Models of binocular rivalry and alteration of interocular balance

Bistable perception occurs whenever two qualitatively different images can be consciously perceived in alternation from stimulation with a single, physically stable image. Numerous examples of such ambiguous stimuli can produce bistable percepts across visual domains ranging from higher-level object recognition, as in the famous young lady versus old women illusion (Fig.1A), to depth (Fig.1B), motion perception (Fig.1C) and others. Binocular rivalry paradigms, where two physically dissimilar images are dichoptically presented, one to each eye (Fig.1D), are often used to study bistable perception. Just as a woman cannot be physically young and old at the same time, the world cannot *be* different whether it is seen from the left of the right eye. The brain therefore suppresses one, or multiple possible internal representations of this world such that only one reaches consciousness, and dominates perception at any given time. This selection and suppression process is intrinsically unstable, the dominant percept eventually vanishing and the suppressed one taking over, alternating every few seconds, hence bistability. Although some stimulus characteristics or top-down cognitive processes like attention can modulate the stochastic statistics of duration of dominance periods, switches are inevitable (Blake and Logothetis, 2002).

The following essay will first describe the key computational features generating bistability in models of binocular rivalry and bistable perception in general. Although a review of the large body of literature on binocular rivalry and its ongoing debates would be of most interest for the current work, an adequate description

covering all existing computational models addressing binocular rivalry can hardly be achieved in this manuscript with reasonable length. Instead, reference to other models and their key features will be made throughout the following sections whenever deemed appropriate. This will allow to further focus on the computational implications of a putative role for the inhibitory neurotransmitter GABA, and of the effect of unbalancing interocular interactions on the dynamics of rivalry. Finally, an implementation of one particular model will be challenged to account for some data from my lab where both neurotransmitter concentrations and rivalry dynamics were measured before and after altering the interocular balance with monocular deprivation.

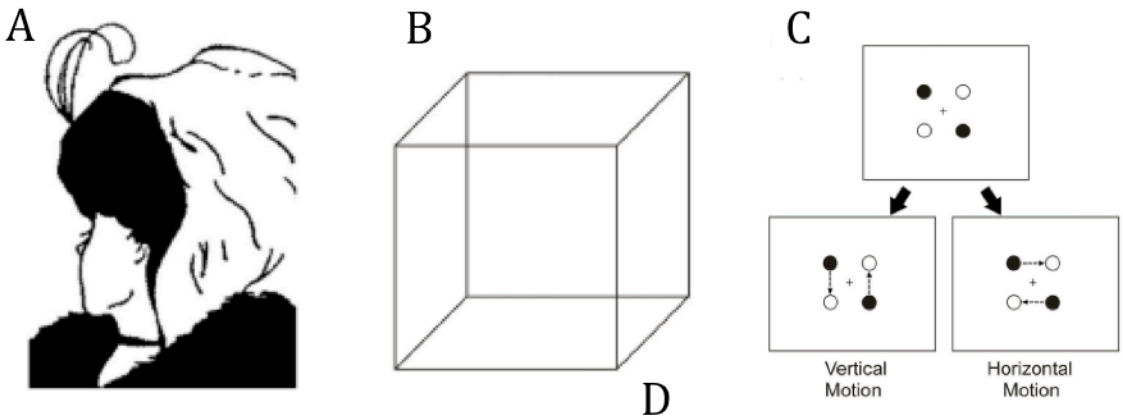

Figure 1. Examples of ambiguous stimuli in A. object recognition (either an old women or a young lady can be perceived), B. depth perception (the front face of the cube can either be the upper or the lower square) and C. motion perception (the circles simultaneously alternating between a white and a black fill can be perceived as apparent vertical of horizontal motion). Adapted from *Scocchia et al. Front Hum Neurosci. 2014*. In binocular rivalry in D., two orthogonal gratings are dichoptically presented, one to each eye. With relatively small stimulus size, perception is dominated by either one orientations, which alternate over time, rather than by a plaid overlay. Adapted from *Tong et al, Trends Cogn Sci. 2006*.

The generic model of rivalry

Mutual inhibition

Early modeling work on binocular rivalry used competitive inhibition for the establishment of dominance of one percept over the other (Sugie, 1982, Lehky, 1988, Blake, 1989), a mechanism that still today is central to the vast majority of models (Blake and Wilson, 2011, Scocchia et al., 2014). In its minimalist form, a model would include two units, X1 and X2, respectively responding to excitatory inputs I_1 and I_2 with an activity level X_1 and X_2 as follow:

$$\tau\partial X_1 = I_1 - X_1$$
$$\tau\partial X_2 = I_2 - X_2 \qquad [1]$$

This could represent a red right-tilted grating in the right eye stimulating unit X1 and a green left-tilted grating in the left eye stimulating unit X2, such that the activity level in a given unit, here solely dependent on the strength of the inputs, reflects the strength of the percept corresponding to the physical image it is driven by (Fig.1A). Mutual inhibition between the two units:

$$\tau\partial X_1 = I_1 - X_1 - \gamma S[X_2]$$
$$\tau\partial X_2 = I_2 - X_2 - \gamma S[X_1] \qquad [2]$$

, where the level of activity of one suppresses activity of the other with gain *gamma* after non-linear transformation ($S[X]=X^{18}$ for $X>=0$ and $S[X]=0$ for $X<0$), will introduce a winner-takes-all competition. An ever slight advantage in activity level of one unit, say X1, may it be by chance, will have it maximally suppress its opponent X2, while lifting inhibition on itself at the same time. Initiated at 0 and

responding to the introduction of constant inputs I_1 slightly larger than I_2, X_1 and X_2 will rapidly converge respectively to their maximum and minimum, and dominance of perception of a red right-tilted grating will be established (Fig.2C).

Adaptation

Driving inputs and mutual inhibition alone are not sufficient for bistability, since the system becomes stable once dominance is established. Another element is needed to disrupt dominance and allow alternations. In our minimalist model, adaptation, depicted as recurrent self-inhibitory connections in Fig.1A and akin to neuronal fatigue, goes as follow:

$$\begin{aligned} \tau\partial X_1 &= I_1 - (1+A_1)X_1 - \gamma S[X_2] \\ \tau\partial X_2 &= I_2 - (1+A_2)X_2 - \gamma S[X_1] \end{aligned} \quad [3] \qquad \begin{aligned} \tau_A\partial A_1 &= -A_1 + \alpha S[X_1] \\ \tau_A\partial A_2 &= -A_2 + \alpha S[X_2] \end{aligned} \quad [4]$$

, where A_1 and A_2 stand for the adaptation level of each unit and modulate the leak term. Adaptation levels are themselves controlled by the differential equations [4], which represents slow (tau_A >> tau) leaky integrators of the level of activity of the corresponding unit. Given this, adaptation will slowly accumulate for the highly active dominant X1 unit (Fig.1D, bottom panel), and as it does, it gradually reduces the activity level of the same unit (Fig.1D, top panel), *ergo* leading to dynamic interactions involving disinhibition of the suppressed X2 unit and inhibition of the dominant X1 unit by the increasingly active X2 unit. This culminates with rapid reversal of dominance once activity level of the (previously highly) suppressed X2 exceeds that of the (now much less) dominant X1, and after the process can start over. Whether this fatigue, generally referred to as adaptation, is implemented

similarly to physiological spike-rate adaptation by up-regulating the leak of the input integrator as above (Noest et al., 2007, van Loon et al., 2013) and/or as synaptic depression where the gain of the excitatory inputs to, or the inhibitory inputs from, the highly active unit is reduced (Laing and Chow, 2002), the behavior of the system will be the same: dominance and suppression wane over time and bistability emerges.

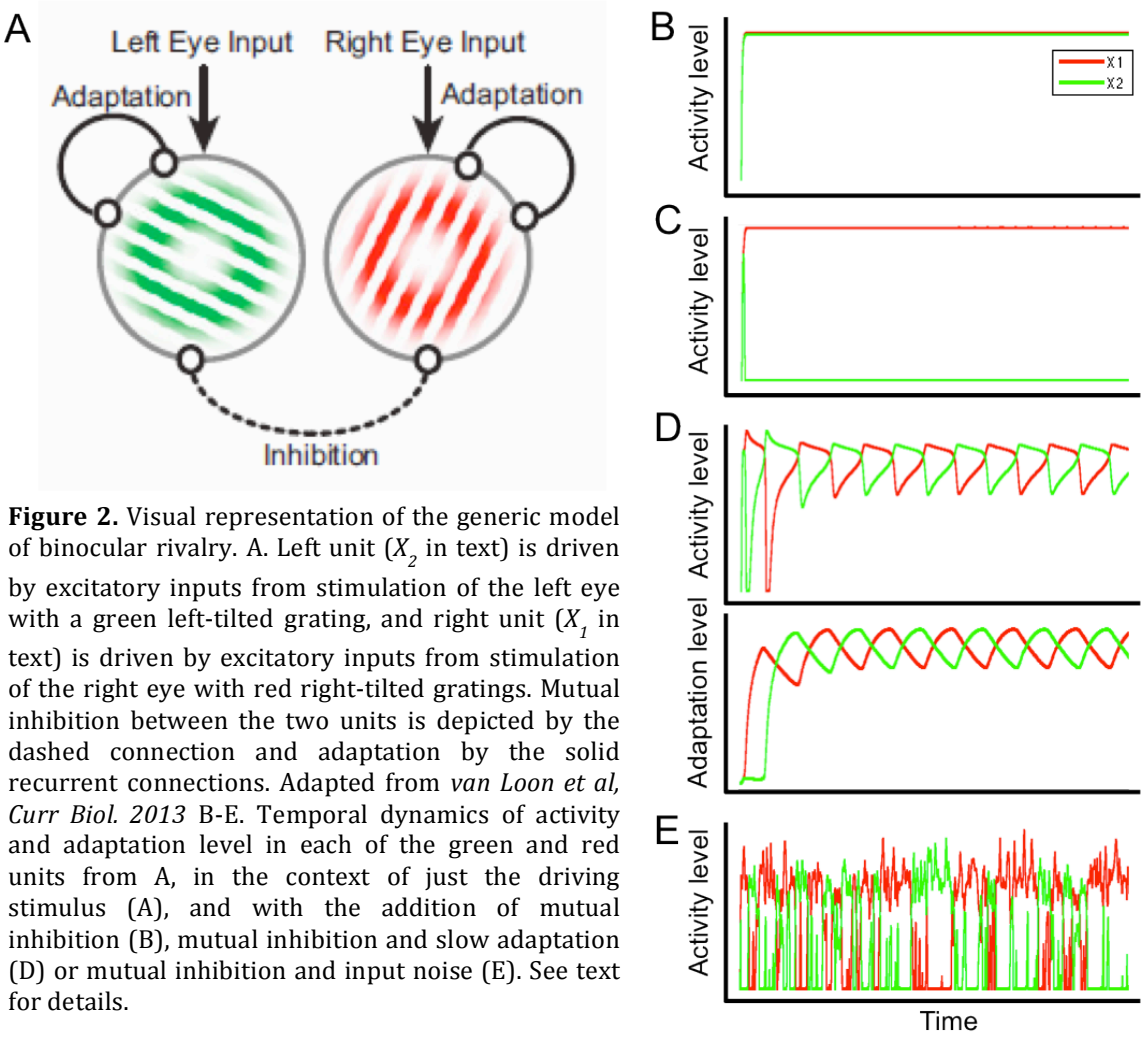

Figure 2. Visual representation of the generic model of binocular rivalry. A. Left unit (X_2 in text) is driven by excitatory inputs from stimulation of the left eye with a green left-tilted grating, and right unit (X_1 in text) is driven by excitatory inputs from stimulation of the right eye with red right-tilted gratings. Mutual inhibition between the two units is depicted by the dashed connection and adaptation by the solid recurrent connections. Adapted from *van Loon et al, Curr Biol. 2013* B-E. Temporal dynamics of activity and adaptation level in each of the green and red units from A, in the context of just the driving stimulus (A), and with the addition of mutual inhibition (B), mutual inhibition and slow adaptation (D) or mutual inhibition and input noise (E). See text for details.

Noise

One must note that adaptation is not an absolute requirement for bistability (Brascamp et al., 2006, Moreno-Bote et al., 2007, Shpiro et al., 2009). If strong enough, and accompanied by mutual inhibition, Gaussian noise of mean 0 and standard deviation *sigma* added to the input signal as follow:

$$\begin{aligned} \tau\partial X_1 &= I_1 - X_1 - \gamma S[X_2] + N(0,\sigma_{X1}) \\ \tau\partial X_2 &= I_2 - X_2 - \gamma S[X_1] + N(0,\sigma_{X2}) \end{aligned} \qquad [5]$$

can momentarily overcome the mutual inhibition-induced dominance and trigger alternations (Fig.2E). Using such a mechanism to generate bistability takes us from the deterministic oscillator-based model described above to a stochastic attractor-based model, which although not explicit in the derivation in [5], represents the two perceptual alternatives as stable minima, the attractors, on an energy plane (Moreno-Bote et al., 2007). Whether triggering a perceptual switch is best explain by energizing an activity space with noise or by attenuating activity level associated with the dominant percept through adaptation processes is an ongoing debate, but an accurate match to experimental data likely requires a balance between both (Shpiro et al., 2009). Importantly, at least some level of noise, whether implemented in the inputs or as fluctuations in the gain of adaptation gain or synaptic depression, is most certainly required, as the deterministic nature of systems in which bistability relies solely on adaptation, as in [3] and [4], cannot produce the stochastic behavior, with gamma or log-normal distributed durations of dominance, that is a psychophysical hallmark of bistable perception (Levelt, 1968). Interestingly, the deterministic, yet chaotic behavior emerging from distributed

neuronal network with Gaussian pattern of connectivity can mimic stochasticity and by producing gamma-distributed dominance durations (Laing and Chow, 2002), challenging this idea of an absolute requirement of noise to accurately account for empirical data.

The role GABAergic inhibition in the competition process

As described above, the role of competitive inhibition is central to the majority of models of binocular rivalry and bistable perception in general, but surprisingly enough, to the best of my knowledge, this assumption has been put to experimental challenge only very recently. van Loon et al., 2013 made use of a generic low-level model of bistable perception implementing both adaptation and input noise in a single stage (see later sections for a detailed description of the model) in order to predict the effect of changes in the level of (putatively GABAergic) mutual inhibition on the duration of dominance periods. Using both Magnetic Resonance Spectroscopy measures of GABA in the occipital cortex and pharmacological modulation of the $GABA_A$ receptor, they confirmed the predictions of the model in three types of bistable perception, including binocular rivalry. Subjects with higher GABA concentrations, and presumably higher levels of competitive inhibition, showed longer dominance durations as expected, and pharmacological inhibition of the receptor further suggested causality of the relation.

It is important to note at this point that the exact locus of the inhibition responsible for dominance is still a matter of debate (Kovacs et al., 1996, Logothetis et al., 1996, Blake and Wilson, 2011), just as is the relevance and nature of a hierarchical structure (Wilson, 2003, Freeman, 2005) and the importance of top-

down interactions (Tong et al., 2006). Interestingly, van Loon et al., 2013's relation between dominance durations and GABA concentrations was specific to the occipital cortex, as it was not found in the dorsolateral prefrontal cortex (DLPFC), a high-level region that may be implicated percept alternation (Vernet et al., 2015). This reinforces the idea that although competition can go on at higher levels, rivalry is likely initiated by competition at lower levels in the visual hierarchy (Blake and Wilson, 2011).

Monocular deprivation and unbalanced rivalry dynamics

The fully developed visual system is known to retain some potential for plastic changes, as revealed by various visual deprivation protocols in human adults (Boroojerdi et al., 2000, Kwon et al., 2009, Zhang et al., 2009). Plasticity induced by one such protocol involving a relatively short period (30 minutes to 3 hours) of monocular deprivation can bias vision towards a greater influence of the deprived eye during binocular combination (Zhou et al., 2013) and greater perceived contrast from the deprived relative to the non-deprived eye (Lunghi et al., 2011). Consistent with that is the fact that contrast sensitivity is increased in the deprived-eye and reciprocally decreased in the non-deprived one (Zhou et al., 2013). Not surprisingly, such monocular deprivation treatment can also bias binocular rivalry dynamics toward longer dominance periods for the deprived-eye (Lunghi et al., 2011, 2013).

At first sight, these recent findings could point toward homeostatic modulation of contrast-gain mechanisms (Mrsic-Flogel et al., 2007). Given van Loon et al., 2013's demonstration of the involvement of GABA in rivalry dynamics, couldn't monocular deprivation act through altering the balance of interocular mutual inhibitory

connections? More importantly, the potency of monocular deprivation-induced plasticity offers an opportunity to challenge current computational models of binocular rivalry by offering a new way to alter processes underlying its dynamics.

Modeling the effect of unbalanced modulations on the rivalry dynamics

In this section, we will explore the dependence of dominance period durations on the different components of its underlying dynamics. In addition to balanced changes, i.e. identical changes to parameters related to the left and the right eye, I will attempt to offer a computational framework for the recent data on monocular deprivation reported above through the assessment of the effect of unbalanced, or unilateral parameter changes. Finally, the behavior of model will be compared to preliminary results from my lab where the dependence of binocular rivalry dynamics on the neurotransmitters GABA and glutamate was assessed using Magnetic Resonance Spectroscopy (MRS) (van Loon et al., 2013), both before and after ~3h of monocular deprivation (Lunghi et al., 2011, 2013).

Simulations will be limited to a single implementation of the generic computational model of binocular rivalry described above, the one from van Loon et al., 2013, which incorporates all of mutual inhibition, adaptation and noise within a single stage. This decision is motivated by the ease of implementation of the model, which also has the advantage of already being shown by the investigators to reflect GABA-related effects on the rivalry dynamics, at least on the basis of inter-individual variations. It could have been of interest to explore more elaborate models implementing elements of hierarchical structure (Wilson, 2003, Freeman, 2005), top-down modulations (Tong et al., 2006) or distributed neuronal networks (Laing

and Chow, 2002), but since our MRS-measures are limited to lower cortical visual areas and given the relatively high explanatory power of generic single-stage models, it should suffice to capture most of the relevant processes.

Methods

Simulations

The levels of activity X_1 and X_2 of the model units X1 and X2 (Fig.2A) respectively responding to inputs I_1 and I_2 are governed by the following set of differential equations:

$$\begin{aligned} \tau\partial X_1 &= I_1 - (1+A_1)X_1 - \gamma_2 S[X_2] + N(0,\sigma_{X1}) \\ \tau\partial X_2 &= I_2 - (1+A_2)X_2 - \gamma_1 S[X_1] + N(0,\sigma_{X2}) \end{aligned} \quad [6] \qquad \begin{aligned} \tau_A\partial A_1 &= -A_1 + \alpha_1 S[X_1] \\ \tau_A\partial A_2 &= -A_2 + \alpha_2 S[X_2] \end{aligned} \quad [7]$$

It implements 1) mutual inhibition similar to [2], where X_1 suppresses X_2 with gain $gamma_1$ and X_2 suppresses X_1 with gain $gamma_2$ after non-linear transformation ($S[X]=X^{18}$ for $X>=0$ and $S[X]=0$ for $X<0$), 2) adaptation by modulation of the leak term with an adaptation levels A_1 and A_2 similar to [3] and 3) Gaussian noise of mean 0 and standard deviation $sigma_1$ and $sigma_2$ similar to [5]. Adaptation levels are governed by the slow (tau=1 whereas tau_A=125) leaky integrators of X_1 and X_2 with gain $alpha_1$ and $alpha_2$, similarly to [7]. Note that this exactly reproduces (van Loon et al., 2013)'s implementation, with the only difference that the *gamma* and *alpha* parameters can now be independently modulated for X1 and X2.

Using constant inputs I_1 and I_2, the dynamical system was solved for X_1, X_2, A_1 and A_2 by integrating the set of 4 differential equations from [5] and [6] in the Matlab computing environment from time 0 to 5000 (arbitrary units) using the Runge-

Kutta method as implement in the ode45.m function. All variable solved were restricted to non-negative values and initiated at 0. Maximum time step allowed was 1 and relative tolerance 10^{-5}. An example of the time series obtained for X_1, X_2, A_1 and A_2 is shown in Fig3. From the reach of equilibrium (arbitrarily defined at 100 time units) to the end of the time series, periods of dominance were identified between to successive crossings of X_1 and X_2. Durations of X1 and X2 dominance periods were calculated and averaged.

When investigating the effect of balanced parameter changes, the two members of each parameter pair always shared the same value, and the value of only one parameter pair at a time was modulated over its range across different simulations, while the other pairs were set to their reference value. Reference values and ranges are indicated in Table1. For example, when testing the effect of input strength I, $I_1 = I_2 = I$, where I varies within [0.95, 1.05] while $gamma_1 = gamma_2 = gamma = 3$, $sigma_1 = sigma_2 = sigma = 0.003$ and $alpha_1 = alpha_2 = alpha = 4$. This was iterated ten times for each of the parameter pairs explored.

For the investigation of unbalanced parameter changes, a similar scheme was used, with the only exception that the parameter corresponding to the first modeled unit X1 within a parameter pair was always set to its reference value, such that only parameters corresponding to X2 varied. For example, when testing the effect of input strength I, $I_1 = I$ but I_2 varies within [0.95, 1.05], while $gamma_1 = gamma_2 = gamma = 3$, $sigma_1 = sigma_2 = sigma = 0.003$ and $alpha_1 = alpha_2 = alpha = 4$. This was also iterated ten times for each of the parameter pairs to explore.

Table 1: Parameter space of simulations

Parameters	Reference Value	Range
I (I_1, I_2)	1	[0.95, 1.05]
$gamma$ ($gamma_1$, $gamma_2$)	3	[2.6, 3.4]
$sigma$ ($sigma_1$, $sigma_2$)	0.003	[0.001, 0.015]
$alpha$ ($apha_1$, $alpha_2$)	4	[3, 5]

Experimental acquisitions

Five subjects participated in this study so far, approved by the ethics committee of the Montreal Neurological Institute of Montréal. They all underwent a Magnetic Resonance Imaging (MRI) session, but one was not available for the follow-up behavioral session.

MRI acquisitions began with anatomical scans to allow the prescription of a 3x3x3cm^3 voxel for ^{1}H-MRS acquisition. These acquisitions used the MEGA-PRESS *J*-coupling editing sequence (Mescher et al., 1998) allowing measurement of GABA and glutamate neurotransmitters, the concentrations of which were normalized as ratios to the simultaneously acquired creatine signal. Two 8-minute measurements were acquired before and immediately after the start of monocular deprivation with an opaque black eye patch. Subjects then either monocularly read or watched television outside the scanner for the ~3 hours of the deprivation treatment before coming back to the scanner for two other measurement immediately before and after removal of the patch.

In a follow-up behavioral session, the binocular rivalry dynamics was assessed similarly to Lunghi et al., 2011. Using polarized filters, two orthogonal (-45° and +45° orientations) high-contrast gabor patches of 3cpd and size 1.5° were dichoptically and continuously presented within a squared frame to facilitate fusion.

With fixation at the center of the gabor, subjects were instructed to press down a key assigned to one gabor whenever that gabor clearly dominated their visual field, and to release the key only when dominance was not clear anymore. A different key was assigned to the other gabor. The median durations of key presses during a 3-minute run were computed and averaged between two consecutive runs to yield one dominance duration measurement for each eye. Separated by about 15 minutes, two such measurements were obtained before and immediately after the same monocular deprivation treatment as administered during the MRI session.

Results

Simulations Results

A section of the time series of variables X_1, X_2, A_1 an A_2 obtained from one simulation using reference values for all parameters is shown in Fig.3A, along with the histogram of dominance period durations compiled across the ten iterations of the simulation (Fig3.B). The expected behavior is expressed, with high levels of activity alternating between X1 and

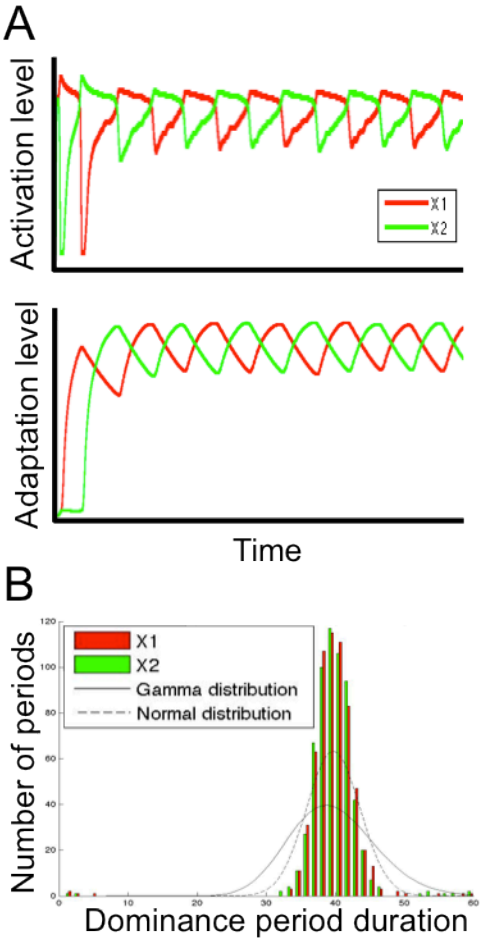

Figure 3. Simulation results when all parameters are set to their reference value. A. Time evolution of the activity and adaptation level of unit X1 and X2. B. Histogram of dominance period durations, collapsed across the ten iterations of the simulations. Gamma and normal distribution are fitted on the combination of X1 and X2 dominance periods.

X2. Adaptation levels vary more slowly and follow the activity level with some time lag, just as it would be expected from a slow leaky integrator. Note that the pattern closely resembles the one from Fig.2D, with the only exception of the addition of a little noise. This is not surprising since the current simulation using [6] and [7] only differs from the simulation in Fig.2D, using [3] and [4], by the addition of the noise term. This noise did allow to break the determinism of the system, as can be seen from the distribution of dominance durations in Fig3.B. Although it does not fit well

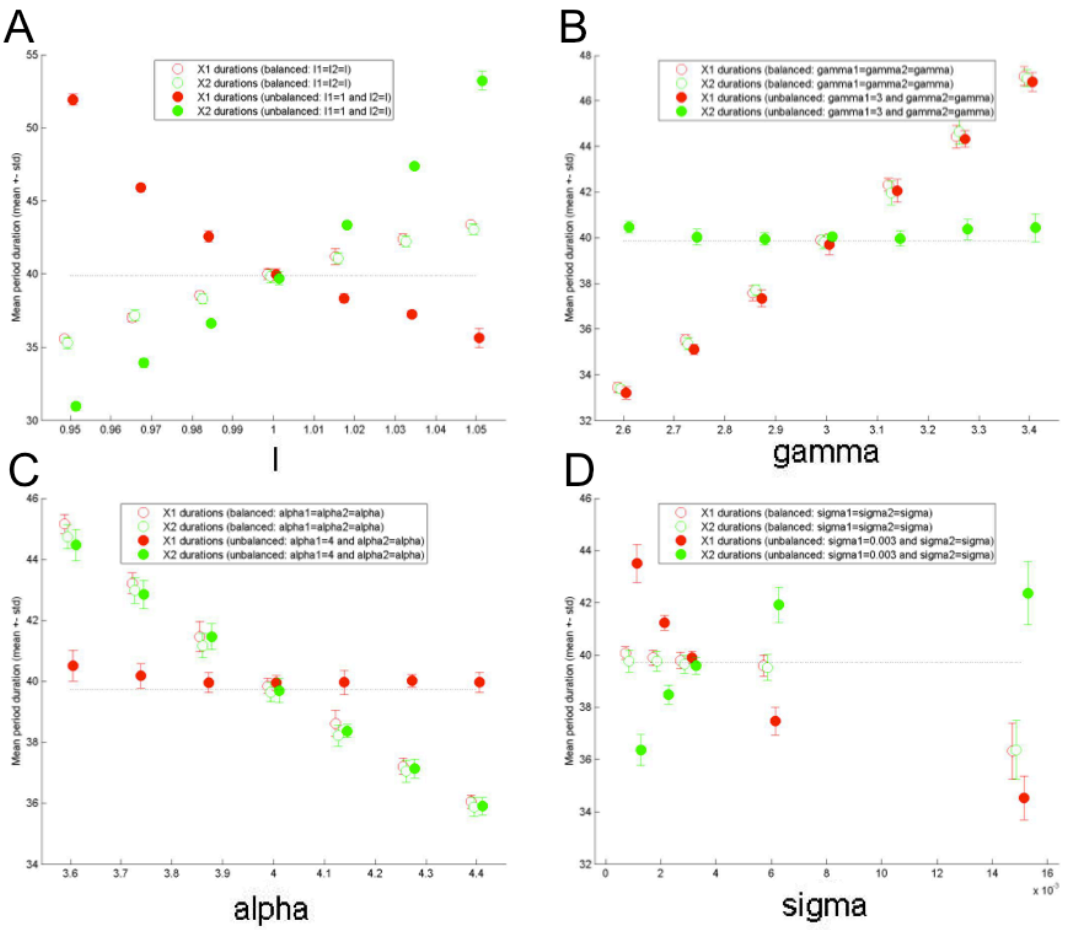

Figure 4. Dependence of dominance period durations on different parameter values. Durations of X1 and X2 dominance (mean and standard deviation across ten simulations) are respectively shown in red and green, and in the case of balanced (open circles) and unbalanced (filled circles) variations of the parameters. The dotted line indicate durations when all parameters are set to their reference value. A. Effect of variations of input *I*. B. Effect of variations of mutual inhibition gain *gamma*. C. Effect of variations of adaptation gain *alpha*. D. Effect of variations of noise gain *sigma*.

the expected gamma distribution, it is nevertheless *mostly* unimodal and skewed toward longer durations, as reported from human psychophysics. The few instances of very short duration are unexpected and will be discussed later.

The dependence of dominance period durations upon the different parameter tested is shown in Fig.4A-D. Open circles represent durations when both parameters of a pair were changed together according the value on the abscissa. Durations unexpectedly increased with input strength *I* (Fig.4A), but was directly related to mutual inhibition *gamma* (Fig.4B) as in van Loon et al., 2013. Durations decreased with increases in both adaptation gain *alpha* (Fig.4C) and noise *sigma* (Fig.4D), but the later did so supra-linearly with larger changes in the upper noise range.

Filled circles in Fig.4 illustrate durations when only the parameter corresponding to unit X2 was changed according the value on the abscissa, the other parameter of the pair under examination being fixed to its reference value. The doted lines indicate durations when all parameters are set to their reference value. Increasing input strength I_2 increased X2 durations, almost linearly, and had the reciprocal effect on X1 durations (Fig.4A). Increasing inhibition from X2 to X1 while keeping fixed the inhibition from X1 to X2 allowed X2 to remain dominant for longer periods of time, but that stronger inhibition on X1 left its dominance durations virtually unaffected (Fig.4B). The effect of unilateral changes in adaptation gain was similarly unilateral, with increases in $alpa_2$ decreasing durations of X2 only. Finally, the effect of noise is much richer. Making noisier only the inputs to X2 increased dominance duration of the later, and had roughly the mirror effect on X1 durations. Contrary to the effect of changing $sigma_1$ and $sigma_2$ together, which accelerated at higher noise

level, the effects of unilateral changes of noise evolve rapidly in the lower and saturate in the higher noise range (Fig.4D).

Empirical Results

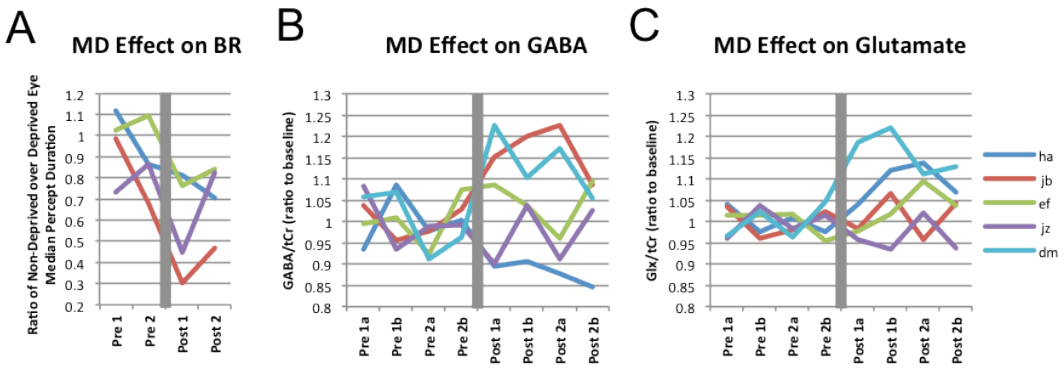

Figure 5. Empirical effect of monocular deprivation (MD) on binocular rivalry (BR) (A) and GABA (B) and glutamate (C) neurotransmitter concentrations. Thick vertical vertical lines mark the location of the 3-hour MD treatment. A. Ordinate axis reflect interocular balance expressed as a ratio of dominance period duration in the non-deprived eye over duration in the deprived eye. B-C. GABA and glutamate concentrations expressed as ratio to total creatine (tCr) normalized as ratio to baseline, calculated as the average of pre-MD measures.

Results of the empirical experiment are summarized in Fig.5 and Fig.6. As expected from Lunghi et al., 2011, 2013, monocular deprivation (MD) did bias the initially balanced interocular dynamics toward the deprived eye, with ratios of duration of percepts from the non-deprived over the deprived eye shifting from around one to lower values. MRS-measures of neurotransmitters did not show evidence of short-term effects of the transitions between binocular and monocular viewing at the onset and offset of the MD treatment. Viewing conditions will not be considered further and all four pre-MD measures (containing two measures during binocular and two during monocular viewing) will be taken as baseline, just as the four post-MD measures will be considered as reflecting time effects only, if any. Although MD did modulate neurotransmitter, it did so in an unsystematic manner,

with both increases and decreases depending on the subject, for glutamate and especially GABA. No sham MD condition or control brain region was acquired, but the relevance of these changes to MD deprivation is supported by their correlation with the behavioral effects of the treatment reported below.

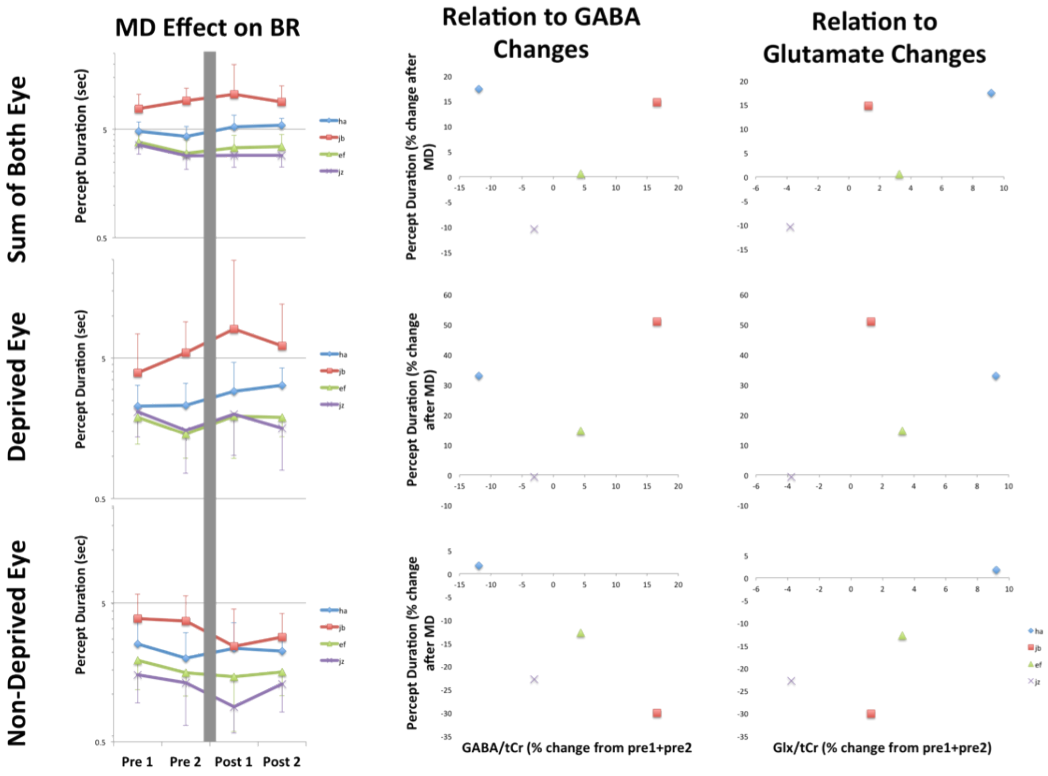

Figure 6. Detailed representation of the effect of monocular deprivation (MD) on binocular rivalry dynamics (left column), along with its relation with MD-induced neurotransmitter changes (middle and right column). Middle and bottom row uses median durations of dominance of percepts corresponding respectively to the deprived and non-deprived eye. The top row represents MD effects on BR that are unspecific to the eye by using the sum of durations from the two eyes. The thick gray line indicates the period of MD. In middle and right columns, both percept durations and neurotransmitter concentrations are expressed as percent change from baseline.

A finer picture of the dynamics of BR is shown in Fig.6, left column, where median dominance durations before (left of the thick gray line) and after (right of the thick gray line) MD are resolved for percept coming from the deprived (middle row) and the non-deprived eye (bottom row). It can be observer that the shift in interocular balance shown in Fig.5A can arise from increased durations in the deprived eye and/or decreased durations in the non-deprived eye, and the proportions varies

between the four subjects tested. Suggesting that the overall effect on the interocular balance might arise from different mechanisms depending on the subject, potentially explaining the highly variable MRS results. When expressed as percent change from baseline and compared to percent neurotransmitter changes in the middle and right columns, an inverse relation between GABA changes and dominance durations stands-out only for the non-deprived eye, such that an increase in GABA predicts a MD-related decrease of the non-deprived-eye percept duration, and vice-versa. Increases in glutamate, on the other hand, seems to predict increased percept duration from both eye after MD, which is more evident in the first row where durations are summed across the eyes in order to better illustrate potential eye-*un*specific changes.

A pattern is emerging from these preliminary empirical data, whereby GABA modulations specifically predict non-deprived eye changes, and glutamate changes relate to dominance durations irrespective of the eye of origin (Fig.6). How does that compare to our simulation results? The patterns of dependence of dominance durations on *gamma* (Fig.4B) and *alpha* (Fig.4C) are candidate for the eye-specific GABA relation to durations, as unilateral modulations of the parameters for one unit (filled circles in Fig.4) also exhibit unit- (or eye-) specificity. Input strength *I* (Fig.4A) and *sigma* (Fig.4D) can be excluded, as unilateral modulations produced reciprocal changes in the two units, a pattern we don't observe between the deprived and non-deprived eye relation to GABA. All parameter modulations produced non-specific duration changes when the change in one member of a parameter pair equated the

change in the other (Fig.4, open circles), and no specific candidate can be identified on the basis of this pattern of change alone.

Discussion

In the present work, we implemented a model of binocular rivalry in an attempt to account for the pattern of results we obtained from the empirical study of the effect of monocular deprivation on both MRS-measured concentrations of occipital GABA and glutamate and the psychophysically assessed dynamics of binocular rivalry. Before trying to relate simulation to empirical results, we must first assess the validity of the chosen model by comparing it against existing data on binocular rivalry.

Validity of the model

We observed earlier that durations produced by our model did not fit well the expected gamma distribution (Blake and Logothetis, 2002, Lunghi et al., 2011, Lunghi et al., 2013). More over, a few dominance periods of very short durations, completely outside of the main distribution peak, were produced (Fig.3B). Closer inspection of time series simulated under the highest level of noise revealed that the only noise-driven dominance reversal present were actually incomplete, and were responsible for the observed very short dominance durations (Fig.7). More specifically, when noisy events brought activity of the suppressed unit

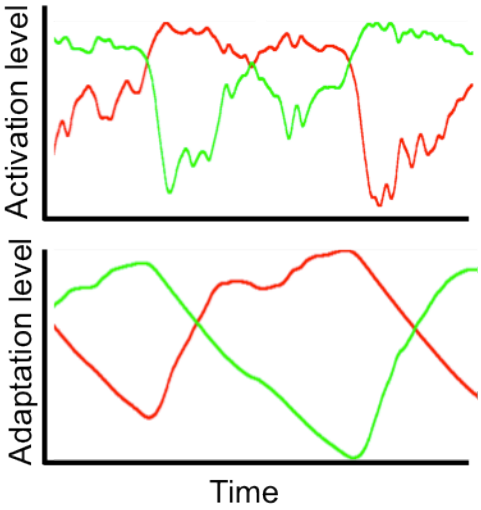

Figure 7. Example of noise-induced failed or incomplete dominance reversal. See text for details.

at a higher level than the dominant one, but at a time when adaptation levels of the suppressed unit was still high, the switch of dominance could not be fully established and the two units returned into their respective dominant and suppressed states. A simple fixe for this misbehavior would be to remove the noise term from the fast dynamics of activity levels in [6] and rather introduce it into the slow dynamics of adaptation levels in [7]. This would not only make the distribution gamma-like as van Ee, 2009 showed, but would likely prevent the observed incomplete noise-induced dominance reversals, as activity levels will only be influenced by noise through the adaptation process, which will then be the only driver of reversals, insuring their completeness. Such a reanalysis is however not needed as despite our distribution being non-gamma, it nevertheless shows the expected skewness and long tail of longer durations. The few very short durations certainly biased our dependent variable, the mean dominance duration, toward lower values, but it is unlikely to have affected most of our analysis, with the exception of simulations with varying noise levels, since the number of short off-distribution durations scaled-up with noise level (data not shown). This analysis of the effect of noise will therefore not be discussed further in the present work.

The effect of simulating variations in input strength *I* to one or the two eyes has a direct psychophysical equivalent that as been extensively studied, the contrast of the rivaling stimuli. Physically increasing the contrast of both left-eye and right-eye stimuli decreases dominance durations according to Levelt's fourth proposition (Levelt, 1968) and more recent experimental data (Brascamp et al., 2006), but our model exhibited the inverse behavior (Fig.4A). Exploration of the full parameter

space of a very similar model implementing all of mutual inhibition, adaptation and noise within a single stage (Shpiro et al., 2009) revealed an inverted U shape for the dependence of durations on input strength. The range of input strength we used might therefore be too high to reproduce experimental data.

Modulating contrast to only one eye while keeping fixed in the other was long thought to primarily affect dominance duration of the other eye, according to Levelt's second proposition (Levelt, 1968). Our model did comply with the expectation that inputs to X2 directly relate to dominance durations of the same unit, and inversely related to dominance duration of the other fixed-input X1 unit. The slopes of these relations are however of roughly the same magnitude, in violation of Levelt's second proposition. Recent psychophysical data suggests that the relative magnitude of these slopes depends on the level of the fixed contrast: a high fixed contrast comply with Levelt's and a low one produce the reverse (greater changes in the eye with variable inputs), while the middle range yield a pattern very similar to the behavior of our system (Shpiro et al., 2009).

Fitting the model on supplementary binocular rivalry data acquired at baseline while modulating contrast of the stimuli in one eye and in both eye would allow finding an appropriate input strength regime. Such an informed model should allow for more valid predictions of the effect of monocular patching, but interpretation should proceed with care until then.

For balanced modulation of the mutual inhibition gain parameters, our model not surprisingly matched the only relevant experimental data from van Loon et al., 2013, with increased inhibition producing longer durations just as less measured

GABA, or pharmacological down-regulation of $GABA_A$ receptor, yielded longer durations in humans. To the best of my knowledge, no data exist on unilateral changes in interocular inhibition and binocular rivalry.

Interestingly, although adaptation processes have received a lot of attention from various experimenters (Roumani and Moutoussis, 2012), to the best of my knowledge, none tried to assess the role of its gain on binocular rivalry. For example, although drifting stimuli ongoing rivalry across a pre-adapted zone of the visual field is a clever way to demonstrate a causal role for adaptation (Blake et al., 2003), it does not inform on the gain of adaptation, which is the element of interest for the validation of our model. Experimentally modulating this gain might be challenging. We could however estimate it in each eye from the slope of the adaptation effect expressed as a function of contrast of the adaptor. In an approach similar to van Loon et al., 2013, correlating inter-individual variations of these adaptation gain measures with binocular rivalry measures could help validating our model. Until then, validation of the dependence of dominance durations on adaptation gains expressed by our model will rely on the assumptions, entailed in the model's formalism, regarding the mechanisms through which adaptation affects binocular rivalry. These assumptions seem reasonable regarding the body of experimental data on the subject (Alais et al., 2010, Roumani and Moutoussis, 2012).

Mapping the effects of monocular deprivation on the model's simulation

As briefly mentioned in the results section, from the patterns of the simulation results, mutual inhibition and adaptation gain (Fig.4B-C) could both be considered as candidate to explain the relation between GABA and dominance durations

specifically in non-deprived eye (Fig.6 middle column). We know from physiology that GABA neurotransmitter mediates interocular inhibition (Blake and Wilson, 2011), such that more of it should mean more mutual inhibition, hence higher *gamma*. Concordant with that, a direct relation between MRS-measured GABA and dominance duration as previously been shown (van Loon et al., 2013). Unless we are willing to consider a convoluted explanation involving sensitivity of MRS *baseline* GABA measures to mutual inhibition (direct relation in van Loon et al., 2013) and sensitivity of MRS measures of GABA *changes* to inhibition of mutual inhibition (our inverse relation), we should discard changes in mutual inhibition as the factor driving monocular deprivation-induced alterations of binocular rivalry.

The pattern of adaptation gain (Fig.4C) is interesting. For it to explain our GABA results, we could imagine a pool of GABA ready to be released on an adapting neuron that would consequently show reduced response. Importantly, the MRS-measured GABA would have to reflect the whole pool of GABA in order to be sensitive to the gain of adaptation, rather then adaptation itself, which would rather depend on the amount of released, or active GABA. This may be far fetched, but it is not so far from common conceptualization of adaptation as recurrent self-inhibition or feedback inhibition, and the concept of adaptation is no stranger to GABAergic inhibition from some empirical studies (Heistek et al., 2010). Importantly, attributing our empirical results to a specific change in adaptation gain allows the testable prediction that monocular deprivation increases adaptation gain specifically in the non-deprived, and that contrary to common sense mutual inhibition is unchanged. Acquisition of the adaptation function in each eye as

described earlier, as well as performance of simple dichoptic masking tasks should be sufficient to test those predictions.

The patterns of dependence of dominance durations on the model parameters (Fig.4) could not narrow down the number of candidate mechanisms explaining our empirical preliminarily evidence for an eye-*un*specific direct relation between glutamate and dominance durations (Fig.6 right column). It could be tempting to equate glutamate increase with increase in input strength for both eyes given the direction of the relation in the simulation of balanced changes in input strength (Fig.4A). One must however remember this direction of the relation, although consistent across our simulation and empirical results, is the inverse that observed empirically by physically modulating input strength through changing the contrast of the stimuli (Levelt, 1968, Brascamp et al., 2006). I am forced to conclude our simulations have very limited power helping to understand the mechanisms of the glutamatergic effect on dominance durations, and to appeal to metaplasticity phenomena (Hulme et al., 2013), where upregulating glutamate could favor other plastic changes, not captured by our model, affecting dominance duration similarly in both eyes.

Conclusion

Binocular rivalry and bistable perception in general is a broad and dynamic field where a variety of computational models are flourishing, and one must arm itself with patience to try to cover them all. It however fells gratifying that one of the simplest models available has such explanatory power. More importantly, the

specific testable predictions its exploration allowed will be extremely useful to guide further empirical investigations.

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