Sampling and asymptotics cheatsheet

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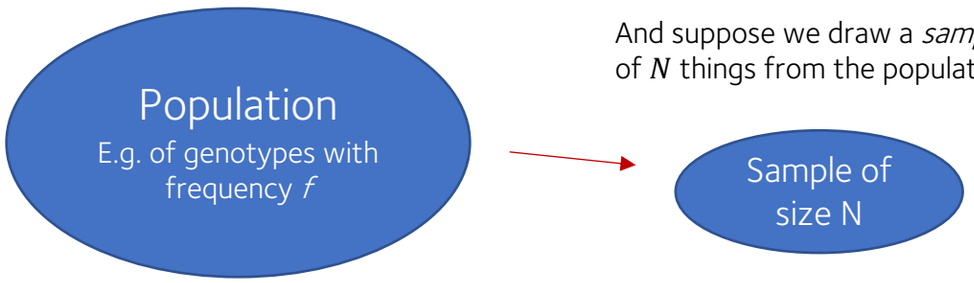
Suppose we have a big bag of things – for example, a population of people, with a particular genotype G that occurs at frequency f:



And suppose we draw a *sample* of N things from the population.

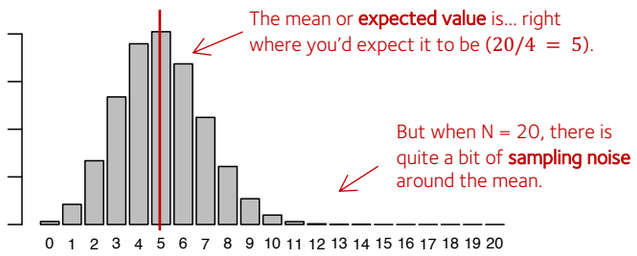
The number of G genotypes in our sample depends on what sample we drew (i.e. it is a "**random variable**") – it would vary from one sample to the next. How does it vary?

It turns out that - if we made sure not to sample the same person twice ("**sampling without replacement**"), then the number has a "hypergeometric distribution". This is actually a bit annoying because that distribution is a bit tricky to work with – it depends on knowing the full population size, and it makes the samples not independent of each other. However, ***if our population is very large and the sample is much smaller*** then we will never sample the same thing twice anyway. We might as well imagine we are **sampling with replacement** instead – that is, we can use the much simpler binomial distribution:

number of G genotypes in the sample $\sim$ binomial(N, f) ← Only depends on the sample size and the true frequency f

This is the situation we're often in in genetics – we have a small sample from a large population, and we would like to make statements about the population by looking at the sample.

For example, here is the distribution of a sample of size 20 when the population frequency $f = 25\%$.

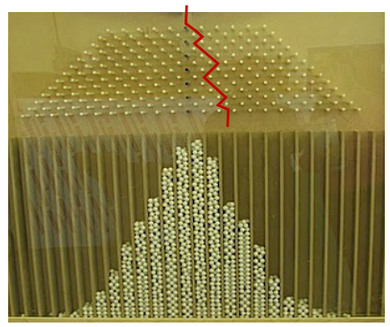


Here is another way to think of sampling – via a Galton board:

We drop marbles in at the top

At each level the ball 'samples' either a left or a right.

After a while the marbles draw a binomial distribution:

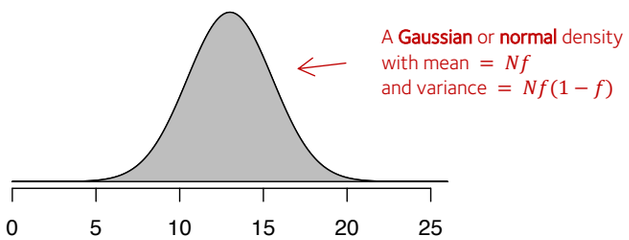


Number of possible routes is given by Pascal's triangle:

```
        1
      1   1
    1   2   1
  1   3   3   1
1   4   6   4   1
  etc.
```

The **number of possible routes** ending up in each box is given by **Pascal's triangle** – in other words, they are the binomial coefficients. Hence the name!

The most crucial fact in all of statistics is that, as we let the number of samples get large, the distribution above becomes approximately *Gaussian*.



This famous fact is known as the central limit theorem. An important consequence is the asymptotic theory of likelihoods explained below.

Example for `glm()`:

```
➢ fit = glm( Y ~ X, data = data, family = "binomial" )

> summary(fit)$coefficient
              Estimate Std. Error   z value     Pr(>|z|)
(Intercept) -1.1155710  0.2409409 -4.630061 3.655588e-06
X           -0.2491656  0.2115801 -1.177642 2.389394e-01
```

$\hat{\beta}$ (the **maximum likelihood estimate** or **MLE**)

se (the standard error of the MLE, estimated from the likelihood curvature)

$z = \beta/\text{se}$ (the **z-score**)

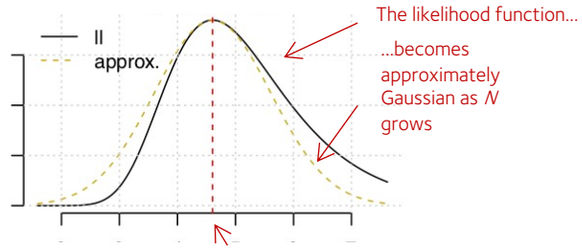
$P = \text{pnorm}(-|z|)\times 2$ (the **P-value**)

Interpretation: our estimate of β is -0.25, but since $P = 0.23$ this is consistent with a true effect of zero and a nonzero observed effect due to random sampling of the outcome varianble Y.

The central limit theorem implies that many likelihood functions 'become gaussian' as the amount of data grows. Specifically:

1. the likelihood function will approximate a Gaussian density (up to a constant) as $N \to \infty$.

And **2.** the location of the likelihood function itself will become approximately Gaussian around the 'true' value as $N \to \infty$.



$\hat{\beta}$ = the **maximum likelihood estimate**, becomes approximately gaussian distributed around 'true' β as N grows

Moreover **3.** these gaussians have the same variance!

Likelihood function: $\mathrm{P}(\text{data}|\beta = \mathrm{x}) \propto N\left(x; \hat{\beta}, \frac{I}{N}\right)$

MLE estimate distribution: $\hat{\beta} \sim N\left(\text{true } \beta, \frac{I}{N}\right)$

These have the same variance, scaling like $1/N$. (Here I is some value that doesn't depend on the data or parameters.)

Conclusion 1: often we only need to report the maximum likelihood estimate and its std. error.

Conclusion 2: the standard error can be read off from the likelihood function.
(This is indeed how standard errors and P-values in functions like `lm()` and `glm()` are often computed.)

This is referred to as 'asymptotic local normality' and 'Le Cam' theory. For them to work the likelihood must be smooth, the 'true β' should be in the interior of parameter space, and the data should have some level of independence.