## S1| Determining arithmetic operations from rate-coded input-output relationships and the confounding effects of nonlinearity

The mathematical operations performed by a neuron can be separated into arithmetic components. For linear input-output (I-O) relationships (e.g **Fig. 5b**) gain changes can be calculated from the change in slope of a fitted linear function and the additive component determined from the change in the x-axis intercept. For nonlinear I-O relationships (e.g. **Fig. 6d**) a nonlinear empirical function is used to fit the data. Hill-type functions (widely used to describe the binding of a ligand to a receptor; (Hill, 1910) are well suited for this because they can take a range of shapes. In this case neuronal firing rate response (R) is defined as a function of the driving input frequency (d) as follows:

$$R(d) = R_{MAX} \frac{d^n}{d_{50}{}^n + d^n}$$

The Hill coefficient (n) determines the shape of the function: n=1 produces a simple saturating function, while higher values of n produce sigmoidal curves of increasing steepness. The additive component can be determined from the value of the driving input that produces a half maximal response ($d_{50}$) before and after modulation(Murphy and Miller, 2003; Rothman et al., 2009). The gain of the I-O relationship can be determined from the average derivative of the Hill function fit over a range of output frequencies. An input gain modulation (**Fig. 1e**) can be distinguished from an output gain modulation (**Fig. 1f**) by determining whether the saturating output rate ($R_{MAX}$) changes after modulation. However, application of this equation is limited to saturating I-O relationships. Alternatively, non-saturating I-O relationships may be fit a *polynomial function*(Ayaz and Chance, 2009; Chance et al., 2002).

Nonlinear properties of I-O relationships complicate the distinction between additive and multiplicative operations, because purely additive shifts along one of the axes can introduce a crude form of multiplication when the gain change is calculated as a function of that axis. Figure S1, which shows a rate-coded I-O relationship with an exponential form, illustrates this effect.

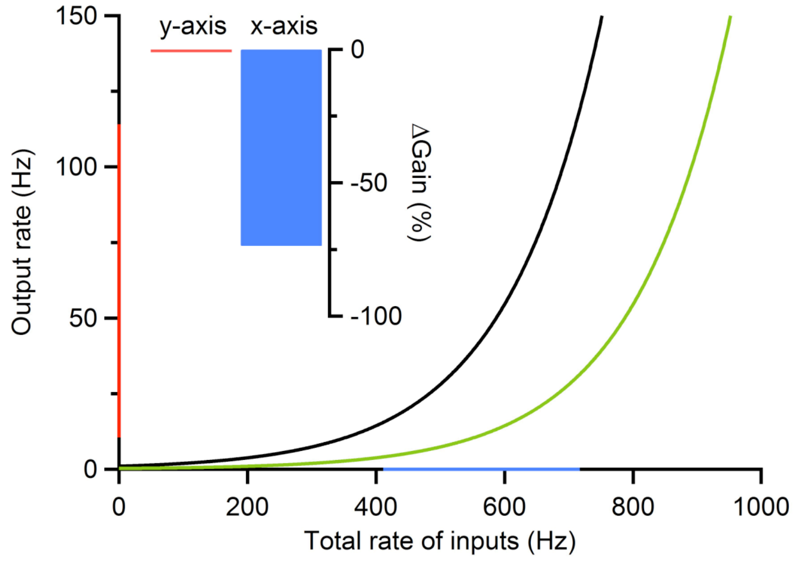


**Figure S1. An additive x-axis shift introduces a multiplicative gain change as a function of the input**

A rightward additive shift along the driving axis (black to green) produced a divisive gain change as a function of input axis (blue bar), because exponential functions have the special property that $e^{(d+m)} = e^{d} \times e^{m}$. This has been termed a 'nonlinear-additive' multiplication, which can be distinguished from 'directly multiplicative' effects(Brozovic et al., 2008) by calculating the gain change with respect to the non-shifted axis y-(Chance et al., 2002). Indeed, the gain change, determined over a range output firing rates (y-axis) for this exponential function, is exactly zero (red bar). Similar effects are observed with other types of nonlinear function. True gain changes can also be distinguished from nonlinear-additive multiplication, for functions other than an exponential, by examining the ratio of the derivatives of the two functions (Brozovic et al., 2008). Although such nonlinear-additive effects have been discounted in some studies(Ayaz and Chance, 2009; Chance et al., 2002), they could potentially allow neurons to perform crude multiplications, especially when combined with an input nonlinearity (Brozovic et al., 2008; Murphy and Miller, 2003.

Ayaz, A., and Chance, F.S. (2009). Gain modulation of neuronal responses by subtractive and divisive mechanisms of inhibition. J Neurophysiol *101*, 958-968.

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Chance, F., Abbott, L., and Reyes, A. (2002). Gain modulation from background synaptic input. Neuron *35*, 773.

Hill, A.V. (1910). The possible effects of the aggregation of the molecules of hæmoglobin on its dissociation curves. Proceedings of the Physiological Society *40*, iv-vii.

Murphy, B.K., and Miller, K.D. (2003). Multiplicative gain changes are induced by excitation or inhibition alone. J Neurosci *23*, 10040-10051.

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**Polynomial function**

A function made up of the sum of a number of terms, each consisting of a coefficient and one or more variables raised to the power of a positive integer (for example, $a + bx + cx^2$)