

vertebrates: a brief review Light-adaptive role of nitric oxide in the outer retina of lower

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Light-adaptive role of nitric oxide in the outer
 Light-adaptive role of nitric oxide in the outer retina of lower vertebrates: a brief review
The same in the outer
The vertebrates: a brief review
The view of lower vertebrates: a brief review

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The role of nitric oxide (NO) as a novel neurochemical mechanism controlling light adaptation of the
outer retina is discussed by consid The role of nitric oxide (NO) as a novel neurochemical mechanism controlling light adaptation of the outer retina is discussed by considering mainly published results. The emphasis is on the retinae of fishes and amphibia, The role of nitric oxide (NO) as a novel neurochemical mechanism controlling light adaptation of the outer retina is discussed by considering mainly published results. The emphasis is on the retinae of fishes and amphibia, outer retina is discussed by considering mainly published results. The emphasis is on the retinae of fishes and amphibia, but some data from the mammalian (rabbit) retinae have also been included for completeness. In the f and amphibia, but some data from the mammalian (rabbit) retinae have also been included for completeness. In the fish retina, application of NO donors in the dark caused light-adaptive photomechanical movements of cones. T ness. In the fish retina, application of NO donors in the dark caused light-adaptive photomechanical
movements of cones. The normal effect of light adaptation in inducing cone contractions was suppressed
by pretreatment of uncoupling the cells' lateral gap junctional interconnections and enhancing negative feedback to cones, by pretreatment of retinae with an NO scavenger. NO donors modulated horizontal cell activity by uncoupling the cells' lateral gap junctional interconnections and enhancing negative feedback to cones, again consistent with uncoupling the cells' lateral gap junctional interconnections and enhancing negative feedback to cones, again consistent with a light-adaptive role of NO. Direct evidence for light adaptation-induced release of NO has been again consistent with a light-adaptive role of NO. Direct evidence for light adaptation-induced release of NO has been obtained in fish (carp) and rabbit retinae. The results strongly suggest that control of retinal light role. light adaptation is under multiple neurochemical control, with NO and dopamine having an interactive
role.
Keywords: nitric oxide; retina; light adaptation; photoreceptor; horizontal cell

1. INTRODUCTION

1. INTRODUCTION
Light adaptation of the retina, which contributes to the
ability of the vertebrate visual system to respond to light **Example 1. INTRODUCTION**
Light adaptation of the retina, which contributes to the
ability of the vertebrate visual system to respond to light
intensities that may vary by ≥ 10 orders of magnitude Light adaptation of the retina, which contributes to the ability of the vertebrate visual system to respond to light intensities that may vary by ≥ 10 orders of magnitude, occurs in several stages (Dowling 1987) A par ability of the vertebrate visual system to respond to light
intensities that may vary by ≥ 10 orders of magnitude,
occurs in several stages (Dowling 1987). A part of this mechanism operates in the outer retina and involves occurs in several stages (Dowling 1987). A part of this
mechanism operates in the outer retina and involves
photoreceptors' (PCs') intrinsic activity and interactions
with second-order neurons in the outer pleviform layer mechanism operates in the outer retina and involves
photoreceptors' (PCs') intrinsic activity and interactions
with second-order neurons in the outer plexiform layer.
Synaptic interactions (feedforward and feedback) photoreceptors' (PCs') intrinsic activity and interactions
with second-order neurons in the outer plexiform layer.
Synaptic interactions (feedforward and feedback)
between PCs and horizontal cells (HCs) are also moduwith second-order neurons in the outer plexiform layer.
Synaptic interactions (feedforward and feedback)
between PCs and horizontal cells (HCs) are also modu-
lated by light or dark adaptation Synaptic interactions (feedforw
between PCs and horizontal cells
lated by light or dark adaptation.
A considerable body of evidence tween PCs and horizontal cells (HCs) are also modu-
ed by light or dark adaptation.
A considerable body of evidence suggests that dopa-
ne (DA) is released in vertebrate retinae during light

lated by light or dark adaptation.
A considerable body of evidence suggests that dopa-
mine (DA) is released in vertebrate retinae during light adaptation and mimics many of the light-adaptive mine (DA) is released in vertebrate retinae during light
adaptation and mimics many of the light-adaptive
changes seen in PCs and HCs (Djamgoz & Wagner 1992).
However in several instances, DA-independent effects of adaptation and mimics many of the light-adaptive
changes seen in PCs and HCs (Djamgoz & Wagner 1992).
However, in several instances, DA-independent effects of
light adaptation have also been found (e.g. Diamgoz et al. changes seen in PCs and HCs (Djamgoz & Wagner 1992).
However, in several instances, DA-independent effects of
light adaptation have also been found (e.g. Djamgoz *et al.*
1996b). This has raised the possibility that retina However, in several instances, DA-independent effects of light adaptation have also been found (e.g. Djamgoz *et al.*) adaptation may involve additional modulators.
This paper briefly reviews evidence showing (i) that 1996 b). This has raised the possibility that retinal light

nitric oxide (NO) is a novel neuromodulator in the outer This paper briefly reviews evidence showing (i) that nitric oxide (NO) is a novel neuromodulator in the outer retina, and (ii) that the effects of NO are consistent with it being involved in the control of several aspects nitric oxide (NO) is a novel neuromodulator in the outer
retina, and (ii) that the effects of NO are consistent with
it being involved in the control of several aspects of the
light-adantation process retina, and (ii) that the ef
it being involved in the c
light-adaptation process.

A number of studies on fish and amphibian retinae have shown that NO can potentially be synthesized by various types of retinal neuron. NO-synthesizing have shown that NO can potentially be synthesized by
various types of retinal neuron. NO-synthesizing
neurons can be visualized either by histochemistry of
nicotinamide adenine dinucleotide phosphate (NADPH). various types of retinal neuron. NO-synthesizing
neurons can be visualized either by histochemistry of
nicotinamide adenine dinucleotide phosphate (NADPH)-
diaphorase or by immunocytochemistry of NO synthase neurons can be visualized either by histochemistry of
nicotinamide adenine dinucleotide phosphate (NADPH)-
diaphorase or by immunocytochemistry of NO synthase
(NOS), which catalyses the synthesis of NO from the nicotinamide adenine dinucleotide phosphate (NADPH)-
diaphorase or by immunocytochemistry of NO synthase
(NOS), which catalyses the synthesis of NO from the diaphorase or by immunocytochemistry of NO synthase
(NOS), which catalyses the synthesis of NO from the
substrate L-arginine. The two methods have given
broadly consistent results: typical localization of (NOS), which catalyses the synthesis of NO from the
substrate L-arginine. The two methods have given
broadly consistent results; typical localization of
NADPH-dianborase in the carn retina is illustrated in substrate L-arginine. The two methods have given
broadly consistent results; typical localization of
NADPH-diaphorase in the carp retina is illustrated in
figure 1. Clearly a wide variety of retinal neurons are broadly consistent results; typical localization of NADPH-diaphorase in the carp retina is illustrated in figure 1. Clearly, a wide variety of retinal neurons are NADPH-diaphorase in the carp retina is illustrated in
figure 1. Clearly, a wide variety of retinal neurons are
potentially capable of synthesizing (and presumably
releasing) NO including HCs binolar amacrine Müller figure 1. Clearly, a wide variety of retinal neurons are
potentially capable of synthesizing (and presumably
releasing) NO, including HCs, bipolar, amacrine, Müller
and ganglion cells with intense staining also occurring i potentially capable of synthesizing (and presumably
releasing) NO, including HCs, bipolar, amacrine, Müller
and ganglion cells, with intense staining also occurring in
PC ellinsoid regions (Diamaga et al. 1996a) A similar releasing) NO, including HCs, bipolar, amacrine, Müller
and ganglion cells, with intense staining also occurring in
PC ellipsoid regions (Djamgoz *et al.* 1996*a*). A similar
extensive distribution of NADPH-dianhorase-nosi and ganglion cells, with intense staining also occurring in
PC ellipsoid regions (Djamgoz *et al.* 1996a). A similar
extensive distribution of NADPH-diaphorase-positive
and/or NOS-immunoreactive cells has also been found i PC ellipsoid regions (Djamgoz *et al.* 1996*a*). A similar extensive distribution of NADPH-diaphorase-positive and/or NOS-immunoreactive cells has also been found in goldfish and catfish retinae. A broad pattern of potent extensive distribution of NADPH-diaphorase-positive and/or NOS-immunoreactive cells has also been found in goldfish and catfish retinae. A broad pattern of potentially NO- synthesizing cells would be indicative of NO having goldfish and catfish retinae. A broad pattern of potentially
NO-synthesizing cells would be indicative of NO having
a diverse functional role in the teleost retina. On the
other hand, such a wide distribution is rather sur NO-synthesizing cells would be indicative of NO having
a diverse functional role in the teleost retina. On the
other hand, such a wide distribution is rather surprising
since the 'sphere of influence' of any NO released is a diverse functional role in the teleost retina. On the other hand, such a wide distribution is rather surprising since the 'sphere of influence' of any NO released is thought to be some hundreds of microns, comparable other hand, such a wide distribution is rather surprising
since the 'sphere of influence' of any NO released is
thought to be some hundreds of microns, comparable
with the whole thickness of a neural retina. This situation since the 'sphere of influence' of any NO released is
thought to be some hundreds of microns, comparable
with the whole thickness of a neural retina. This situation

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Marghinical Laboratory,

^{2.} LOCALIZATION OF NITROGEN OXIDE-SALIZATION OF NITROGEN OXIDE-
SYNTHESIZING CELLS IN FISHES
AND AMPHIPIAN PETINAE **AND AMPHIBIAN RETINAE**
AND AMPHIBIAN RETINAE

Figure 1. An overview of the staining of cellular layers within Figure 1. An overview of the staining of cellular layers with
the carp retina by histochemistry of NADPH-diaphorase.
PR /EL/OS, photorecentor ellipsoid and outer segment regi Figure 1. An overview of the staining of cellular layers within
the carp retina by histochemistry of NADPH-diaphorase.
PR/EL/OS, photoreceptor ellipsoid and outer segment region.
ONL. outer nuclear layer. OPL. outer plexif PR/EL/OS, photoreceptor ellipsoid and outer segment region.
ONL, outer nuclear layer. OPL, outer plexiform layer. HCL, horizontal cell layers. INL, inner nuclear layer. IPL, inner ONL, outer nuclear layer. OPL, outer plexiform layer. HCL,
horizontal cell layers. INL, inner nuclear layer. IPL, inner
plexiform layer. Scale bar, 26 μm. Modified from Djamgoz *et*
al (1996α) *al*. (1996*a*).
al. (1996*a*).

may have important implications for the mode of action may have impo
of retinal NO.

3. CELLULAR EFFECTS OF NITRIC OXIDE IN THE FECTS OF NITRIC O
OUTER RETINA S. CELLOLAR EFFECTS OF NITRIC OXIDE IN THE

OUTER RETINA

The putative effects of NO could be studied by treating

a retina with NO donor compounds such as sodium

The putative effects of NO could be studied by treating
the retina with NO donor compounds such as sodium
nitronrusside (SNP) S-nitroso-N-acetylenicillamine The putative effects of NO could be studied by treating
the retina with NO donor compounds such as sodium
nitroprusside (SNP), S-nitroso-N-acetylpenicillamine
 $(SNA P)$ S-nitrosoclutathione $(SNOG)$ or S-nitrosocysteine the retina with NO donor compounds such as sodium
nitroprusside (SNP), S-nitroso-N-acetylpenicillamine
(SNAP), S-nitrosoglutathione (SNOG) or S-nitrosocysteine nitroprusside (SNP), S-nitroso-N-acetylpenicillamine
(SNAP), S-nitrosoglutathione (SNOG) or S-nitrosocysteine
(SNC). As regards the possible role of endogenous NO,
some NO 'scavenger' compounds have been used (SNAP), S-nitrosoglutathione (SNOG) or S-nitrosocysteine
(SNC). As regards the possible role of endogenous NO,
some NO 'scavenger' compounds have been used,
including haemoglobin and $2-(4-carboxunbenv)$. (SNC). As regards the possible role of endogenous NO,
some NO 'scavenger' compounds have been used,
including haemoglobin and $2-(4\text{-carboxyphenyl})-$
 $4.4-5.5\text{-terramethul-imidazoline-l-ovvl-3-ovide not assium}$ some NO 'scavenger' compounds have been used,
including haemoglobin and 2-(4-carboxyphenyl)-
4,4,5,5-tetramethyl-imidazoline-1-oxyl-3-oxide potassium (cPTIO).

(a) *Photoreceptor cells*

(a) **Photoreceptor cells** *Ionotropic glutamate receptors*
Light and dark adaptation of PCs incorporates both Application of SNP to (a) **Photoreceptor cells**
Light and dark adaptation of PCs incorporates both
structural/biochemical and physiological changes in
which NO has been shown to have a putative role Light and dark adaptation of PCs incorporates
structural/biochemical and physiological chang
which NO has been shown to have a putative role. which NO has been shown to have a putative role.
(i) *Electrophysiological aspects*

pathway in PCs is the second messenger cyclic guanosine An integral component of the phototransduction
pathway in PCs is the second messenger cyclic guanosine
 $3'$,5'-monophosphate (cGMP), which gates cation chan-
nels in the plasma membrane. The identification in PCs of pathway in PCs is the second messenger cyclic guanosine
3',5'-monophosphate (cGMP), which gates cation channels in the plasma membrane. The identification in PCs of
both soluble guanylate cyclase (sGC: an enzyme respon- $3\frac{'}{5}$ -monophosphate (cGMP), which gates cation channels in the plasma membrane. The identification in PCs of both soluble guanylate cyclase (sGC; an enzyme respon-
sible for cGMP synthesis and a primary target of NO nels in the plasma membrane. The identification in PCs of
both soluble guanylate cyclase (sGC; an enzyme respon-
sible for cGMP synthesis and a primary target of NO) both soluble guanylate cyclase (sGC; an enzyme responsible for cGMP synthesis and a primary target of NO) and NOS would suggest that NO could act as a modulator of PC activity. In fact, application of SNP to sible for cGMP synthesis and a primary target of NO)
and NOS would suggest that NO could act as a
modulator of PC activity. In fact, application of SNP to
isolated rods of *Rana esculenta* was found to accelerate the and NOS would suggest that NO could act as a modulator of PC activity. In fact, application of SNP to isolated rods of *Rana esculenta* was found to accelerate the *Phil. Trans. R. Soc. Lond.* B (2000)

recovery phase of the light-evoked response (Schmidt *et* recovery phase of the light-evoked response (Schmidt *et al.* 1992). This was suggested to be due to an increased rate in cGMP turnover induced by NO enhancement of recovery phase of the light-evoked response (Schmidt *et al.* 1992). This was suggested to be due to an increased rate in cGMP turnover induced by NO enhancement of sGC activity. Conversely suppressing endogenous NO al. 1992). This was suggested to be due to an increased
rate in cGMP turnover induced by NO enhancement of
sGC activity. Conversely, suppressing endogenous NO
production by inhibiting NOS with N^{ω} -monomethyl-Lrate in cGMP turnover induced by NO enhancement of
sGC activity. Conversely, suppressing endogenous NO
production by inhibiting NOS with N^o-monomethyl-L-
arginine slowed down the recovery phase of the PC $\rm sGC$ activity. Conversely, suppressing endogenous NO
production by inhibiting NOS with $\rm N^{\omega}$ -monomethyl-L-
arginine slowed down the recovery phase of the PC
response to light Importantly this occurred even though production by inhibiting NOS with N®-monomethyl-L-
arginine slowed down the recovery phase of the PC
response to light. Importantly, this occurred even though
solitary PCs (dissociated from the retina) were used (see arginine slowed down the recovery phase of the PC
response to light. Importantly, this occurred even though
solitary PCs (dissociated from the retina) were used (see $§ 3(a)(ii)$.

(ii) *Photomechanical movements*

PC cells of 'lower' vertebrates (fishes and amphibia), (ii) *Photomechanical movements*
PC cells of 'lower' vertebrates (fishes and amphibia),
which have no or only a weak pupillary response, possess
the ability to undergo photomechanical movements PC cells of 'lower' vertebrates (fishes and amphibia),
which have no or only a weak pupillary response, possess
the ability to undergo photomechanical movements
(PMMs) Thus during light adaptation cones (and which have no or only a weak pupillary response, possess
the ability to undergo photomechanical movements
(PMMs). Thus, during light adaptation, cones (and
melaning granules of pigment epithelial cells) move the ability to undergo photomechanical movements
(PMMs). Thus, during light adaptation, cones (and
melanin granules of pigment epithelial cells) move
towards the outer limiting membrane while rods move (PMMs). Thus, during light adaptation, cones (and melanin granules of pigment epithelial cells) move towards the outer limiting membrane while rods move away from it melanin granules of pigment epithelial cells) move
towards the outer limiting membrane while rods move
away from it.
Greenstreet & Djamgoz (1994) originally and towards the outer limiting membrane while rods move
away from it.
Greenstreet & Djamgoz (1994) originally and

away from it.

Greenstreet & Djamgoz (1994) originally and

Haamedi (1999) subsequently showed that application of

a variety of NO donors (SNP SNAP or SNOG) to dark-Greenstreet & Djamgoz (1994) originally and
Haamedi (1999) subsequently showed that application of
a variety of NO donors (SNP, SNAP or SNOG) to dark-
adapted retinae of cynrinid fishes (roach and carn) Haamedi (1999) subsequently showed that application of
a variety of NO donors (SNP, SNAP or SNOG) to dark-
adapted retinae of cyprinid fishes (roach and carp)
produced light-adaptive cone contractions Pretreatment a variety of NO donors (SNP, SNAP or SNOG) to dark-
adapted retinae of cyprinid fishes (roach and carp)
produced light-adaptive cone contractions. Pretreatment adapted retinae of cyprinid fishes (roach and carp)
produced light-adaptive cone contractions. Pretreatment
of the retinae with cPTIO largely blocked the effect of
test light-adaptation consistent with light-evoked release produced light-adaptive cone contractions. Pretreatment
of the retinae with cPTIO largely blocked the effect of
test light adaptation, consistent with light-evoked release
of endogenous NO of the retinae with
test light adaptation,
of endogenous NO.
At present, the cell It light adaptation, consistent with light-evoked release
endogenous NO.
At present, the cellular origin(s) of NO modulating the
bt-evoked PC responses including cone PMMs is not

of endogenous NO.
At present, the cellular origin(s) of NO modulating the
light-evoked PC responses, including cone PMMs, is not
clear. It is generally thought that NO acts upon cells At present, the cellular origin(s) of NO modulating the
light-evoked PC responses, including cone PMMs, is not
clear. It is generally thought that NO acts upon cells
other than those that produce it due to the conflicting light-evoked PC responses, including cone PMMs, is not clear. It is generally thought that NO acts upon cells other than those that produce it, due to the conflicting clear. It is generally thought that NO acts upon cells
other than those that produce it, due to the conflicting
 Ca^{2+} requirements of sGC and NOS, i.e. the intracellular
 Ca^{2+} levels required to activate NOS should in other than those that produce it, due to the conflicting Ca^{2+} requirements of sGC and NOS, i.e. the intracellular Ca^{2+} levels required to activate NOS should inhibit sGC activity. However, the electrophysiological d Ca^{2+} requirements of sGC and NOS, i.e. the intracellular Ca^{2+} levels required to activate NOS should inhibit sGC activity. However, the electrophysiological data obtained from the solitary rods would suggest that th Ca^{2+} levels required to activate NOS should inhibit sGC
activity. However, the electrophysiological data obtained
from the solitary rods would suggest that the unique
compartmentalized structure of the PC could permit activity. However, the electrophysiological data obtained
from the solitary rods would suggest that the unique
compartmentalized structure of the PC could permit NO
production in one region and action at a different intrafrom the solitary rods would suggest that the unique
compartmentalized structure of the PC could permit NO
production in one region and action at a different intra-
cellular site. Further work is required to investigate th compartmentalized structure of the PC could permit NO
production in one region and action at a different intra-
cellular site. Further work is required to investigate the effects of NO on both electrophysiological and contractile cellular site. Further work is required to investigate the effects of NO on both electrophysiological and contractile activities of PCs, and to substantiate the evidence that PCs may indeed respond to NO that the cells the effects of NO on both electrophysiological and contractile
activities of PCs, and to substantiate the evidence that
PCs may indeed respond to NO that the cells themselves
could produce activities of PCs
PCs may indeed
could produce.

(b) *Horizontal cells*

(i) *Cone^HC feedforward synaptic transmission*

The neurotransmitter glutamate released from PCs acts (i) *Cone–HC feedforward synaptic transmission*
The neurotransmitter glutamate released from PCs acts
upon HCs at both ionotropic and metabotropic receptors.
NO affects both sets of synaptic transmission The neurotransmitter glutamate released from
typon HCs at both ionotropic and metabotropic
NO affects both sets of synaptic transmission. *NO* affects both sets of synaptic transmission.

Electrophysiological aspects
An integral component of the phototransduction analogue of cGMP), was probably mediated by a Application of SNP to dissociated hybrid bass HCs had Ionotropic glutamate receptors

Application of SNP to dissociated hybrid bass HCs had

two modulatory effects on the glutamate-evoked currents

(McMahon & Schmidt 1999) First, the affinity of the Application of SNP to dissociated hybrid bass HCs had
two modulatory effects on the glutamate-evoked currents
(McMahon & Schmidt 1999). First, the affinity of the
synaptic receptors for glutamate was decreased. This two modulatory effects on the glutamate-evoked currents
(McMahon & Schmidt 1999). First, the affinity of the
synaptic receptors for glutamate was decreased. This
effect also seen with 8-Br-cGMP (a membrane-nermeable (McMahon & Schmidt 1999). First, the affinity of the synaptic receptors for glutamate was decreased. This effect, also seen with 8-Br-cGMP (a membrane-permeable analogue of ϵ GMP) was probably mediated by a synaptic receptors for glutamate was decreased. This
effect, also seen with 8-Br-cGMP (a membrane-permeable
analogue of cGMP), was probably mediated by a
pathway involving sGC cGMP and a cGMP-dependent pathway involving sGC, cGMP and a cGMP-dependent analogue of cGMP), was probably mediated by a
pathway involving sGC, cGMP and a cGMP-dependent
protein kinase (PKG). Second, the maximal current was
increased This was probably due to recentor desensitipathway involving sGC, cGMP and a cGMP-dependent
protein kinase (PKG). Second, the maximal current was
increased. This was probably due to receptor desensiti-
zation being blocked, since the effect was not seen with protein kinase (PKG). Second, the maximal current was
increased. This was probably due to receptor desensiti-
zation being blocked, since the effect was not seen with
the pop-desensitizing agonist kainate and was suppresse increased. This was probably due to receptor desensitization being blocked, since the effect was not seen with the non-desensitizing agonist kainate and was suppressed zation being blocked, since the effect was not seen with
the non-desensitizing agonist kainate and was suppressed
by the glutamate receptor desensitization blocker
cyclothiazide Accordingly in the dark (when the glutathe non-desensitizing agonist kainate and was suppressed
by the glutamate receptor desensitization blocker
cyclothiazide. Accordingly, in the dark (when the gluta-
mate release would be high) NO donors would depolarize by the glutamate receptor desensitization blocker
cyclothiazide. Accordingly, in the dark (when the gluta-
mate release would be high), NO donors would depolarize

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the resting membrane potential of HCs and such an effect the resting membrane potential of HCs and such an effect
has indeed been recorded in the isolated retina of carp
(M_B_A_Diamgoz_unpublished_data)_However_any the resting membrane potential of HCs and such an effect
has indeed been recorded in the isolated retina of carp
(M. B. A. Djamgoz, unpublished data). However, any
possible presynantic effect of NO on glutamate release (M. B. A. Djamgoz, unpublished data). However, any possible presynaptic effect of NO on glutamate release itself was not studied. possible presynaptic effect of NO on glutamate release

Metabotropic glutamate receptors

It is becoming increasingly apparent that H1 type HC *Metabotropic glutamate receptors*

It is becoming increasingly apparent that H1 type HC

responses generated by long wavelength (LW) versus

short wavelength (SW) stimuli are processed differently It is becoming increasingly apparent that H1 type HC
responses generated by long wavelength (LW) versus
short wavelength (SW) stimuli are processed differently
in the cynrinid fish $(carn)$ retina (Diamoga et al. 1996b responses generated by long wavelength (LW) versus
short wavelength (SW) stimuli are processed differently
in the cyprinid fish (carp) retina (Djamgoz *et al.* 1996*b*,
1998; Furukawa *et al.* 1997). In particular, SW-driv in the cyprinid fish (carp) retina (Djamgoz *et al.* 1996*b*, 1998; Furukawa *et al.* 1997). In particular, SW-driven synaptic input to H1 HCs may involve a 2-amino-4-phos-phonophutyrate (APB)-sensitive metabotronic gluta 1998; Furukawa *et al.* 1997). In particular, SW-driven synaptic input to H1 HCs may involve a 2-amino-4-phos-
phonobutyrate (APB)-sensitive metabotropic glutamate
receptor mechanism negatively coupled to a cGMPsynaptic input to H1 HCs may involve a 2-amino-4-phos-
phonobutyrate (APB)-sensitive metabotropic glutamate
receptor mechanism negatively coupled to a cGMP-
dependent pathway (as in the case of centre-depolarizing phonobutyrate (APB)-sensitive metabotropic glutamate
receptor mechanism negatively coupled to a cGMP-
dependent pathway (as in the case of centre-depolarizing
binolar cells). Thus during light stimulation cGMP receptor mechanism negatively coupled to a cGMP-
dependent pathway (as in the case of centre-depolarizing
bipolar cells). Thus, during light stimulation, cGMP
production in the H1 HC is increased and this activates dependent pathway (as in the case of centre-depolarizing
bipolar cells). Thus, during light stimulation, cGMP
production in the H1 HC is increased and this activates
a depolarizing conductance. A role for NO in the bipolar cells). Thus, during light stimulation, cGMP
production in the H1 HC is increased and this activates
a depolarizing conductance. A role for NO in the enhancement of the SW-transmission pathway has been a depolarizing conductance. A role for NO in the
enhancement of the SW-transmission pathway has been
established. Furukawa *et al.* (1997) measured the change
in input resistance of carp H1 HCs during IW- or SWenhancement of the SW-transmission pathway has been
established. Furukawa *et al.* (1997) measured the change
in input resistance of carp H1 HCs during LW- or SW-
light stimulation. Light adaptation induced a chromatic established. Furukawa *et al.* (1997) measured the change
in input resistance of carp H1 HCs during LW- or SW-
light stimulation. Light adaptation induced a chromatic
difference in the light-evoked change in equal-voltage in input resistance of carp H1 HCs during LW- or SW-
light stimulation. Light adaptation induced a chromatic
difference in the light-evoked change in equal-voltage
input resistance, thereby suggesting the possible presence light stimulation. Light adaptation induced a chromatic
difference in the light-evoked change in equal-voltage
input resistance, thereby suggesting the possible presence
of at least two different receptor or channel mechan difference in the light-evoked change in equal-voltage
input resistance, thereby suggesting the possible presence
of at least two different receptor or channel mechanisms input resistance, thereby suggesting the possible presence
of at least two different receptor or channel mechanisms
in the H1 HCs. Application of SNP to dark-adapted
retina mimicked the effect of light adaptation while APB of at least two different receptor or channel mechanisms
in the H1 HCs. Application of SNP to dark-adapted
retina mimicked the effect of light adaptation while APB
eliminated the chromatic difference in input resistance in the H1 HCs. Application of SNP to dark-adapted
retina mimicked the effect of light adaptation while APB
eliminated the chromatic difference in input resistance
change. Furthermore, light, adaptation, sharpened, the retina mimicked the effect of light adaptation while APB
eliminated the chromatic difference in input resistance
change. Furthermore, light adaptation sharpened the
spectral sensitivity profile of the Hl HC in the red eliminated the chromatic difference in input resistance
change. Furthermore, light adaptation sharpened the
spectral sensitivity profile of the H1 HC in the red
region of the spectrum (figure 2a) and it was proposed change. Furthermore, light adaptation sharpened the spectral sensitivity profile of the H1 HC in the red region of the spectrum (figure $2a$) and it was proposed that this was due to potentiation of the depolarizing SW spectral sensitivity profile of the H1 HC in the red
region of the spectrum (figure $2a$) and it was proposed
that this was due to potentiation of the depolarizing SW
component (Diamgoz *et al.* 1996*b*; Yamada *et al.* 1 region of the spectrum (figure 2a) and it was proposed effect similar to that of light adaptation was produced by component (Djamgoz *et al.* 1996*b*; Yamada *et al.* 1999). An effect similar to that of light adaptation was produced by application of NO donors to dark-adapted retinae (figure 2*h*). Thus it would seem that NO enhances effect similar to that of light adaptation was produced by
application of NO donors to dark-adapted retinae
(figure 2*b*). Thus, it would seem that NO enhances the
SW transmission to H1 HCs and sharpens their spectral application of NO donors to dark-adapted retinae
(figure $2b$). Thus, it would seem that NO enhances the
SW transmission to H1 HCs and sharpens their spectral
response neak mimicking the effect of light adaptation (figure 2*b*). Thus, it would seem that NO enhances the SW transmission to H1 HCs and sharpens their spectral response peak, mimicking the effect of light adaptation (*Yamada et al.* 1999). Indeed pretreatment of the reti SW transmission to H1 HCs and sharpens their spectral
response peak, mimicking the effect of light adaptation
(Yamada *et al.* 1999). Indeed, pretreatment of the retinas
with haemoglobin blocked the spectral effect of ligh (Yamada et al. 1999). Indeed, pretreatment of the retinas with haemoglobin blocked the spectral effect of light (Yamada *et al.* 1999). Indeed, pretreatment of the retinas
with haemoglobin blocked the spectral effect of light
adaptation, consistent with release of endogenous NO
(forure $2c$) with haemo
adaptation,
(figure 2*c*). (figure $2c$).
(ii) HC -cone feedback

 H HC \emph{cond} $\emph{feedback}$ pathway between cones and HC s H $\emph{oserves several important functions}$ in visual processing (ii) HC–cone feedback
The negative feedback pathway between cones and HCs
subserves several important functions in visual processing.
Roth electronbysiological mechanisms and morphological The negative feedback pathway between cones and HCs
subserves several important functions in visual processing.
Both electrophysiological mechanisms and morphological
aspects of this interaction have been studied subserves several important functions in visua
Both electrophysiological mechanisms and m
aspects of this interaction have been studied.

Electrophysiological aspects

Electrophysiological aspects
In isolated cone terminals of the tiger salamander retina, Electrophysiological aspects

In isolated cone terminals of the tiger salamander retina,

Savchenko *et al.* (1997) identified clusters of cGMP-gated

(CNG) channels which could be activated by SNC. In order In isolated cone terminals of the tiger salamander retina,
Savchenko *et al.* (1997) identified clusters of cGMP-gated
(CNG) channels which could be activated by SNC. In order
to determine whether NO enhancement of the CNG Savchenko *et al.* (1997) identified clusters of cGMP-gated
(CNG) channels which could be activated by SNC. In order
to determine whether NO enhancement of the CNG
conductance could affect sunantic transmission from the (CNG) channels which could be activated by SNC. In order
to determine whether NO enhancement of the CNG
conductance could affect synaptic transmission from the to determine whether NO enhancement of the CNG
conductance could affect synaptic transmission from the
cone terminal, dissociated catfish HCs were used as `biosen-
sors` to monitor glutamate release from the terminals. App conductance could affect synaptic transmission from the
cone terminal, dissociated catfish HCs were used as 'biosen-
sors' to monitor glutamate release from the terminals. Appli-
cation of SNC or a membrane permeable analo cone terminal, dissociated catfish HCs were used as 'biosen-
sors' to monitor glutamate release from the terminals. Appli-
cation of SNC or a membrane permeable analogue of cGMP
to the PC–HC pair, induced an increase in th sors' to monitor glutamate release from the terminals. Application of SNC or a membrane permeable analogue of cGMP
to the PC–HC pair induced an increase in the current
variance of the HC consistent with NO increasing neuro cation of SNC or a membrane permeable analogue of cGMP
to the PC–HC pair induced an increase in the current
variance of the HC consistent with NO increasing neuro-
transmitter release. It was suggested that the NO-induced to the PC–HC pair induced an increase in the current
variance of the HC consistent with NO increasing neuro-
transmitter release. It was suggested that the NO-induced
enhancement of the mainly voltage-independent CNG variance of the HC consistent with NO increasing neuro-

transmitter release. It was suggested that the NO-induced In the teleost

enhancement of the mainly voltage-independent CNG suggested to occur

Figure 2. Spectral profiles of H1 HCs in carp retinae under Figure 2. Spectral profiles of H1 HCs in carp retinae under
different light- and dark-adaptive experimental conditions.
Data are shown as means + s e (n = 5–14 cells) (a) Dark-Data are shown as means \pm s.e. ($n = 5-14$ cells). (*a*) Dark-
and light-adapted control retinae (filled and open circles, different light- and dark-adaptive experimental conditions.
Data are shown as means \pm s.e. ($n = 5-14$ cells). (*a*) Dark-
and light-adapted control retinae (filled and open circles,
respectively). The dotted curve repr Data are shown as means \pm s.e. $(n = 5-14$ cells). (*a*) Dark-
and light-adapted control retinae (filled and open circles,
respectively). The dotted curve represents the absorption
spectrum of the cyprinid red-sensitive and light-adapted control retinae (filled and open circles,
respectively). The dotted curve represents the absorption
spectrum of the cyprinid red-sensitive cone obtained by
microspectrophotometry (b) \overline{B} ffect of 0. respectively). The dotted curve represents the absorption
spectrum of the cyprinid red-sensitive cone obtained by
microspectrophotometry. (*b*) Effect of 0.25 mM SNOG on
the spectral sensitivity in dark-adapted retinae (op spectrum of the cyprinid red-sensitive cone obtained by
microspectrophotometry. (b) Effect of 0.25 mM SNOG on
the spectral sensitivity in dark-adapted retinae (open circles).
The data obtained with normal Ringer solutio microspectrophotometry. (*b*) Effect of 0.25 mM SNOG on
the spectral sensitivity in dark-adapted retinae (open circles
The data obtained with normal Ringer solution are also
shown (filled circles) (*c*) Effects of 10 uM h the spectral sensitivity in dark-adapted retinae (open circles).
The data obtained with normal Ringer solution are also
shown (filled circles). (*c*) Effects of 10 μM haemoglobin on
the spectral sensitivity in light-adapt The data obtained with normal Ringer solution are also
shown (filled circles). (c) Effects of $10 \mu M$ haemoglobin on
the spectral sensitivity in light-adapted retinae (filled circles).
The data obtained with normal Ring shown (filled circles). (*c*) Effects of 10 μ M haemoglobin on
the spectral sensitivity in light-adapted retinae (filled circles
The data obtained with normal Ringer solution are also
shown (open circles). Data modified The data obtained with normal Ringer solution are also shown (open circles). Data modified from Yamada *et al.* (1999).

(1999).
channel in the cone terminal could be responsible for
neurotransmitter release at the hyperpolarized potentials channel in the cone terminal could be responsible for
neurotransmitter release at the hyperpolarized potentials
encountered during retinal light adaptation channel in the cone terminal could be res
neurotransmitter release at the hyperpolarize
encountered during retinal light adaptation. encountered during retinal light adaptation.

In the teleost retina, HC-cone feedback has been suggested to occur via HC spinules, finger-like extensions

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of HC dendrites positioned laterally at synaptic ribbons
within cone pedicles (Wagner & Diamooz 1993) Appliof HC dendrites positioned laterally at synaptic ribbons
within cone pedicles (Wagner & Djamgoz 1993). Appli-
cation of NO donors (SNP SNAP or SNOG) to darkof HC dendrites positioned laterally at synaptic ribbons
within cone pedicles (Wagner & Djamgoz 1993). Appli-
cation of NO donors (SNP, SNAP or SNOG) to dark-
adapted cyprinid fish (roach and carp) retinae produced within cone pedicles (Wagner & Djamgoz 1993). Appli- occurred through amacrine and centre-depolarizing cation of NO donors (SNP, SNAP or SNOG) to dark-
adapted cyprinid fish (roach and carp) retinae produced Sekaran *et al* cation of NO donors (SNP, SNAP or SNOG) to dark-
adapted cyprinid fish (roach and carp) retinae produced
HC spinules, mimicking the effect of normal light adapt-
ation (Greenstreet & Diamgoz 1994: Haamedi 1999) adapted cyprinid fish (roach and carp) retinae produced
HC spinules, mimicking the effect of normal light adaptation (Greenstreet & Djamgoz 1994; Haamedi 1999).
These effects were concentration dependent and were HC spinules, mimicking the effect of normal light adaptation (Greenstreet & Djamgoz 1994; Haamedi 1999).
These effects were concentration dependent and were
completed within 10–20 min following a given treatment ation (Greenstreet & Djamgoz 1994; Haamedi 1999).
These effects were concentration dependent and were
completed within 10-20min following a given treatment. These effects were concentration dependent and were
completed within 10–20 min following a given treatment.
Pretreatment with cPTIO largely (but not completely)
blocked the normal light adaptation-induced formation of completed within 10–20 min following a given treatment.
Pretreatment with cPTIO largely (but not completely)
blocked the normal light adaptation-induced formation of
spinules consistent with (i) endogenous NO being blocked the normal light adaptation-induced formation of
spinules, consistent with (i) endogenous NO being produced during light adaptation, and (ii) HC spinules being under NO control.

(iii) *Electronic coupling of HCs*

(iii) *Electronic coupling of HCs*
HCs of the same subtype form gap junction-coupled
syncytia imparting upon these cells wide receptive fields.
In teleosts HC coupling is dynamically regulated by the HCs of the same subtype form gap junction-coupled
syncytia imparting upon these cells wide receptive fields.
In teleosts, HC coupling is dynamically regulated by the
adaptational state of the retina. Light adaptation syncytia imparting upon these cells wide receptive fields.
In teleosts, HC coupling is dynamically regulated by the
adaptational state of the retina. Light adaptation
decreases coupling resulting in an increase in the spat In teleosts, HC coupling is dynamically regulated by the
adaptational state of the retina. Light adaptation
decreases coupling resulting in an increase in the spatial
resolution whereas in the dark the HCs are strongly adaptational state of the retina. Light adaptation
decreases coupling resulting in an increase in the spatial
resolution, whereas in the dark the HCs are strongly
coupled so as to increase the absolute sensitivity of the decreases coupling resulting in an increase in the spatial resolution, whereas in the dark the HCs are strongly coupled so as to increase the absolute sensitivity of the resolution, whereas in the dark the HCs are strongly
coupled so as to increase the absolute sensitivity of the
system. DA was found initially to decrease HC coupling,
mimicking the effects of light adaptation (Diamgoz & coupled so as to increase the absolute sensitivity of the
system. DA was found initially to decrease HC coupling,
mimicking the effects of light adaptation (Djamgoz &
Wagner 1992): NO has been shown subsequently also to system. DA was found initially to decrease HC coupling,
mimicking the effects of light adaptation (Djamgoz &
Wagner 1992); NO has been shown subsequently also to
have a similar role (e.g. Lu. & McMahon 1997) Applicamimicking the effects of light adaptation (Djamgoz & Wagner 1992); NO has been shown subsequently also to have a similar role (e.g. Lu & McMahon 1997). Application of SNP or 8-Br-cGMP to pairs of cultured hybrid
bass HCs decreased the amplitude of the junctional
that NO is a novel signal of light adaptation in the outer
retina and may account for some of the interesting prophave a similar role (e.g. Lu & McMahon 1997). Application of SNP or 8-Br-cGMP to pairs of cultured hybrid bass HCs decreased the amplitude of the junctional coupling current (Lu & McMahon 1997). The effects of tion of SNP or 8-Br-cGMP to pairs of cultured hybrid
bass HCs decreased the amplitude of the junctional
coupling current (Lu & McMahon 1997). The effects of
SNP could be blocked by the application of IV-83583 bass HCs decreased the amplitude of the junctional
coupling current (Lu & McMahon 1997). The effects of
SNP could be blocked by the application of LY-83583,
an inhibitor of sGC or intracellular injection of coupling current (Lu & McMahon 1997). The effects of SNP could be blocked by the application of LY-83583,
an inhibitor of sGC, or intracellular injection of RKRARKE a PKG inhibitor It was proposed that NO SNP could be blocked by the application of LY-83583,
an inhibitor of sGC, or intracellular injection of $RKRARKE$, a PKG inhibitor. It was proposed that NO
modulation of HC electrical coupling occurs via PKG an inhibitor of sGC, or intracellular injection of $\overline{RKRARKE}$, a PKG inhibitor. It was proposed that NO modulation of HC electrical coupling occurs via PKG inhers the canonical coupling occurs via PKG in RKRARKE, a PKG inhibitor. It was proposed that NO modulation of HC electrical coupling occurs via PKG phosphorylation of the gap junctions.

modulation of HC electrical coupling occurs via PKG
phosphorylation of the gap junctions.
Interestingly, a chromatic difference in the receptive
field size of carp HI HCs has been observed (Djamgoz et Interestingly, a chromatic difference in the receptive *al.* 1998). In the light-adapted retina, the receptive field of field size of carp H1 HCs has been observed (Djamgoz *et al.* 1998). In the light-adapted retina, the receptive field of H1 HCs was found to be smaller for SW- in comparison with LW-light stimulation. APB application supp al. 1998). In the light-adapted retina, the receptive field of H1 HCs was found to be smaller for SW- in comparison
with LW-light stimulation. APB application suppressed
the chromatic difference whereas intracellular cGMP HI HCs was found to be smaller for SW- in comparison
with LW-light stimulation. APB application suppressed
the chromatic difference whereas intracellular cGMP
injection increased it. The differential effects of the specwith LW-light stimulation. APB application suppressed
the chromatic difference whereas intracellular cGMP
injection increased it. The differential effects of the specthe chromatic difference whereas intracellular cGMP
injection increased it. The differential effects of the spec-
tral stimulation on the receptive field size was suggested
to be due to the APB-sensitive conductance-decrea injection increased it. The differential effects of the spectral stimulation on the receptive field size was suggested
to be due to the APB-sensitive, conductance-decreasing
SW input to the H1 HC as described above NO has tral stimulation on the receptive field size was suggested
to be due to the APB-sensitive, conductance-decreasing
SW input to the H1 HC, as described above. NO has been
linked to the enhancement of the SW-transmission to be due to the APB-sensitive, conductance-decreasing
SW input to the Hl HC, as described above. NO has been
linked to the enhancement of the SW-transmission listed evidence concerning the role of NO in vertebrate retinae SW input to the H1 HC, as described above. NO has been
linked to the enhancement of the SW-transmission
pathway and so it is possible that NO could also be
involved in the modulation of the chromatic difference in linked to the enhancement of the SW-transmission
pathway and so it is possible that NO could also be
involved in the modulation of the chromatic difference in
the HI HC recentive field size during light adaptation pathway and so it is possible that NO could also k
involved in the modulation of the chromatic difference i
the H1 HC receptive field size during light adaptation.

4. LIGHT-EVOKED RETINAL PRODUCTION OKED RETINAL PROD
OF NITRIC OXIDE

4. LIGHT-EVOKED RETINAL PRODUCTION
OF NITRIC OXIDE
Recent evidence suggests that endogenous NO produc-**EXECUTE:**
Recent evidence suggests that endogenous NO production does indeed occur during light adaptation in both
fish and mammalian retinae. Neal *et al.* (1998) used a Recent evidence suggests that endogenous NO production does indeed occur during light adaptation in both fish and mammalian retinae. Neal *et al.* (1998) used a method based upon pitrate reductase activity and election does indeed occur during light adaptation in both fish and mammalian retinae. Neal $et \ al.$ (1998) used a method based upon nitrate reductase activity and elecfish and mammalian retinae. Neal *et al.* (1998) used a method based upon nitrate reductase activity and electrochemical detection to assay NO in perfusates of rabbit retinae treated experimentally *in ring* in various di method based upon nitrate reductase activity and electrochemical detection to assay NO in perfusates of rabbit
retinae treated experimentally *in vivo* in various different
wavs This method gave more consistent data compar trochemical detection to assay NO in perfusates of rabbit
retinae treated experimentally *in vivo* in various different
ways. This method gave more consistent data, compared
with attempts to measure NO production directly retinae treated experimentally *in vivo* in various different ways. This method gave more consistent data, compared with attempts to measure NO production directly. Thus, ways. This method gave more consistent data, compared
with attempts to measure NO production directly. Thus,
both steady and flickering light adaptation led to
production of NO. Interestingly, these effects were with attempts to measure NO production directly. Thus,
both steady and flickering light adaptation led to
production of NO. Interestingly, these effects were
blocked by $cis-2$ 3-piperiding
discriboxylic acid and \triangle PR both steady and flickering light adaptation led to production of NO. Interestingly, these effects were blocked by *cis*-2,3-piperidinedicarboxylic acid and APB, *Phil. Trans. R. Soc. Lond.* B (2000) *Phil. Trans. R. Soc. Lond.* B (2000)

indicating that the corresponding synaptic control
occurred through amacrine and centre-depolarizing indicating that the corresponding synaptic control
occurred through amacrine and centre-depolarizing
binolar_cells_respectively indicating that the cor

occurred through amacr

bipolar cells, respectively.

Sekaran et al. (1999) a

HCs of the same subtype form gap junction-coupled the level of NO, but APB blocked both steady and flicker
ncytia imparting upon these cells wide receptive fields. light adaptation-induced NO production, suggesting that Sekaran *et al.* (1999) applied this technique to the isolated retina of carp and also found light-adaptation-Sekaran *et al.* (1999) applied this technique to the isolated retina of carp and also found light-adaptation-
induced synthesis of NO. An interesting aspect of NO
production in the carp retina was that it was associated isolated retina of carp and also found light-adaptation-
induced synthesis of NO. An interesting aspect of NO
production in the carp retina was that it was associated
with a very narrow operating range $(\leq 1 \log$ unit). It induced synthesis of NO. An interesting aspect of NO
production in the carp retina was that it was associated
with a very narrow operating range (\leq 1log unit). It
followed therefore that NO could have a 'switching' production in the carp retina was that it was associated
with a very narrow operating range $(\leq 1 \log \text{unit})$. It
followed, therefore, that NO could have a 'switching'
(rather than a graded) role in the light-adaptation with a very narrow operating range $(\leq 1 \log \text{unit})$. It followed, therefore, that NO could have a 'switching' (rather than a graded) role in the light-adaptation process We have also recently shown that both steady and followed, therefore, that NO could have a 'switching' (rather than a graded) role in the light-adaptation process. We have also recently shown that both steady and flicker light enhanced NO release in the carp retina, process. We have also recently shown that both steady and
flicker light enhanced NO release in the carp retina,
flicker stimulus being relatively more effective. The cellular
origin of the light-evoked NO release was inves flicker light-enhanced NO release in the carp retina,
flicker stimulus being relatively more effective. The cellular
origin of the light-evoked NO release was investigated.
6-Cyano-7-nitroquinoxaline-2.3-dione, had no effe flicker stimulus being relatively more effective. The cellular
origin of the light-evoked NO release was investigated.
6-Cyano-7-nitroquinoxaline-2,3-dione had no effect on
the level of NO but APB blocked both steady and f origin of the light-evoked NO release was investigated. 6-Cyano-7-nitroquinoxaline-2,3-dione had no effect on
the level of NO, but APB blocked both steady and flicker
light adaptation-induced NO production, suggesting that
the centre-depolarizing bipolar cell pathway plays an the level of NO, but APB blocked both steady and flicker light adaptation-induced NO production, suggesting that
the centre-depolarizing bipolar cell pathway plays an
important role in the light-evoked release of NO
(Sekaran et al. 2000) the centre-depolarizin
important role in t
(Sekaran *et al.* 2000).

**5. CONCLUDING REMARKS: MULTIPLICITY 5. CONCLUDING REMARKS: MULTIPLICITY
OF NEUROCHEMICAL CONTROL OF RETINAL
LIGHT ADAPTATION** DING REMARKS: MULTIF
HEMICAL CONTROL OF
LIGHT ADAPTATION **LIGHT ADAPTATION**
The available evidence taken together suggests strongly

The available evidence taken together suggests strongly
that NO is a novel signal of light adaptation in the outer
retina and may account for some of the interesting prop-The available evidence taken together suggests strongly
that NO is a novel signal of light adaptation in the outer
retina and may account for some of the interesting prop-
erties of this process, such as its spread. Since that NO is a novel signal of light adaptation in the outer
retina and may account for some of the interesting prop-
erties of this process, such as its spread. Since DA is
another well-established light-adaptative modulato retina and may account for some of the interesting properties of this process, such as its spread. Since DA is
another well-established light-adaptative modulator, it
follows that retinal light-adaptation is under multiple erties of this process, such as its spread. Since DA is
another well-established light-adaptative modulator, it
follows that retinal light adaptation is under multiple
neurochemical control. It is likely that this multipli another well-established light-adaptative modulator, it follows that retinal light adaptation is under multiple
neurochemical control. It is likely that this multiplicity is
interactive rather than independent. In fact, bo follows that retinal light adaptation is under multiple
neurochemical control. It is likely that this multiplicity is
interactive rather than independent. In fact, both antago-
nistic and synergistic modes of NO-DA interac neurochemical control. It is likely that this multiplicity is
interactive rather than independent. In fact, both antago-
nistic and synergistic modes of NO-DA interaction have interactive rather than independent. In fact, both antagonistic and synergistic modes of NO-DA interaction have
been found (e.g. Djamgoz *et al.* 1995; McMahon &
Schmidt 1999) Such multiplicity and potential intricacy mistic and synergistic modes of NO-DA interaction have
been found (e.g. Djamgoz *et al.* 1995; McMahon &
Schmidt 1999). Such multiplicity and potential intricacy
of signalling would imply that the neurochemical control been found (e.g. Djamgoz *et al.* 1995; McMahon &
Schmidt 1999). Such multiplicity and potential intricacy
of signalling would imply that the neurochemical control
of retinal light adaptation is even more complex than Schmidt 1999). Such multiplicity and potential intricacy
of signalling would imply that the neurochemical control
of retinal light adaptation is even more complex than
previously thought. In the case of aquatic or semi-aqu of signalling would imply that the neurochemical control
of retinal light adaptation is even more complex than
previously thought. In the case of aquatic or semi-aquatic
vertebrates, such control probably reflects the dyna of retinal light adaptation is even more complex than
previously thought. In the case of aquatic or semi-aquatic
vertebrates, such control probably reflects the dynamic
nature of the visual environment under water. previously thought. In the case of aquatic or semi-aquatic

mature of the visual environment under water.
We are aware that regretfully we could not include all the pub-
lished evidence concerning the role of NO in vertebrate retinae We are aware that regretfully we could not include all the published evidence concerning the role of NO in vertebrate retinae
due to space limitations. Our work is supported by the UK Bio-We are aware that regretfully we could not include all the published evidence concerning the role of NO in vertebrate retinae
due to space limitations. Our work is supported by the UK Bio-
technology and Biological Science lished evidence concerning the role of NO in vertebrate retinae
due to space limitations. Our work is supported by the UK Bio-
technology and Biological Sciences Research Council (special
studentship to S.S.) grants from t due to space limitations. Our work is supported by the UK Biotechnology and Biological Sciences Research Council (special studentship to S.S.), grants from the European Union (STRIDE Programme) and the Sardinian Regional G technology and Biological Sciences Research Council (special studentship to S.S.), grants from the European Union (STRIDE Programme) and the Sardinian Regional Government (A.R.A., S.V. and I.H.), and The British Council To studentship to S.S.), grants from the European Union (STRIDE Programme) and the Sardinian Regional Government (A.R.A., S.V. and J.H.), and The British Council, Tokyo (M.B.A.D. and M.Y).

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tion of dopam
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diaphorase—a [marker for neuronal nitric](http://rudolfo.ingentaselect.com/nw=1/rpsv/cgi-bin/linker?ext=a&reqidx=/0197-0186^28^2928L.283[aid=536129,doi=10.1016/0197-0186^2895^2900090-9,nlm=8813246]) oxide synthase—in
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