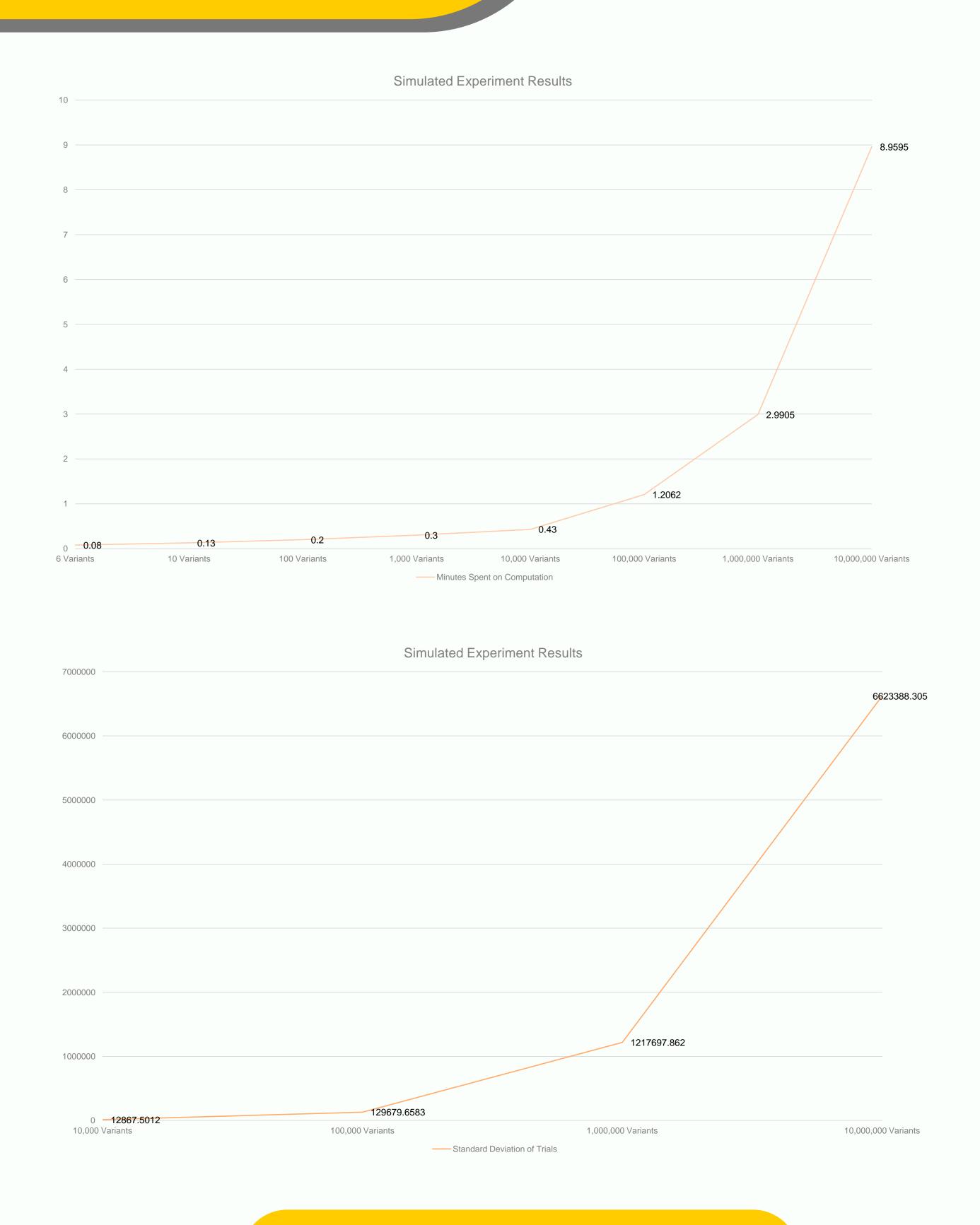
Suppose you have a contest involving many teams in which three teams compete at a time in each match. Several rooms are set up with three teams in each room competing simultaneously. Our task has been to develop an algorithm which would improve upon the existing software for this scenario. The current software was developed over 30 years ago. Our hope was to use newer tools (and perhaps even newer mathematical results) to streamline the process of tournament scheduling which can now take weeks.

In our case, we decided on using Google's OR-Tools suite to allow us to feed in a four-dimensional matrix of all zeros and ones as well as our seven constraints on the resulting matrix so that it would be possible to find out in a reasonable amount of time whether our tournament of interest with a given set of parameters has a feasible solution. Such a result could also assist us in designing experiments to compare our biological constructs. Our partial solution to the scheduling problem allows for the user to specify how many teams, quizzes, rooms, and matches will be used in a given tournament, modularly designing a favorable outcome. Our software also has the advantage of being able to immediately inform the user of unfeasible tournament scenarios.

Results

When running *Variant Sampler* with the number of trials used gradually decreasing by a factor of ten, we can still see the average necessary number of wells finding increasingly larger values. When extending this notion of variant sampling to a higher quantity of variants at a time, we can see the average necessary number of wells increases almost exponentially. Our software gives us the ability to find incredibly precise solutions to computationally complex simulations in a reasonable amount of time.





Conclusions

For future work, we hope to find a means of expanding the results of our experiment simulation software to provide insights into how well certain *in vitro* solutions work with different combinations of promoters, ribosome binding sites, alleles, and other biological constructs. We also hope to find a complete solution to the Scheduling Problem by successfully identifying and deriving all possible constraints for our system built in Python using the OR-Tools suite. Further advances in each of these directions would yield promising results for not only synthetic biologists but also mathematicians and computer scientists.

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