APS-Acel, Aend, Aflu, Agij, Ahea, Alun, Areg, Jap, and Phys Gen

(APS: dg-japp, h0-acel, h1-aend, h2-aflu, h3-agij, h4-ahea, h5-alun, h6-areg, h7-phys)

USE STANDARD SGML CODING

S-Proof

Visual Contents

Typeface(s)	Times Roman with **Bold** <ff;0> **Bookman with bold** <**ff;3**> Avant Garde with **Bold** <ff;1> Kabel with **bold** <**ff;111**> Helvetica with **bold** <ff;2> `Prestige with bold <ff;12>`
<zstyle>	Refer to p. 7 for use of <zstyle>
<lite>	outputs italic
Saved info for output within frills	Article Opening Tag Lines. <copy;278;1;January;2000;000–000;2000;J807-0e> First field is Volume No. Second field is Issue No. Third field is Month Fourth field is Year Fifth field is Page Range Sixth field is Copyright Year
<zpub;?> <zdoi;?>	<zpub;?> ?=online published date. <zdoi;?> ?=doi information. Macros output information at top of opening page. <zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpcell.00000.2001> outputs ''First published April 26, 2001; doi:10.1152/ajpcell.00000.2001.'' <zpub;First published April 26, 2001><zdoi;> outputs ''First published April 26, 2001.'' <zpub;><zdoi;doi:10.1152/ajpcell.00000.2001> outputs ''doi:10.1152/ajpcell.00000.2001.'' **NOTE:** when first published date is present, journal info line above ends with a period; when first published date is not present, journal info line above ends with a semicolon. See page 60 for style without published information.
Running Heads	<px;;2>SHORT TITLE<pa> 8 pt. Times Roman ×43, SET ALL CAPS. Left & right pages carry short title. Set chemical compounds small caps. If no wording is given on ms., set ''PLEASE SUPPLY WORDING''. Invited Reviews, Brief Reviews, Minireviews, and Historical Perspectives will have a subject-related short title (i.e., running head, like we do for regular articles). There will be no running heads (pages 2 to last) for Editorial, Commentary, Prologue, Invited Editorial, Invited Medical Editorial, Editorial Focus, In Focus, and Special Communication since they repeat the article-type section headings above the gray bar.
<<sh>> **<<sh;1>>**	<<sh>> Change wording as needed. Set C/lc. <<sh;1>> Use for ''IN NEXT ISSUE''
<<title>> **<<title;1>>**	Set initial cap/lc. Used in announcements; set as Cap/lc.
<<aut>>	Set C/lc. Set <bx;1> and <ba> around author names (see page 54). Set the <ba> after the comma and footnote symbols following the last name. Code <cm;1>c<cm;0> for small cap letters in author names.
<<aff>>	Use <rosup;?> to code superior number to correspond with author in <<aut>>
<<abs>> **<<abs;1>>** **<zcopy>** **<<key>>,** **<<key;1>>**	Set a spaceband before the <mc>. Use <<abs;1>> for abstract ×25 (centered ×43 picas) **NOTE:** Invited & Brief Reviews, Minireviews & Historical Perspectives are the only articles to carry centered abstracts. <zcopy> macro computer generates journal title, volume, issue, page range, year, and em dash. Set lc, proper nouns set cap/lc, separated by a semicolon. Use <<key>> for keywords. <<key;1>> will delete 18 pica gray rule when it falls at the bottom of the column.
<<hd1>> & **<<smhd1>>**	Set cap/lc, computer will make all caps. First line to be longest; no one-word runovers.
<<hd2>> & **<<smhd2>>**	Set cap/lc. Italic terms stay italic. Signs of operation set italic. See example on page 9. First line to be longest; no one-word runovers.
<<hd3>> & **<<smhd3>>**	Set initial cap/lc. Set spaceband before <mc>. Italic terms stay italic. Signs of operation set italic. See example on page 9. Proper nouns set cap/lc.

<<hd4>> & <<smhd4>>	Set all lc. Computer will generate small caps. Set a spaceband before the <mc>.
<<altfoot>> <<foot>>	8/9 Times Roman ×21, para style. Use superior numbers or full-size symbols followed by a thin space. The full length rules above all footnotes will be generated by the computer.
<<sigau>> <<sigau;1>> <<sigaff>>	10/11 Times Roman. All lines align on left. Flush right on longest. Runovers indent 1 em. Use <<sigau;1>> for 9/10 Times Roman
Figure Coding	See page 5 for specific coding for Figure Pickups.
Size-condition tags	<<in0>>, <<in1>>, <<in2>>, <<in3>>, <<in4>>, <<align>>, <<ment>>, <<ment2>>
<<note>>	''Note added in proof''—set head all lowercase, computer will make small caps. Precedes <<smtexp>> text.
MATH Equations	10/11 Times Roman, ×21. 18 pts b/b above and below to text. 18 pts b/b to consecutive equations. Bracketed expressions should not be broken if possible. Equations that run 2 lines should set flush left and flush right. Equations that run 4–5 lines should set across 2 columns. Display across 2 columns set as pickup with rules above and below.
Equation numbers	Italic arabic number in roman parens, flush right, center vertically on equation as a whole. Use <zsid>, i.e. <id;zsid;1>. In the appendix section, the numbers and letters are italic.
Math variables	Variables are roman unless marked for italic or bold.
Trig terms	Style 2
Math signs	In text: Signs of operation stay up. In display: Signs of operation go down. Superior/Inferior: 2 units of space around signs of operation.
Fraction style	Superior/Inferior: Em-piece **To set sup/inf fractions code <supfrax;?;?> or <inffrax;?;?>** In Text: Em-Piece (when a fraction must be built, build all of them in the same area); shilling for ratios. In Display: Em-piece unless build-up is required; shilling for ratios.
Alignment:	Single Equations: Center Consecutive Single Line Equations with Equals: Center each equation unless alignment is marked on the manuscript. Multiple Line Equations: Follow established alignment procedures.
Other Info	$P > 0.05$ intensities <90 μA intervals ~1 min Set integral same point size as surrounding text. Key summation sign in text, (Not cap sigma). Greek: Straight greek. Stack charges.
<<conhd1>>	Set cap/lc, computer will make ALL CAPS!
<zsym> <zsymx>	For 6 pt symbols in figure legends, <zsym> will drop you 2 pt sizes to set your symbol, <zsymx> will return you to 8 pt.
<<hdr>>, <<ref>>, <<refa>>	set cap/lc, computer will make c/smcap. Set ''and'' all lowercase, computer will make smallcap. <<refa>> is used for reference numbers with ''a''. <<hdr>>: set Cap/lc, computer will make ALL CAPS!
<zart;?>	The **<zart;?>** (where the ? is the graphic name) macro will float artwork in the remaining space at the bottom of the last page of an article. See page 16.
GENERAL INFO	E-mail and URL addresses can be broken accordingly: 1. Squeeze to fit to one line if possible. 2. Break before @. 3. Break after /, after //, or after a period. 4. Keep http:// together. 5. If break is necessary, never add hyphen. Always justify line. 6. Break after E-mail: 7. Break words within URL only if absolutely necessary. Do not add hyphen. 45°C in vitro in situ *P* i.e. magnification ×3,100 **CW spacing:** key en dashes tight. Inferiors/superiors marked for space within, key a <mh;2u> (2 unit spaces) within text. Set a thin space following footnote symbols in captions and table footnotes. In tables, set a thin space around signs of operations in the table body and around signs of operation within inferior/superior. **In-house spacing:** key 1 unit space around all en dashes. Inferiors/superiors marked for space within, key 2 unit spaces. Key 2 units of space following footnote symbols in captions and table footnotes. In tables, key 2 units of space around signs of operations in table body and around signs of operation within inferior/superior. **Widows:** In text avoid widows (≤3 characters) at ends of paragraphs. Four characters is not considered a widow. Do not count punctuation. Superiors and inferiors do count. **Customer coding on hard copy:** 1. Title: T=set copyright; T1=delete copyright. 2. Abstract: ABS2=set ×21 and position in text column; ABS=set ×25 and center by page width. For JAP's Highlighted Topic series, the article type (e.g., Invited Review, Selected Contribution, Historical Perspectives) will be dropped from the title and used instead in the section head (except for Selected Contribution, which will be dropped altogether). After ''Translational Physiology'' there is a vertical gray bar, but no series title follows. Ref. citations: (5) (6, 9) (9–11) (en dash) ALWAYS break ''ischemia'' and ''ischemic'' like this: is-che-mia is-che-mic Break ''apoptosis'' and ''apoptotic'' like this: apop-to-sis apop-totic Try to make author lines as equal length as possible. Customer likes ''box'' appearance. In affiliation lines, do not break city, state, and zip code. Also, try to make affiliation lines as equal length as possible.
Order of elements at end of article	(1) text; (2) Appendix; (3) Note Added in Proof; (4) Acknowledgments; (5) Grants; (6) Disclosures; (7) References.

<zast>	This macro takes you to superior, changes to 9 pt, sets the asterisk and then returns to correct point size and resets to baseline.
<ini;???>	This macro is to appear with each article following the <artno;???> macro at beginning of article. Macro contains initials for customer use and outputs in the slug line.

<<enote>>AQ1 Please indicate correct pages for reference 28.
<mc>AQ2 Please correct the volume number or year for reference 30.
COTTAGE WORKERS: set author queries as the last element of the division.
XYVISION SYSTEM OPERATORS: delete all queries in AA stage.

Tag List

<<abs>> — page 9
<<ack>> — page 16
<<aff>> — page 9
<<align>> — page 12
<<altfoot>> — page 9
<<aut>> — page 9
<<bl>> — page 11
<
> — page 23
<<brtitle>> — page 23
<<cona>> — page 29
<<conf>> — page 29
<<conhdf>> — page 32
<<conhd1>> — page 29
<<conhd>> — page 29
<<cont>> — page 29
<<cor>> — page 25
<<eq>> — page 10
<<disc>> — page 16
<<extf>> — page 11
<<extp>> — page 13
<<foot>> — page 9
<<grant>> — page 16
<<guest>> — page 28
<<guesthd1>> — page 28
<<hd1>> — page 9
<<hd2>> — page 9
<<hd3>> — page 9
<<hd4>> — page 9
<<hdack>> — page 16
<<hdds>> — page 16
<<hdgr>> — page 16
<<hdlet>> — page 21
<<hdr>> — page 16
<<in0>> — page 12
<<in1>> — page 12
<<in2>> — page 12
<<in3>> — page 12
<<in4>> — page 12
<<key>> — page 9
<<letexf>> — page 21
<<letexp>> — page 21
<<ment2>> — page 15
<<ment>> — page 12
<<note>> — page 16
<<pict>> — page 11
<<pictcon>> — page 13
<<rec>> — page 9
<<ref>> — page 16
<<refa>> — page 16
<<sh>> — page 17
<<ssh>> — page 49
<<sshtitle>> — page 49
<<sigaff>> — page 21
<<sigau>> — page 21
<<smhd1>> — page 13
<<smhd2>> — page 13
<<smhd3>> — page 13
<<smhd4>> — page 13
<<smtexf>> — page 15
<<smtexp>> — page 13
<<tabft>> — page 4
<<tech>> — page 17
<<texf>> — page 9
<<texp>> — page 9
<<title>> — page 9
<<tt>> — page 4
<<vconhd>> — page 31
<<vconhdt>> — page 31

Table Guidelines for APS
(Acel, Aend, Aflu, Agij, Ahea, Alun, Areg, Japp, Phys. Gen.)

Table Measures: ×21, ×43, ×55.6 broadside; maximum depth is ×55.6p. Do not drop point size for Table Number or Title. Reduce point size of table body to 7½/8½ or 7/8 to fit ×43 before setting broadside. Before setting any table broadside, break BEFORE ± to fit ×43 pica measure. If breaking before ±, footnote symbols are positioned after the first line of the entry; the column(s) aligns on the right and the footnote symbols hang. Tables can set 8/8 to keep to one page.

Table Number & Title (tt): Word ''Table'' is set 10/11 Times Roman cap/lc, flush left, number is set 10/11 Times Roman full-size Arabic, followed by a period and <ens> (the <ens> is computer generated), run in to Title. Set Title 10/11 Times Roman italic × table width, initial cap/lowercase, flush left, rr w/o hyphenation. Italic terms stay italic. Signs of operation set italic. See example on page 9. Avoid 1-word runovers. Lines to be ⅔ (top line) to ⅓ (last line).
6 pts b/b below to ½ pt rule; 2 pts b/b to another ½ pt rule; 10 pts b/b below double rule to column heads.
Set justifiers around signs of operation.

Table Column Heads & Straddle Heads: Column and Straddle Heads set 7/8 Times Roman; centered; bottom align. Column heads set cap/lc OR initial cap/lc per manuscript. Straddle heads set cap/lc.
Straddle Heads have 5.5 pts b/b below to ½ pt rule, 9 pts b/b below rule; Column Heads have 5.5 pts b/b below to ½ pt rule, 10 pts b/b below rule to TB.

Table Spanner Heads: 8/9 Times Roman italic; cap/lc; centered × table width; positioned in the table body. Spanner head below rule beneath column heads has 10 pts b/b above and 13 pts b/b below; subsequent spanner heads have 13 pts b/b above and 13 pts b/b below.

Table Body: 8/9 Times Roman; stub column positions flush left as a unit on the longest line in the column head or column; 5.5 pts b/b below Table Body to ½ pt rule, 10 pts b/b below rule to Table Footnotes. Align numerical columns on decimal where feasible. Use 2 units of space around signs of operation in column heads and table body. **Note:** Columns that contain math signs align only on math sign. Do not align decimals in columns containing math signs. Gutters to 5 pica max. (can go to 5½ picas as a last resort). Proof needs to specify width of side box or gutter space when indicating to indent left & right.

Table Footnote (tabft): 8/9 Times Roman × table width, para style. Use 2 unit spaces between footnote symbols and footnote text. Footnote symbols set full-sized. Footnote letters set superior. Use justifier space around signs of operation in footnote (justified copy), or if item is surrounded by parens, e.g., (a = 2), use the 2 unit space. Set footnote symbol in table title in roman to match symbol in footnote.

Do not key dumline if table has only 1 column
Dumline is set up for 8 pt Times Roman
Use <zcolhd> in the dumline for the column head wording — <nx><zcolhd>Column head wording<nx>
The first column is setup for a 1 em runover indent

NOTE:
For a 1 column table set **<</PICK;t?;0;0;block>>**
For a 2 column table set **<</PICK;t?;0;0;page>>**

<<tt>>Table 2.**<mc>** *Effects of respiratory substrates on MDH-LAC gene expression and quantitative metabolic patterns in 24-hr urine samples*
<starttab;# header rows;# of columns> <dumline>. . . <nx>. . . <nx>. . . <enddum>

	<Tc;;2><urule;1>Galactosidase Activity*	
<Tr;2>Addition†	**<Tr>**Glucose activity	**<Tc>**Glycerol activity
<Tr>None	**<Tc>**1,120±321	**<Tc>**NG‡
<Tr>Oxygen	**<Tc>**226±73	**<Tc>**4,420
<Tr>Nitrate	**<Tc>**1,090±218	**<Tc>**3,120
<Tr>TMAO	**<Tc>**178±1,135	**<Tc>**6,370
<Tr>Fumarate	**<Tc>**1,000±90	**<Tc>**6,420

<endtab><<tabft>> *<ths>Cells were grown in a glucose minimal or glycerol minimal medium either aerobically or anaerobically as described in the text. †<ths>Units are given in nanomoles of ONPG hydrolyzed per minute per milligram of protein. ‡<ths>NG, no growth.**</.>**

Alignment Styles					
	flush left	2nd	3rd	4th	right hang
1	$	. ⊞ * †		. * †	
2	$	/			)%
3	$	.*†‡			
4	$	em dash	en dash	-	
5	$	± en dash = ×	(		
6	$	. ⊞ § ¶	± × =	. § ‖	

SYSTEM OPERATOR NOTE: key 2 control u following footnote symbols in captions and table footnotes. (Cottage is keying <ths> — this is being converted to 2 unit spaces.

In-House Style Guidelines

Trim: 8⅜ × 10⅞ inches
Head Margin: ½ inch (36 pts)
Gutter: ⅝ inch (44 pts)
Depth: 2p + 55.6 picas—61 lines of 10/11 pt text per column
No. of Columns: 2
Page Width: 43 picas
Column Width: 21 picas
Typefaces: Times Roman Kabel Helvetica (Helv) **Bookman** Prestige (monospace)
Text: 10/11 Times Roman × 21 picas; para indent is 1 em.
Footnotes: 8/9 Times Roman ×21, para style (1 em para indent). ½-pt rule ×21 positions 3 pts above footnotes. Text footnotes position at bottom of column where mentioned. Footnotes on opening page are placed at bottom of left column. Allow approx. 18q space between text above and footnote rule.
Opening page footnotes: Most articles include ''advertisement'' footnote. The following sections do not carry this footnote. They may have a different footnote or none at all. They are Invited Review, Brief Report, Editorial, Special Medical Editorial, Invited Editorial, Distinguished Lectureship, Corrigendum, Commentary, Themes, and Editorial Focus. Journal zh7-phys does not carry ''advertisement'' footnote at all.
Figure Legends: 8/9 Times Roman, justified w/hyphens. Set word ''Fig.'' and number followed by a period and <en> space. 6 pts visual space from graphic to caption. ×21 (1 col), ×43 (2 col), ×55.6 (broadside). Single line captions set flush left.
Figure Symbols: Symbols such as ○, ●, □, ■, ◇, ◆, etc., are set 6pt in figure captions. See p. 2 for coding.
Figure Labels: Set 12 pt Helvetica Bold caps when type is sans serif (e.g., Helvetica); 12 pt Times Roman Bold caps when type has serifs (e.g., T.R., Bask.).
Appendix: 9/10 Times Roman ×21, para style (10 pt para indent); precedes Acknowledgments. See visual guide pages 15 and 16.
Acknowledgments: 8/9 Times Roman ×21, para style (10 pt para indent); precedes References.
Received Line: 8/9 Times Roman ×21, 6-pt# above, initial Cap/lc, begins FL. Follows Affiliation line(s) on article opening page.
Note Added in Proof: head is 8/11 Times Roman ×21, caps, FLRR, set in cap/lc, computer will make caps. <<smtexp>> to text, 9/10 Times Roman ×21, paragraph style (10 pt para indent); precedes References.
References: 8/9 Times Roman, numbered, followed by period and <ens> (computer generated) overruns align with first author. Clear for 10 or 100 as necessary. <<hdr>> above. Run-in after all other elements. Last page squares off.

CODING FOR FIGURE PICKUPS

To set Figures ×21p or less set **<</PICK;f1;0;0;block>>**.

To set Figures >31p–43p set **<</PICK;f1;0;0;page>>**.

To set Figures between 22p–30.11p set **<</PICKCS;f1;0;0;page>>**.

NOTE: The system will insert **<px><ig;000000000000><pa><xs;3600;%igwidth><zsidecap>** after the **<pict>** macro in all side captions. This will measure the graphic and insert the side caption flush outside, 1 pica from the graphic. If the side caption should be positioned flush inside (see Side Captions guidelines on visual guide p. 6), make the macro **<zsidecap;1>** and change the ''Xorig'' of the graphic block to ''flip''. The gutter between the graphic and caption is set to be 12 points; if a different amount is wanted, put that amount in points in the second field of the <zsidecap> macro (for example if an 18 pt gutter is wanted set **<zsidecap;;18>**).

To set Figures for announcements set **<</PICK2;f1;0;0;block>>**

To set block for advertising footnote on opening page set **<</PICKF;a1;0;0;block>>**

Pagination Guidelines

Articles: Articles begin on left or right pages; no blanks. Continuous pagination within volume.

Long or short: Pages may run 1 to 2 lines short. No long pages. **NOTE:** Opening page always runs normal depth (no short pages). **Note:** Each page in Phys. Gen. articles has a running foot. Therefore, there can be no long pages with <zstyle;9>.

Drop folios: 8 pt Times Roman drop folios are flush outside on opening pages and base align with copyright info. which centers at bottom of opening page. Designated journal letter to precede folio (set closed up to folio)

Folios: 10 pt Times Roman, flush outside, top align w/RHs. Designated journal letter to precede folio (set closed up to folio). RHs set 8 pt Times Roman, centered. First pages get dummy folios. Pagination is consecutive within the volume.

Running Feet: 8 pt. Times Roman, centered at bottom of all pages except opening page. Running foot may be dropped if necessary to fit a full page figure or table.

Text Requirements: Facing pages align unless one or both of the pages contains full-page artwork.

Stub: 5 lines minimum.

Make-up Guidelines:

1. NO orphan or widow lines allowed.
2. Open space above NOT below heads to balance columns/pages.
3. If abstract fills first column, delete swell rule at bottom of column.
4. Do NOT place the very first or last line of acknowledgments copy in a separate column.
5. If reference entry must break, allow at least two lines at top or bottom of column.

Figures and Tables: Place as soon after citation as possible, top or bottom of the page. May precede citation as long as it appears on the same page. Allow a minimum of 1 pica and a maximum of 2.6 picas space around figs and tables. When 2 figs/tables appear on a page, stagger top and bottom. Figures and tables center horizontally within the column. It is okay to place two small figures top/bottom in outside column to keep closer to mention. As a last resort, it is okay to stack figs/tables if necessary for page layout but query editor regarding page layout when stacking. If a figure is almost a full page/column and will not fit with caption, place caption at bottom of facing page/column (see visual guide page 15.) (NEVER place caption at top of page/column). If 4 lines of text will fit on page/column with figure, always place figure at bottom of page/column. If 4 lines of text will NOT fit on page/column with figure, center figure (and caption if it fits) vertically on page/column. Continued figures, captions, and tables begin on facing pages. Figures and tables may **NOT** 1) appear directly before or after equations, 2) appear on page with references. Figs/tables on same page as references is a last resort. Editor must be queried to see if layout is acceptable when figures/tables appear with references. If you MUST place figs/tables on page with references, you MUST have some text separating figs/tables from references.

Text lines between figures/tables: 4 lines minimum

Captions: 6-pt space from figure to caption. Multi-line captions are block-style ×21 (1 col), ×43 (2 col), ×55.6 (broadside). Single line captions flush left. Captions may not be broken.

Side Captions: Figures measuring 22–30.11 picas use side captions. Side captions position flush outside on page. Side captions position 1 pica away from figure. Side captions center vertically. If the caption is 1 q to 1 pica deeper than the figure, center the figure vertically on the caption. If the caption exceeds the depth of the artwork by >1 pica, reset the caption ×43 and position FL beneath figure. Figure centers ×43 picas. When 2 figures with side captions appear on a page without text, stagger captions (top caption outside, bottom caption inside). When 2 figures with side captions appear on a page with text, both captions position flush outside.

Continued Figures: Set ''Fig. 2—*Continued*''

Continued Vertical Tables: Set ''Table 2.—*Continued*'' and column heads on each continued page. Set closing rule at bottom of each page of the table. Set ''*Continued*'' in 8 pt. Times Roman italic, 10 pts. b/b below and flush right on closing rule at bottom of each continued page. Code **<ztabcontin>** following **<endtab>** at bottom of tables that continue. Set closing rule at end of table. Table footnotes are at the end of the table.

Broadside Figs and Tables: When broadside figs and tables fit in 1 column, place text, figures, and/or tables in facing column. Single-column broadside tables must appear in outside column of page.

End of Article Logos: Logos are placed on the last page of some articles when AAs come back and articles are paginated. Logos center horizontally and vertically on remaining text area of last page of article. Logos are used when depth of text & RH are <26 picas. Logo selection is random—do NOT use the same logo on two consecutive articles. Use a small logo (logos 1–11) when depth of text (including RH) is 20 to 26 picas. Use a large logo (logos 13–24) when depth of text (including RH) is <20 picas. **See pages 7 and 8.** When depth of text (including RH) is >26 picas, no logo is used. Pagechecker must carry ''NO LOGO'' on those pages without a logo. If text is added to or deleted from the last page, text depth needs to be rechecked to determine if a logo is or is not needed.

Page Styles for regular articles

<ps;1>—Regular 2 column page style.
<ps;2>—Normal no running head (full page figs).
<ps;4>—Table of contents.
<ps;5>—Volume table of contents.
<ps;7>—1 line short, facing pages.
<ps;9>—1 line short (entire article).
<ps;10>—1 main text block, Announcement, Corrigenda
<ps;11>—normal page layout for Phys. Gen. (phys)
<ps;16>—full page figs (long) no running head or running foot
<ps;17>—full page figs (short) no running head
<ps;20>—Ads (center on trim)

AD LAYOUTS—Dummy divisions in ''JOB_r0-ads''

<ps;70>—Use for Full Page Ad—(layout - adfull)
<ps;71>—Use for Bleed Ad—(layout - adbleed)
<ps;72>—trim size page—no bleed (layout - adtrim)
<ps;73>—1/2 page ads (layout - 12ad)
<ps;74>—1/2 page ad top and two 1/4 on bottom (layout - 12adtop)
<ps;75>—1/2 page ad bottom and two 1/4 on top (layout - 12adbtm)
<ps;76>—1/4 page ads (layout - 14ad)
<ps;78>—1/2 page ad vertical left and two 1/4 on right (layout - 12adverl)
<ps;79>—1/2 page ad vertical right and two 1/4 on left (layout - 12adverr)
<ps;80>—1/2 page ads vertical (layout - 12adv)

<zstyle>

<zstyle;1;1> Argument 1 determines journal designation, argument 2 determines ''no copyright'' layout.

The first argument of this macro outputs correct information for each journal in <zcopy> line in abstract, correct journal title etc, in opening page volume line, correct ISBN Number and letter with folio on opening page running foot, and correct letter with folio on running heads; and running foot wording.

When the second argument is 1 there will be no copyright information on opening page running foot.

<zstyle;1> = AJP-Cell Physiology (acel) ''C'' ISBN Number 0363-6143
Running Foot Wording:
AJP-Cell Physiol • VOL 281 • AUGUST 2001 • www.ajpcell.org

<zstyle;2> = AJP-Endocrinology and Metabolism (aend) ''E'' ISBN Number 0193-1849
Running Foot Wording:
AJP-Endocrinol Metab • VOL 281 • AUGUST 2001 • www.ajpendo.org

<zstyle;3> = AJP-Renal Physiology (aflu) ''F'' ISBN Number 0363-6127
Running Foot Wording:
AJP-Renal Physiol • VOL 281 • AUGUST 2001 • www.ajprenal.org

<zstyle;4> = AJP-Gastrointestinal and Liver Physiology (agij) ''G'' ISBN Number 0193-1857
Running Foot Wording:
AJP-Gastrointest Liver Physiol • VOL 281 • AUGUST 2001 • www.ajpgi.org

<zstyle;5> = AJP-Heart and Circulatory Physiology (ahea) ''H'' ISBN Number 0363-6135
Running Foot Wording:
AJP-Heart Circ Physiol • VOL 281 • AUGUST 2001 • www.ajpheart.org

<zstyle;6> = AJP-Lung Cellular and Molecular Physiology (alun) ''L'' ISBN Number 1040-0605
Running Foot Wording:
AJP-Lung Cell Mol Physiol • VOL 281 • AUGUST 2001 • www.ajplung.org

<zstyle;7> = AJP-Regulatory, Integrative and Comparative Psychology (areg) ''R'' ISBN Number 0363-6119
Running Foot Wording:
AJP-Regul Integr Comp Physiol • VOL 281 • AUGUST 2001 • www.ajpregu.org

<zstyle;8> = Journal of Applied Physiology (japp) no letter ISBN Number 8750-7587
Running Foot Wording:
J Appl Physiol • VOL 91 • AUGUST 2001 • www.jap.org

<zstyle;9> = Physiological Genomics (phys) no letter ISBN Number 1094-8341
Running Foot Wording:
Physiol Genomics • VOL 6 • www.physiolgenomics.org

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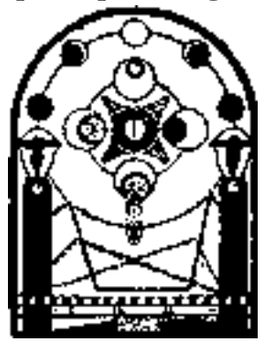

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<copy;91;1;August;2001;000–000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/japplphysiol.00361.2001><zstyle;8>
<px;;2>SPATIOTEMPORAL PATTERNS AT THE RETINAL OUTPUT<pa>

J Appl Physiol 91: 000–000, 2001.
First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.

CG

<<title>>Spatiotemporal patterns at the retinal output (set 16/22 Times Roman med)

<<aut>>**Adam L. Jacobs,[1,*] Todd A. McBride,[2,*] and Frank S. Werblin[1,†] (set 10/12 Times Roman bold)**

<<aff>>[1]<rosup;1>*Department of Molecular and* [2]<rosup;2>*Cellular Biology, University of California, Berkeley, California (set 9/12 Times Roman mdit)*

<<rec>>Submitted 14 May 1999; accepted in final form 31 August 1999 (set 8/9 Times Roman med)

<<abs>>**Jacobs, Adam L., Todd A. McBride, and Frank S. Werblin.** <mc>Spatiotemporal patterns at the retinal output. <zcopy>*J Appl Physiol* 91: 000–000, 2001. First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.— Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in the salamander retina these interactions do little to enhance edge enhancement. To demonstrate this we recorded extraedge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition. (set 9/10 Times Roman med)

<<key>>abdomen; rib cage; diaphragmatic contractility; phrenic stimulation; diaphragm fiber length(set 9/10 Times Roman med)

<<texf>><cm;1><foot;fu;10><pick;a1;0>RECORDING NUMBER <zsmcap>12 <rs><cm;1>FROM THE SIMULTANEOUS<cm;0> population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid that cell[1]<foot;f1;10> (<zref>3–5, 7, 10<zrefx>) (set 10/11 Times Roman med).

<<hd1>>INTRODUCTION AND EXTRA TEXT (set 8/11 Times Roman bold)

<<texp>>Our objective was to determine the patterns of activity elicited in a layer of reginal neurons by increments. Playing back all of these recordings simultaneously simulated the pattern of responses that the center of the representation the pattern of responses that the center of the representation collapsed, leaving a γ-aminobutyric acid-C (GBA_C) receptors a flashed stimulus square subtending -30 of visual angle.

<<hd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials (set 10/11 Times Roman mdit)*

<<texp>>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we cell and shifting the square to -2,000 different positions the center of the representation collapsed, leaving a in cell and shifting the square to -2,000 different positions the center of the representation collapsed, leaving a in a 54 × 36-position grid with 25 μm spacing.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

<<hd3>>*Ca^{2+}-rMLC phosphorylation relationship (set 10/11 Times Roman mdit).* <mc>The following coding is used to set an italic sign of operation: <ff;110><fv;0>+<rs>. A green LED attached to the tip of the robot's arm) in a dark room for 2 s. Then a tone instructed the subject to begin moving.

<mc>By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis.

<<hd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION (set 10/11 Times Roman med). <mc>The resulting reconstructed the patterns by recording from a single reconstructed the patterns by recording from a single distribution was symmetric and concentrated around an average value of 200 ms. With t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells.

<<hd1>>RESULTS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<hd2>>*Existence of PFSs in Cortical Activity*

<<texp>>For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal value, the mean value, and the maximal value.

<</FOOT;fu>><<altfoot>>* Adam L. Jacobs and Todd A. McBride contributed equally to this work.<mc>

† Deceased 31 October 1999 (set 8/9 Times Roman med).<mc>

Address for reprint requests: D. Johnson, George R. Brown School of Engineering, Rice University, 6100 Main, 2041 Duncan Hall, Houston, TX 77005-1892.<</.>>

<</FOOT;f1>><<foot>>[1] In addition to UT-A1 and UT-A, the gene appears to produce at least two other transcripts, ''UT-A1'' and ''UT-A4'' whose cDNAs have recently been cloned.<</.>>

<</PICKF;a1;0;0;block>><<altfoot>><advertisement>The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

NOTE: Wording for this footnote is system generated</.>

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NOTE: Footnotes on this page show order of ''worst case'' example of footnotes on opening page.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<hd1>>RESULTS

<<hd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells.

<<hd1>>RESULTS

<<hd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL).

<<hd2>>*Existence of PFSs in Cortical Activity*

<<hd3>>*Statistics of the interunit, intrapfs time intervals and what they mean.* **<mc>**For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal value, the mean value, and the maximal value.

<<hd2>>*Unit Composition of PFSs*

<<hd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<<texp>>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis.[1]**<foot;f1; 10>**

<mc>The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate

$$\text{<<eq>>}CV = \frac{s^2(H - H*F)}{E(H)}\text{<mx>} \qquad (1)$$

<<texf>>not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.Levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<hd1>>RESULTS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<hd2>>*Existence of PFSs in Cortical Activity*

<<hd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three additional experiments.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<hd1>>RESULTS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<hd2>>*Existence of PFSs in Cortical Activity*

<<hd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three more experiments.

<<hd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma.

<<hd3>>*Statistics of the interunit.* **<<hd4>>**MEAN INTERVAL. **<mc>**We studied the temporal characteristics of the timing of spikes within PFSs pursuing the following issues: *1*) what are the maximal and minimal delays between spikes within a PFS? *2*) Are there any signs of oscillation in the temporal intervals composing a PFS? *3*) Are there any given preferred intervals found in PFSs between any given pair of units? and *4*) What is the temporal precision of PFSs? The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo. The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are

<</FOOT;f1>><<foot>><sup>[1]**<reset><ths>** The muscle data do show that as femoral blood flow falls, so does blood volume, reflecting chemoreflex-mediated peripheral vasoconstriction.**</.>**

typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2.

<mc>With t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells value.

<pick;eq2;0;1>

<</PICK;eq2;0;0;page>><zeq>

<</PICK;f1;0;0;block>>Fig. 1. **<ens>**Action potential broadening during step depolarization is enhanced in the presence of conopressin. **<mdit>***A***<med>**: increase in action potential duration during 15-s step depolarization. **<mdit>***B***<med>**: sample action potentials under control conditions. (set 8/9 Times Roman med)**</.>**

neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually first proto-oncogene identified that was found to contribute to

$$\text{<<eq>>}CV = \frac{\varsigma^2(H - H*F)}{E(H)}\text{<mx><zendeq>} \quad (2)$$

<mc>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division.

<mc>We studied the temporal characteristics of the timing of spikes within PFSs pursuing the following issues: *1*) what are the maximal and minimal delays between spikes within a PFS? *2*) Are there any signs of oscillation in the temporal intervals composing a PFS? *3*) Are there any given preferred intervals found in PFSs between any given pair of units? and *4*) What is the temporal precision of PFSs?**<<bl>>**

- Apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells. (set 10/11 Times Roman med)
- Gradually accumulate not because they are dividing more inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells.
- Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they accelerating cell division, but rather by slowing cell have an average lifespan of only a few hours in vivo.

<<texp>>The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually first proto-oncogene identified that was found to contribute to apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo (Fig. 1).**<pick; f1;0>**

<<extf>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover by apoptosis. (set 9/10 Times Roman med)

<mc>The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo (Fig. 2).**<pick;f2;0>**

<<texp>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromo-

NOTE: 2 column equations are set as pickups (editing use only). Text reads down entire 1st column before going to 2nd column. Default outputs rules on left side. Code <zeq;1> for rules to flush right

<</PICKCS;f2;0;0;page>>Fig. 2. **<ens>**Conopressin enhances the fast sodium current of anterior Jobe neurons. **<mdit>***A***<med>**: with voltage-clamp recording ◆ of an anterior lobe ● neuron in one of the sodium-selective saline.**</.>**

somal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL) (Fig. 3).**<pick;f3;0>** The discovery of *BCL*-2 more than 12 years ago represents a milestone dividing more rapidly than normal B cells, but because have an average lifespan of only a few minutes to hours in vivo.

<<hd2>>*Glossary***<<align>>**RANGE**<<ment>>**

PF	**<mc>**prefrontal cortex (set 10/11 Times Roman med)**<mc>**
CD	**<mc>**caudate nucleus**<mc>**
GPi	**<mc>**internal segment of the last globus pallidus**<mc>**
T	**<mc>**thalamus**<mc>**
MAX	**<mc>**maximum random becomes any synaptic weight**<mc>**
RANGE	**<mc>**range of random synaptic weight distrbution**<mc>**
V	**<mc>**volume of random synaptic height minus the weight distribution and primed**<mc>**

<<texp>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL).

<mc>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because accelerating cell division, but rather by slowing cell do apoptosis; they have an average lifespan of only a few minutes to hours in vivo (Table 1).**<pick;t1;0>**

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in minutes to hours in vivo.**<pick;f4;0>**.

<zis;5q;II.;A.;1.;b.;ii.><<in0>>

I. **<mc>**This is an outline setup. PKC is activated by various transmitters, including glutamate and acetylcholine. (set 10/11 Times Roman med)**<mc>**
II. **<mc>**This is an outline setup.**<<in1>>**
   A. **<mc>**This is the first level of the outline. PKC is activated by various transmitters, including glutamate and acetylcholine.**<mc>**
   B. **<mc>**Second level in outline.**<<in2>>**
      1. **<mc>**Third level in outline. PKC is activated by various transmitters, including glutamate and acetylcholine.**<mc>**
      2. **<mc>**Third level in outline.**<<in3>>**
         a. **<mc>**Fourth level in outline. PKC is activated by various transmitters, including glutamate and acetylcholine.**<mc>**
         b. **<mc>**Fourth level in outline.**<<in4>>**
            i. **<mc>**Fifth level in outline. PKC is activated by various transmitters, including glutamate and acetylcholine.**<mc>**
            ii. **<mc>**Fifth level in outline.

<<texp>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first

<</PICK;f3;0;0;page>>Fig. 3. **<ens>**Localization of all the recorded units in the AHMP region shown on the frontal section of the rat brain 7.2 to 8.2 mm from the zero, interaural plane. All cells localized on the right side of the brain were tested with carbachol, and all the cells localized on the left side of the brain from the zero, interaural plane. All cells localized on the right side of the brain were tested with carbachol, and all the cells localized on the left side of the brain were tested for effects of stimulation of the laterodorsal tegmental nucleus, inhibitory responses**</.>**

Table 1. *Variables n- and c-terminus truncation of NDP-MSH peptide with additional text to show three or more than three lines in a table title*

Stub Column 1†	Column 2‡	This Is a Straddle Head Over Column 3 and 4§	
		Aperature (R)	Adjustments
This is Row 1	17 yrs.	1,000	54.5*
This is Row 2	15 yrs.	1,500	54.5**
This is Row 3	24 yrs.	500	.5***

*Values are means + SD. All peptide activities were tested at a range concentrations. *MCT+CHO; †Significant difference +3; ‡Significant difference +4; §Significant differences. (set 8/9 Times Roman med)

discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's cell division, but rather by slowing cell turnover caused by apoptosis.**<pick;f5;0>**

<<extp>>The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells (set 9/10 Times Roman med).

<mc>Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<texf>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in monly observed in low-grade, B-cell, non-Hodgkin's cell than normal B cells, but because they survive longer center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<smhd1>>METHODS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN (set 8/11 Times Roman bold)

<<smtexp>>For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing is the first proto-oncogene identified that was found to contribute to translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing is the first proto-oncogene identified that was found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more rapidly value, the mean value, and the maximal value.

<<smhd2>>*Existence of PFSs in Cortical Activity (set 9/10 Times Roman mdit).*

<<smtexp>>For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal value, the mean value, and the maximal value.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of than 12 years ago represents a milestone in tumor that was found to contribute to neoplastic cell growth.

<<smhd3>>*Visual target presentation. (set 9/10 Times Roman mdit).* **<mc>**The target was presented to the subject retracted. After 1.5 s, another auditory tone instructed the subject to begin moving. (set 9/10 Times Roman med)

<mc>By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis.

<<smhd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. (set 9/10 Times Roman med) **<mc>**The resulting distribution was symmetric and concentrated around an average value of 200 ms.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL).

<<smhd1>>METHODS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<smhd2>>*Existence of PFSs in Cortical Activity*

<<smtexp>>For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal value, the mean value, and the maximal value.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<smhd1>>METHODS

<<smhd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells.

<<smhd1>>METHODS

<<smhd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL).

<<smhd2>>*Existence of PFSs in Cortical Activity*

<<smhd3>>*Statistics of the interunit, intrapfs time intervals and what they mean.* **<mc>**For each group of group of intervals (of the 207 groups), three intervals were computed: is the first proto-oncogene identified that was found to contribute to neoplastic cell growth

<<pictcon>>Fig. 4. **<ens>**This is an example of a continued figure legend. NOTE: this tag is for system operator use only! Composite diagram of stimulation sites in the pontomesencephalic tegmentum shown on frontal sections of the rat brain. (set 8/9 Times Roman med)

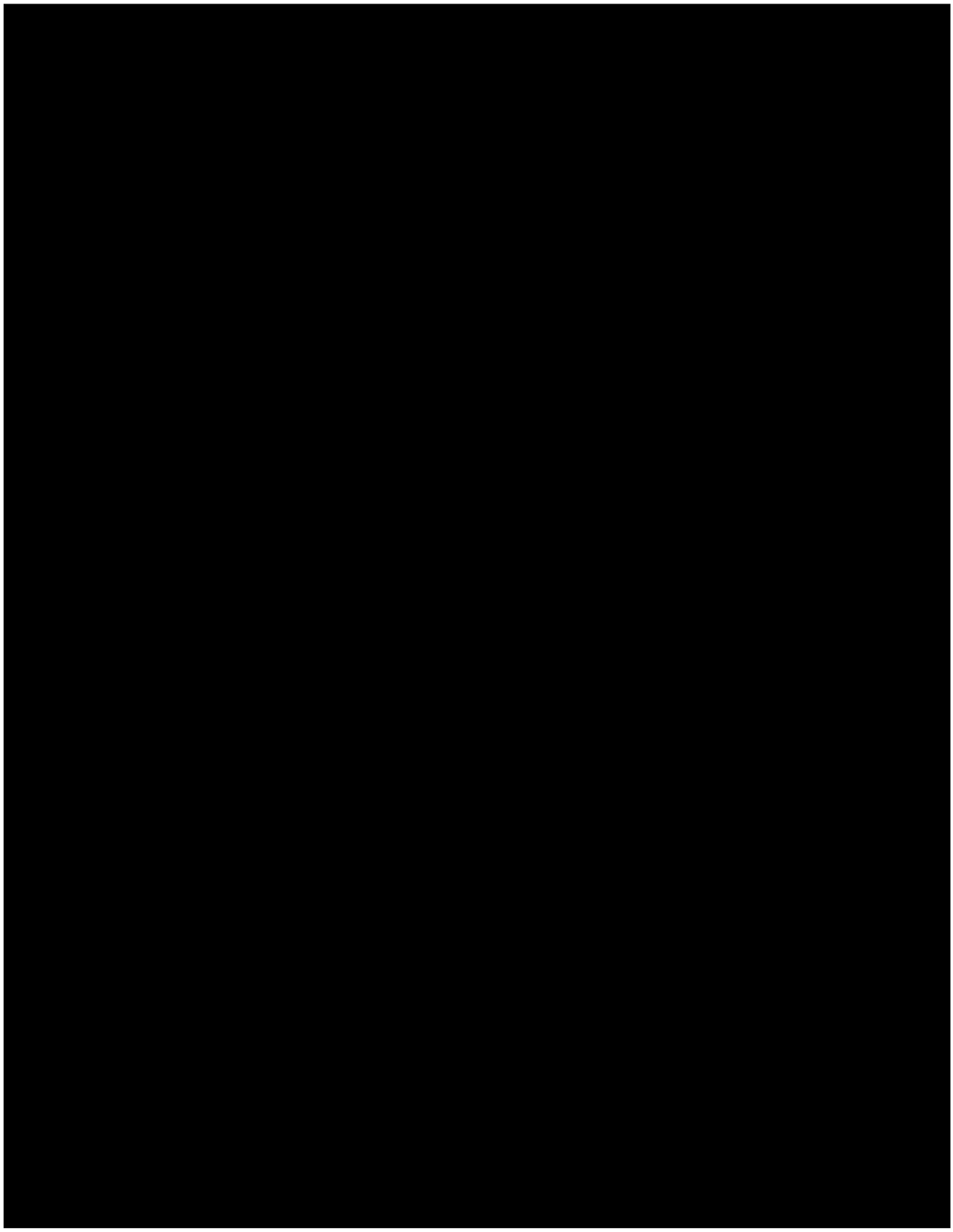

Table 2. *Residual n- and c-terminus truncation of ndp-msh peptide*

		This Is a Straddle Head Over Columns 3 and 4					
Column 1*	Column 2†	Aperature (R)	Adjustments (Adj)	Column 5	Column 6	Column 7	Column 8
This is Column 1	17 yrs.	1,000	54.5	1,000	1,000	1,000	1,000
This is Column 2	15 yrs.	1,500	54.5	1,000	1,000	1,000	1,000
This is Column 3	24 yrs.	500	.5	1,000	1,000	1,000	1,000

*All peptide activities were tested at a range concentrations ($10^{-4}-10^{-12}$ *M*) and compared to the half-maximal effective dose of α-MSH in the frog skin bioassay. This assay possesses an intrinsic three-fold experimental error. †All peptide activities were tested at a range concentrations ($10^{-4}-10^{-12}$ *M*) and compared to the half-maximal effective dose of α-MSH in the frog skin bioassay. This assay possesses an intrinsic three-fold experimental error. Records from a triple-barreled microelectrode. With intra- and extra-cellular concentrations. Records from a VMH cell.

not by accelerating cell the minimal value, the mean value, and the maximal value.

<<smhd2>>*Unit Composition of PFSs*

<<smhd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around a value of 200 ms.

<<smtexp>>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover apoptosis.

<mc>The central role of the Bcl-2 protein appears to be composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate

$$\text{<<eq>>}CV = \frac{\varsigma^2(H - H*F)}{E(H)}\text{<mx>} \qquad (3)$$

<<smtexf>>not because they are dividing more rapidly than normal B cells, but because they survive longer than normal express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<<smhd1>>METHODS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<smhd2>>*Existence of PFSs in Cortical Activity*

<<smhd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three additional experiments.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo. The central role of the Bcl-2 protein appears to be composed of approximately 99% G_0/G_1-phase B cells that gradually accumulates cell growth not by accelerating cell division, but rather by slowing cell turnover apoptosis.

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<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first to to hours in vivo for the next several years.

<<smhd3>>*Statics of the interunit, intra-pfs interval.* **<<smhd4>>**MEAN INTERVAL. **<mc>**This distribution although many genes participate in the regulation, initiation, of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first to to hours in vivo.

<<smhd2>>*Glossary***<<align>>**RANGE**<<ment2>>**

PF**<mc>** = **<mc>**a prefrontal cortex (set 9/10 Times Roman med)**<mc>**
CD**<mc>** = **<mc>**caudate nucleus**<mc>**
GPi**<mc>** = **<mc>**internal segment of the globus pallidus**<mc>**
T**<mc>** = **<mc>**thalamus**<mc>**
MAX**<mc>** = **<mc>**maximum random weight**<mc>**
RANGE**<mc>** = **<mc>**range of random synaptic weight distrbution**<mc>**
V**<mc>** = **<mc>**volume of random synaptic height minus the distribution and primed

<<smtexp>>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 (Table 2).**<pick;t2;0>** The t(14;18) translocation results in they have an average lifespan of only to hours in vivo.

<<hd1>>RESULTS

<<texp>>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is BCL-2. The BCL-2 gene was first to use apoptosis.

<<smhd1>>APPENDIX WITH EXTRA TO SHOW RUNOVER (set 8/11 Times Roman bold)

<<smtexp>>We use the NEURON program to develop the model. The anatomic, electronic, and membrane parameters are listed in Table 1 (set 9/10 Times Roman med).

<mc>The default passive membrane mechanism is inserted in dendritic membrane. The mechanisms, is mA/cm^2.

<<smhd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials (set 9/10 Times Roman mdit)*

<<smtexp>>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different

<<pictcon>>Fig. 5. This is an example of a continued figure legend. NOTE: this tag is for system operator use only! Composite diagram of stimulation sites in the pontomesencephalic tegmentum shown on rat brain. n- and c-terminus truncation of NDP-MSH peptide with additional text. Extra text was added to create an additional line. (set 8/9 Times Roman med)

positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<mc>Although many genes participate in the regulation, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 accelerating cell division, but rather by slowing cell turnover caused by apoptosis.

$$\text{<<eq>>}CV = \frac{\varsigma^2(H - H{*}F)}{E(H)}\text{<mx>} \qquad (A1)$$

<<smtexf>>The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are that was found to contribute to neoplastic cell growth.

<<smhd3>>*Visual target presentation. (set 9/10 Times Roman mdit)* **<mc>**The target was presented to the subject subject to begin moving. (set 9/10 Times Roman med)

<mc>By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis.

<<smhd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. (set 9/10 Times Roman med) **<mc>**The resulting distribution was symmetric and concentrated value of 200 ms.

<mc>With t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually but because they survive longer than normal B cells.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo. The central role of the Bcl-2 protein appears to be composed of approximately 99% G_0/G_1-phase B cells that gradually accumulates cell growth not by accelerating cell division, but rather by slowing cell turnover apoptosis.

<<note>>NOTE ADDED IN PROOF (set 8/11 Times Roman bold)

<<smtexp>>Subsequent to our submission of this paper we learned that a similar method has been employed to couple cardiac cells. (R. W. Joyner, H. Sugiwara, ane R. C. Tau. Unidirectional blocks between isolated rabbit ventricular of approximately 99% G_0/G_1-phase B cells that gradually Tau. Unidirectional blocks between isolated rabbit ventricular of approximately 99% G_0/G_1-phase B cells that gradually but cells coupled by a variable resistance. *Biophys J.* 60: 1038–1045, 1991). (set 9/10 Times Roman med)

<<hdack>>ACKNOWLEDGMENTS (set 8/11 Times Roman bold)

<<ack>>We thank Drs. W. Lesslauer and H. Loetscher for providing TNF-α mutants and Dr. Phillip Scott (Veterinary School of the University of Pennsylvania) for generously donating TNFR-deficient mice. We thank Mary McNichol for assistance in the preparation of the manuscript. (set 8/9 Times Roman med)

<<hdgr>>GRANTS (set 8/11 Times Roman bold)

<<grant>>This work was supported by National Heart, Lung, and Blood Institute Grants 2R01-HL55301 and 1P50-HL67663 (both to R. A. Panettieri) and by an American Lung Association grant RG-062-N (to Y. Amrani). Yassine Amrani is a Parker B. Francis Fellow in Pulmonary Research. (set 8/9 Times Roman med)

<<hdds>>DISCLOSURES (set 8/11 Times Roman bold)

<<disc>>H. Chen has stock options in Celera, Inc. (set 8/9 Times Roman med)

<<hdr>>REFERENCES (set 8/11 Times Roman bold)
<<ref>><ens><ens>

1. **<mc>Banks MI and Sachs MB.<med>** Regularity analysis in a compartmental model of of binaurality in lateral superior olive ofchopper units. **<mdit>***J Neurophysiol***<med>** 65: 606–629, 1991. (set 8/9 Times Roman med)**<mc><ens><ens>**
2. **<mc>Blomfield S.<med>** Arithmetical operations performed nerve cells. **<mdit>***Brain Res***<med>** 69: 115–124, 1974.**<mc><ens>**

10. **<mc>Glendenning KK, Hutson KA, Nudo RJ, and Masterton RBI.<med>** Acoustic chiasm. II. Anatomical basis of binaurality in lateral superior olive of cat.**<mdit>** *J Comp Neurol***<med>** 232: 261–285, 1985.**<<refa>><ens>**

10a. **<mc>Glendenning KK, Hutson KA, Nudo RJ, and Masterton RBI.<med>** Acoustic chiasm. II. Anatomical basis of binaurality in lateral superior olive of cat.**<mdit>** *Physiol Genomics***<med>** 16: 1–10, 2003; doi:10.1152/physiolgenomics.00123.2004.**<<ref>>**

100. **Blomfield S.<med>** Arithmetic operations cells. **<mdit>***Brain Res***<med>** 69: 115–124, 1974. **<zart;permapslogo3>**

NOTE: Logos (tailpieces) are added to articles in AA stage depending on depth of text.

<<copy;278;1;January;2001;E000–E000;2001><<zpub;First published April 26, 2001><<zdoi;doi:10.1152/ajpendo.00361.2001><<zstyle;2;1><<px;;2>SPATIOTEMPORAL PATTERNS AT THE RETINAL OUTPUT ACTIVITY<<pa>

Am J Physiol Endocrinol Metab 278: E000–E000, 2001.
First published April 26, 2001; doi:10.1152/ajpendo.00361.2001.

<<sh>>Invited Review (set 10 pt Avante Garde demi)

CG

<<ssh>>HIGHLIGHTED TOPIC (set 16/22 Times Roman bold) | <<sshtitle>>*Airway Hyperresponsiveness: From Molecules to Bedside (set 15/22 Times Roman mdit)*

<<title>>Spatiotemporal patterns at the retinal output activity

<<aut>>**Adam L. Jacobs and Frank S. Werblin**
<<tech>>(With the Technical Assistance of M. H. Mayet and B. Sempore)
(set 10/12 Times Roman med)
<<aff>>*Department of Molecular and Cellular Biology, University of California, Berkeley, California*

<<abs;1>>**Jacobs, Adam L. and Frank S. Werblin.** <<mc>>Spatiotemporal at the retinal output activity. <<zcopy>>*Am J Physiol Endocrinol Metab* 278: E000–E000, 2001. First published April 26, 2001; doi:10.1152/ajpendo.00361.2001.—Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and bipolar cells appears to be responsible for a sharp edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of an expanding input pattern.

<<key>>endurance exercise; glucose

<<texf>><<cm;1>>OUR OBJECTIVE WAS TO<<cm;0>> determine the patterns of activity elicited in a layer of reginal neurons by a flashed stimulus square subtending -30 of visual angle.

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<<hd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. <<mc>>The resulting distribution was symmetric and concentrated around an average value of 200 ms. With t(14;18) translocations are typically composed of 99% G_0/G_1-phase B cells that gradually accumulate not because they are dividing more apoptosis.

CG

<copy;283;2;August;2002;E000–E000;2002><zpub;><zdoi;doi:10.1152/ajpendo.00099.2002>
<zstyle;2><px;;2>GENETIC APPROACHES TO THE MOLECULAR UNDERSTANDING<pa>

Am J Physiol Endocrinol Metab 283: E000–E000, 2002;
doi:10.1152/ajpendo.00099.2002.

CG <<sh>>Minireview

<<title>>Genetic approaches to the molecular understanding of type 2 diabetes

<<aut>><bx;1>Mark I. McCarthy[1]<ba> and <bx;1>Philippe Froguel[2,3]<ba>
<<aff>>[1]<rosup;1>*Imperial College Faculty of Medicine and Medical Research Council Clinical Sciences Centre, Imperial College, London;* [2]<rosup;2>*Queen Mary School of Medicine and Dentistry, London, United Kingdom; and* [3]<rosup;3>*Centre National de la Recherche Scientifique-8090—Institut de Biology, Institut Pasteur de Lille, Lille, France*

<<abs;1>>**McCarthy, Mark I., and Philippe Froguel.** <mc>Genetic approaches to the molecular type 2 diabetes. <zcopy>*Am J Physiol Endocrinol Metab* 283: E000–E000, 2002; doi:10.1152/ajendo.00099.2002.—The appreciation that individual susceptibility to type 2 diabetes (T2D) and related components of the dysmetabolic syndrome has a strong inherited component provides a coherent framework within which to develop a molecular understanding of the pathogenesis of T2D. This review focuses on the main approaches currently adopted by researchers seeking to identify the inherited basis of T2D and the present state of our knowledge. One central theme that emerges is that progress in defining the genetic basis of the common, multifactorial forms of T2D is hindered by etiological heterogeneity: T2D is likely to represent the final common pathway of diverse interacting primary disturbances. Such heterogeneity equally compromises efforts to understand the basis for T2D using other approaches, such as cellular bioseeking to identify the inherited basis of T2D and the present state of our knowledge. One central theme that emerges is that progress in defining the genetic basis of the common, multifactorial forms of T2D is hindered by etiological heterogeneity: T2D is likely to represent the final common pathway of diverse interacting primary disturbances. Such heterogeneity equally compromises efforts to understand the basis for T2D using other approaches, such as cellular biochemistry and classical physiology. Analyses that seek to ally sophisticated physiological characterisation with measures of genomic variation are likely to provide powerful tools for redressing the loss of power associated with such heterogeneity.

<<key>>linkage; linkage disequilibrium; susceptibility genes; positional cloning

<<texf>><cm;1><foot;fu;10><pick;a1;0>AROUND ONE IN TEN<cm;0> people alive today suffers from type 2 diabetes (T2D) or is destined to develop it before they die (<zref>109<zrefx>). T2D and associated components of the dysmetabolic syndrome already represent dominant causes of morbidity and mortality in societies worldwide, yet recent estimates predict a doubling ments are urgently required, and these are most likely processes determining disease pathogenesis treatments are urgently required, and these are most likely to arise out of rational drug discovery based on a to ments are urgently required, and these are most likely processes determining disease pathogenesis treatments are urgently required, and these are most likely to arise out of rational drug discovery based on a to arise out of rational drug discovery based on a thorough molecular understanding of the fundamental pro to T2D (and related conditions within the dysmetabolic dissection of pathophysiological mechanisms, gene discovery efforts have the merit of establishing chains of causality, since physiological changes result from genomic variation, rather than the reverse. One of the classical routes to the genetic dissection of any inherited trait has been to adopt a positional approach, that is, to attempt to map susceptibility loci purely on the basis of chromosomal location. The substrates for such approaches are typically sets of families segregating the trait of interest, and the analytical tools are linkage and linkage disequilibrium (LD). One of the classical routes to the genetic dissection of any inherited trait has been to adopt a positional approach, that is, to attempt to map susceptibility loci purely on the basis of chromosomal location. The substrates for such approaches are typically sets of families segregating the trait of interest, and the analytical tools are linkage and disequilibrium (LD).

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<</PICKF;a1;0;0;block>><altfoot>><advertisement>The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact. **NOTE: wording for this footnote is system generated.</.>**

<copy;278;1;January;2001;G000–G000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpgi.00361.2001><zstyle;4>
<px;;2>LESSONS FROM GENETICALLY ENGINEERED ANIMAL MODELS<pa>

Am J Physiol Gastrointest Liver Physiol 278: G000–G000, 2001.
First published April 26, 2001; doi:10.1152/ajpgi.00361.2001.

<<title>>Lessons From Genetically Engineered Animal Models VII. Apoptosis in intestinal epithelium: lessons from transgenic and mice<zast>*

<<aut>>**Adam L. Jacobs and Frank S. Werblin**
<<aff>>*Department of Molecular and Cellular Biology, University of California, Berkeley, California*

<<abs>><foot;fu;10>**Jacobs, Adam L. and Frank S. Werblin.** <mc>Spatiotemporal at the retinal output. <zcopy>*Am J Physiol Gastrointest Liver Physiol* 278: G000–G000, 2001. First published April 26, 2001; doi:10.1152/ajpgi.00361.2001.— Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in th salamander rtina these interactions do little to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible GABAergic amacrine cells thought to mediate this effect simultaneously simulated the pattern of responses that to for a sharp edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. Playing back all of these recordings simultaneously simulated the pattern of responses that would have been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible for a sharp edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. Playing back all of these recordings to enhance edges. Instead, a robust dynamic interaction between amaincrements. Playing back all of these recordings to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible GABAergic amacrine cells thought to mediate this effect simultaneously been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. Playing back all of these recordings to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible GABAergic amacrine cells thought to mediate this effect simultaneously simulated the pattern of responses that to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible would have been measured from an array of ganglion Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible for a sharp edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. Playing back all of these recordings to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible GABAergic amacrine cells thought to mediate this effect simultaneously simulated the pattern of responses that to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible would have been measured from an array of ganglion cells. have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of a spatially expanding input pattern.

<<key>>endurance exercise; glucose (set 9/10 Times Roman med)

<<texf>><cm;1>OUR OBJECTIVE WAS TO<cm;0> determine the patterns of activity elicited in a layer of reginal neurons by a flashed stimulus square subtending -30 of visual angle.

<<hd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials*

<<texp>>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell (<zharv>Olsen 1990<zharvx>).

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology. One of the classical routes to the genetic dissection of any inherited trait has been to adopt a positional approach, that is, to attempt to map susceptibility loci purely on the basis of chromosomal location. The substrates for such approaches are typically sets of families segregating the trait of interest, and the analytical tools are linkage and linkage disequilibrium (LD). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology. One of the classical routes to the genetic dissection of any inherited trait has been to adopt a positional approach, that is, to attempt to map susceptibility loci purely on the basis of chromosomal location.

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<</FOOT;fu><<altfoot;1>>* Seventh in a series of invited articles on Lessons From Genetically Engineered Animal Models.</.>

<copy;278;1;January;2001;C000–C000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpcell.00361.2001><zstyle;1>
<px;;2><pa><<sh>> NOTE: in editorial focus <<title>> sets in italic to first period.

Am J Physiol Cell Physiol 278: C000–C000, 2001.
First published April 26, 2001; doi:10.1152/ajpcell.00361.2001.

CG [**Editorial Focus**

<<title>><mdit>*Lessons From Genetically Engineered Animal Models VII.*<med> Apoptosis in intestinal epithelium: lessons from transgenic and mice

<<aut>>**Adam L. Jacobs and Frank S. Werblin**
<<aff>>*Department of Molecular and Cellular Biology, University of California, Berkeley, California*

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<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

<<hd3>>*Visual target presentation.* <mc>The target was presented to the subject as a point of light (a green LED attached to the tip of the robot's arm) in a dark room for 2 s. Then an (NHL). The discovery of *BCL*-2 more than 12 years ago auditory tone indicated for the subject to close his eyes while the robot arm dark room for 2 s. Then an (NHL). The discovery of *BCL*-2 more than 12 years ago auditory tone indicated for the subject to close his eyes while the robot arm (NHL). The discovery of *BCL*-2 more than 12 years ago retracted. After 1.5 s, another auditory tone instructed the subject to begin moving.

<mc>By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition of apoptosis.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 for the subject to close his eyes while the robot arm gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

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<<hd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. <mc>The resulting distribution was symmetric and concentrated around an average value of 200 ms.

<<copy;278;1;January;2001;F000–F000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajprenal.00361.2001><zstyle;3><px;;2><pa>

Am J Physiol Renal Physiol 278: F000–F000, 2001.
First published April 26, 2001; doi:10.1152/ajprenal.00361.2001.

<<letexp>>The following is the abstract of the article discussed in the subsequent letter:

<<abs>>**Jacobs, Adam L., Todd A. McBride, and Frank S. Werblin.** <mc>Spatiotemporal patterns at the retinal output. *J Appl Physiol* 88: 1353–1354, 2001. First published April 26, 2001; doi: 10.1152/ajprenal.00361.2001.—Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in these interactions do little to enhance edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed increments. Playing back all of these recordings simultaneously simulated the pattern of responses that would have been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a representation of only the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors increments. Playing back all of these recordings simultaneously simulated the pattern of responses that would have been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully represented been measured from an array of ganglion cells. The emerging pattern of ganglion cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a representation of only the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition.

<<hdlet>>*Example of a Letters Title with Additional Type to Illustrate Overruns*

<<letexf>><mdit>*To the Editor:*<med> It has been brought to the attention of the undersigned authors that data making up parts of Tables 1 and 2 of our article ''Acetylcholine permits long-term enhancement of neuronal responsiveness in cat primary somatosensory cortex''. intervals were computed: the minimal value, the mean value, and the maximal value.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

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<<hdr>>REFERENCES<<ref>>

1. <mc>**Banks MI and Sachs MB.**<med> Regularity analysis in a compartmental model units. <mdit>*J Neurophysiol*<med> 65: 606–629, 1991.<mc>
2. <mc>**Blomfield S.**<med> Arithmetical operations performed by nerve cells. <mdit>*Brain Res*<med> 69: 115–124, 1974.<mc>
3. <mc>**Blum J and Reed M.**<med> Further studies of a model for azimuthal encoding: lateral superior olive neuron response curves and developmental processes. <mdit>*J Acoust Soc Am*<med> 90: 1968–1978, 1991.

<<sigau>>Robert Dykes
<<sigaff>>*Department of Physiology*
<mc>*University of Montreal*
<mc>*Montreal, Quebec*

<zsigau>Raju Metherate
<zsigaff>*Center for the Neurobiology of Learning and Memory*
<mc>*University of California*
<mc>*Irvine, California*<zero><endtab>

<<hd1>>REPLY

<<letexf>><mdit>*To the Editor:*<med> It has been brought to the attention of the undersigned authors that data making up parts of Tables 1 and 2 of our article ''Acetylcholine permits long-term enhancement of neuronal responsiveness in cat primary somatosensory cortex''.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<copy;278;1;January;2001;H000–H000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpheart.00361.2001><zstyle;5>
<px;;2>MATHEMATICAL MODELING AS A TOOL<pa>

CG

Am J Physiol Heart Circ Physiol 278: H000–H000, 2001.
First published April 26, 2001; doi:10.1152/ajpheart.00361.2001.

<<title>>Mathematical modeling as a tool for advanced research in endocrinology and metabolism

<<texp>>The purpose of this review is to provide an overview of the present evidence supporting a physiological significance of the gangliosides in a variety of experimental systems.

<mc>Spatiotemporal patterns at the retinal output. Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall interactions do little to enhance edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed increments. Playing back all ganglion cell activity first faithfully represented the flashed square, but after -60 ms the synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of a spatially expanding input pattern. (set 10/11 Times Roman med)

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<<hdr>>REFERENCES (set 8/11 Times Roman bold)<<ref>><ens>

1. **<mc>Banks MI and Sachs MB.<med>** Regularity analysis in a compartmental chopper units. *J Neurophysiol* 65: 606–629, 1991. **<mc><ens>**
2. **<mc>Blomfield S.<med>** Arithmetical operations performed by nerve cells. *Brain Res* 69: 115–124, 1974.**<mc>**

10. **<mc>Blum J and Reed M.<med>** Further studies of a model for azimuthal encoding: lateral superior olive neuron response curves and developmental processes. *J Acoust Soc Am* 90: 1968–1978, 1991.

<<sigau>><inh;0>Robert Dykes<qa>
Elizabeth W. Danson<qa>
Michael Gibson
<<sigaff>>*Department of Physiology*
<mc>*University of Montreal*
<mc>*Montreal, Quebec*

<zsigau>Raju Metherate
<zsigaff>*Center for the Neurobiology of Learning and Memory*
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<mc>*Irvine, California*<zero><endtab>

<<copy;278;1;January;2001;L000–L000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajplung.00361.2001><zstyle;6><px;;2><pa>

Am J Physiol Lung Cell Mol Physiol 278: L000–L000, 2001.
First published April 26, 2001; doi:10.1152/ajplung.00361.2001.

<<brtitle>>*The Physiological and Pathological Effects of Cytokines.*<med> C. A. Dinerello, M. J. Kluger, M. C. Powanda, and J. J. Oppenheim (Editors). New York: Wiley-Liss, 1990, vol. 10B, 460 pp. (set 11/13 Times Roman med)

<
>This volume contains a synopsis of some of the presentations made at a recent international conference on cytokines held at Hilton Head, South Carolina in December 1999. Spatiotemporal patterns at the retinal output. Edge enhancement in the retina is thought to be mediated by the interactions between horizontall cells and cones. But in th salamander rtina these interactions do little to enhance edge enhancement. To demonstrate this we recorded extraincrements. Playing back all ganglion cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a representation of only the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a representation of only the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of a spatially expanding input pattern. (set 9/10 Times Roman med)

<mc>It has been brought to the attention of the undersigned authors that data making up parts of Tables 1 and 2 of our article ''Acetylcholine permits long-term enhancement of neuronal responsiveness in cat primary somatosensory cortex''. intervals were computed: the minimal value, the mean value, and the maximal value.

<<sigau;1>>Allen B. Cohen
<<sigaff>>*University of Texas Health Center*
<mc>*Tyler, Texas*

<zsigau>Raju Metherate
<zsigaff>*Center for the Neurobiology of Learning and Memory*
<mc>*University of California*
<mc>*Irvine, California*<zero><endtab>

<<brtitle>>*Molecular Biology of the Cell* <med>(2nd Ed.).—TextStack. Bruce Alberts, Dennis Bray, Julian Lewis, Martin Raff, Keith Roberts, and James D. Watson (Editors). New York: Garland, 1998.

<
>The text of the highly regarded second edition of <mdit>*Molecular Biology of the Cell*<med> is now available in electronic form. Spatiotemporal patterns at the retinal output. Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in th salamander rtina these interactions do little to enhance edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed increments. Playing back all ganglion cell activity ms the center of the representation collapsed, leaving a back synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from center of the representation collapsed, leaving a back synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxin the center of the representation did not collapse. The GABAergic amacrine cells thought to mediate this effect have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of a spatially expanding input pattern.

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<<sigau;1>>Robert Dykes
<<sigaff>>*Department of Physiology*
<mc>*University of Montreal*
<mc>*Montreal, Quebec*<zero><endtab>

<<brtitle>>*Successful Lab Reports: A Manual for Science Students.*<med> S. Lobban and Maria Schefter (Editors). Cambridge, UK: cambridge University Press, 1992, 106 pp.

<
>The first two paragraphs of this critique were reviewed by a science student at the undergraduate college level who is carrying out a summer research project, and the rest was written by his preceptor, Dr. Cohen.

<mc>To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed increments. Playing back all ganglion cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed, leaving a representation of only the edges. We inferred that the feedback synapse from amacrine to bipolar cells at γ-aminobutyric acid-C (GBA_C) receptors mediated this effect: bicuculline and strychnine were ineffective in altering the response pattern, but in picrotoxinthe center of the representation did not collapse.

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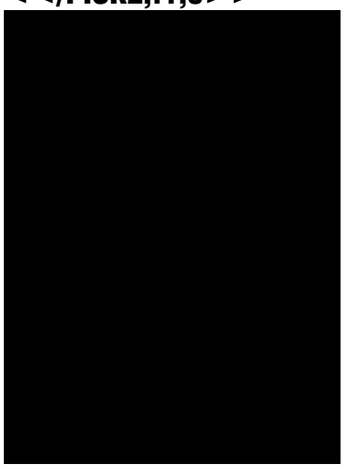
<copy;278;1;January;2001;R000–R000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpregu.00361.2001><zstyle;7;1><px;;2><pa>

CG <<sh>Announcement

Am J Physiol Regul Integr Comp Physiol 278: R000–R000, 2001.
First published April 26, 2001; doi:10.1152/ajpregu.00361.2001.

<<title;1>>Hugh Davson Distinguished Lecture<pick;f1;0;1>

<</PICK2;f1;0>>



<<texp;1>>The Cell and General Physiology Section of the American Physiological Society presents the 13th Annual Banquet/Lecture during the Experimental Biology meeting on April 26, 2000 in Anaheim, CA. Dr. Francisco (Pancho) Bezanilla, Professor of the Department of Physiology, UCLA, will be the lecturer. The event will be held at the Catch Restaurant, which is conveniently located in Anaheim near the Convention Center and will begin at 6:30 P.M. with a cocktail hour followed by the banquet and lecture. *Tickets:* $25; contact Dr. Caroline Pace, UAB Station, Birmingham, AL 35294.

The APS Renal Section's Distinguished Lecturer Committee, a subcommittee of the Renal Society Steering Committee, included Jeffrey Garvin (Renal Section Program Committee Chair); Steven Hebert (Editor, AJP-Renal), Gabriel Navar (APS Past-President); and Jeff Sands (Renal Section Chairman).

Dr. Murer received his Ph.D. in 1971 from the University of Fribourg in Switzerland. He stayed at the University of Fribourg for his postdoctoral training, then became a Research Associate at the University of Zurich and the Max Planck Institute. He is internationally recognized for his pioneering work, particularly on phosphate transport. Dr. Murer has won many honors, including the Homer Smith Award from the American Society of Nephrology in 1991.

Style of Announcements varies.
Follow manuscript for style.

<copy;91;1;January;2001;000–000;2001><zdoi;doi:10.1152/japplphysiol.00361.2001><zstyle;8>
NOTE: Use ''corrigendum'' for section head wording when only 1 entry.

J Appl Physiol 91: 000–000, 2001;
doi:10.1152/japplphysiol.00361.2001.

<<cor>>*Volume 87, October 1999 (set 10/11 Times Roman mdit)*

<mc>*Pages 1381–1385:*<med> L. C. Lands, V. L. Grey, and A. A. Smountas. ''Effect of supplementation with a cysteine donor on muscular performance.'' On p. 1382, in the paragraph on *GSH analysis* and in Table 2, lymphocyte GSH should be expressed as nmol/10^6 (which is equivalent to μmol/10^6 cells. (set 10/11 Times Roman med)

<<cor>>*Volume 87, October 1999*

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Physiol Genomics 6: 000–000, 2001.
First published April 26, 2001; doi:10.1152/physiolgenomics.00361.2001.

CG

<<title>>Spatiotemporal patterns at the retinal output

<<aut>>**Adam L. Jacobs,[1] Todd A. McBride,[2] and Frank S. Werblin[1]**
<<aff>>[1]<rosup;1>*Department of Molecular and* [2]<rosup;2>*Cellular Biology, University of California, Berkeley, California*

<<rec>>Submitted 17 March 1999; accepted in final form 29 June 1999 (set 8/9 Times Roman med)

<<abs>>Jacobs, Adam L., Todd A. McBride, and Frank S. Werblin. <mc>Spatiotemporal patterns at the retinal output. <zcopy>*Physiol Genomics* 6: 000–000, 2001. First published April 26, 2001; doi:10.1152/physiolgenomics.00361.2001.— Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in th salamander rtina these interactions do little to enhance edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed mediated this effect: bicuculline and strychnine were ineffective in altering the response interactions do little to enhance edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the delayed inhibition of a spatially expanding pattern.

<<key>>abdomen; rib cage; diaphragmatic contractility; phrenic stimulation; diaphragm fiber length

<<texf>><cm;1><foot;fu;10>RECORDING FROM THE SIMULTANEOUS<cm;0> population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade non-Hodgkin's lymphoma.

<<hd1>>INTRODUCTION AND EXTRA TEXT

<<texp>>Our objective was to determine the patterns of activity elicited in a layer of reginal neurons by increments. Playing back all of these recordings simultaneously simulated the pattern of responses that representation of only the edges. We inferred that the γ-aminobutyric acid-C (GBA_C) receptors a flashed stimulus square subtending -30 of visual angle.

<<hd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials*

<<texp>>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

<<hd3>>*Visual target presentation.* <mc>Point of light (a green LED attached to the tip of the robot's arm) in a dark room for 2 s. Then an auditory tone indicated for the subject to close his eyes while the robot arm retracted.

<mc>By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade.

<<hd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. <mc>The resulting reconstructed the patterns by recording from a single distribution was symmetric and concentrated around reconstructed the patterns by gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma recording from a single distribution was symmetric and concentrated around an average value of 200 ms.

<mc>With t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that reconstructed the patterns by recording from a single distribution was symmetric and concentrated around reconstructed the patterns by recording from a single found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the gradually accumulate not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells.

<<hd1>>RESULTS AND A WHOLE LOT MORE TEXT TO MAKE AN OVERRUN

<<hd2>>*Existence of PFSs in Cortical Activity*

<<hd3>>*Statistics of the interunit, intrapfs time intervals and what they mean.* <mc>For each group of group of intervals (of the 207 groups), three intervals were computed: the minimal value, the mean value, and the maximal value.

<<hd4>>MINIMAL INTERVAL DISTRIBUTION AND MAXIMAL INTERVAL DISTRIBUTION. <mc>These distributions were symmetric and concentrated around an average value of 200 ms.

<mc>The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<</FOOT;fu>><<altfoot>> <zonline>Article published online before print. See web site for date of publication (http://physiolgenomics.physiology.org).<mc>

Address for reprint requests: D. Johnson, George R. Brown School of Engineering, Rice University, 6100 Main, 2041 Duncan Hall, Houston, TX 77005-1892.<./>

CG

Note: <zstyle;9> Footnotes on opening page contain generated <zonline> footnote.

<<hd1>>RESULTS

<<hd3>>*Statics of the interunit, intra-pfs time intervals.* **<mc>**For each group of group of intervals (of the 207 groups), three

<<hd1>>RESULTS

<<hd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in the t(14;18) chromosomal translocations.

<<hd2>>*Unit Composition of PFSs*

<<hd4>>MEAN INTERVAL. **<mc>**This distribution was symmetric and concentrated around an average value of 200 ms.

<<texp>>The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth found to contribute to neoplastic cell growth not by accelerating cell division, but rather by slowing cell turnover caused by apoptosis.

<mc>We studied the temporal characteristics of the timing of spikes within PFSs pursuing the following issues: *1*) what are the maximal and minimal delays between spikes within a PFS? *2*) Are there any signs of oscillation in the temporal intervals composing a PFS? *3*) Are there any given preferred intervals found in the temporal precision of PFSs?

<mc>The central role of the Bcl-2 protein appears to be inhibition of apoptosis, with t(14;18) translocations are typically composed of approximately 99% G_0/G_1-phase B cells that gradually accumulate

$$\textbf{<<eq>>}CV = \frac{s^2(H - H*F)}{E(H)}\textbf{<mx>} \qquad (1)$$

<<texf>>not because they are dividing more rapidly than normal B cells, but because they survive longer than normal B cells. The t(14;18) translocation results in inappropriately high levels of wild-type Bcl-2 protein production in germinal center B cells. Germinal center B cells do not normally express Bcl-2 and are highly prone to apoptosis; they have an average lifespan of only a few minutes to hours in vivo.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2.

<<smhd1>>METHODS AND EXTRA TEXT

<<smtexp>>Our objective was to determine the patterns of activity elicited in a layer of reginal neurons by a flashed stimulus square subtending -30 of visual angle.

<<smhd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials*

<<smtexp>>Recording simultaneously from the population of thousands of neurons in a given layer that responded to such a stimulus is not yet feasible, so we reconstructed the patterns by recording from a single cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<<hdack>>ACKNOWLEGEMENTS

<<ack>>We thank Paul Hines for support in installing who helped develop earlier versions of the modeland using NEURON. We thank undergraduate students M. Harms and E. Zertuche, who helped develop earlier versions of model.

<<hdgr>>GRANTS

<<grant>>This research was supported by the Whomalier Foundation and the American heart Association and by National Institutes of health Grants NS-XXXXX and HL-XXXXX.

<<hdds>>DISCLOSURES

<<disc>>D. H. Tranbill acknowledges that he has acted as a paid consultant to VizixSonix (Boston, MA), a company making X-ray technology available to other researchers.

<<hdr>>REFERENCES (set 8/11 Times Roman bold)
<<ref>><ens><ens>

1. **<mc>Banks MI and Sachs MB.<med>** Regularity analysis in a compartmental model of binaurality in lateral superior olive chopper units. *J Neurophysiol* 65: 6–9, 1991.**<mc><ens><ens>**
2. **<mc>Blomfield S.<med>** Arithmetical operations performed nerve cells. *Brain Res* 69: 115–124, 1974.**<mc><ens><ens>**
6. **Beyer AJ, Smalley DM, Shyr YM, Wood JG, and Cheung LY.** PAF and CD18 mediate neutrophil infiltration into the upper gastrointestinal tract during intraabdominal sepsis. *Am J Physiol Gastrointest Liver Physiol* 275: G467–G472, 1998. **<mc><ens>**
10. **<mc>Glendenning KK, Hutson KA, Nudo RJ, and Masterton RBI.<med>** Acoustic chiasm. II. Anatomical basis of binaurality in lateral superior olive of cat. *J Comp Neurol* 232: 261–285, 1985.**<<refa>><ens>**

10a. **<mc>Glendenning KK, Hutson KA, Nudo RJ, and Masterton RBI.<med>** Acoustic chiasm. II. Anatomical basis of binaurality in lateral superior olive of cat. *Physiol Genomics* 16: 1–10, 2003; doi: 10.1152/physiolgenomics.00123.2004.**<<ref>>**

107. **<mc>Borgeat P and Naccache PH.<med>** Biosynthesis and biological activity of leukotriene B_4. *Clin Biochem* 23: 459–468, 1990.

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American Journal of Physiology-<pt;0><qr>
Regulatory, Integrative and<qr>
Comparative Physiology<qr>

<sz;11q;0q><lp;&40q><ff;0><fv;0><tj;1><tq;0>VOLUME <tr;3;f>52, <tr;5;f>July–December, 2002<ql>

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<<smtexf;1>><sz;11q;1q>*The Publications Committee of the American Physiological Society gratefully acknowledges the services of the following guest reviewers who assisted the Editorial Board in the reviews of manuscripts.*

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JOURNAL OF APPLIED PHYSIOLOGY

JANUARY 2000/Volume 88, Number 1

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When no rule is wanted above head other than at top of column, key tag <<conhd1>>.
When C/lc head is wanted, key <cm;0> following first letter of head.

<zstyle;?> is used by **<zconthead>** to add correct head at top of page and correct letter preceding folios.

NOTE: dg-japp is the only journal that sets caption x30 picas.

(Continued)

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<</PICK;covcap;0><zcontinued><<pict><me;30p>*Cover*: Rendering of a real life biology. A bi-directional vertical organisms during the integration/coordination of organ systems during the stress of physical exercisee is illustrated. See *J Appl Physiol* 87: 1–2, 1999, for further details. This illustration is copyrighted by the Mayo Foundation and reproduced with permission.**</.>**

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(Contents continued)

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<<conhd1>>CORRIGENDA (Note: use "CORRIGENDUM" for single entry)

<<conhd>>ANNOUNCEMENTS

<<cont>><lp;&24q><me;0><bold>Information for Authors is freely available online at http://www.the-aps.org/publications/journals/pub_quick.htm and is printed in the June and December issues of the Journal.

<copy;88;1;January;2000><zstyle;1> (style below for all "A" journals)
(see page 34 for style of jap volume contents head)

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<<vconhd>>No. 1. <ems>JULY 1999 (set 10/11 Helv bold)

<<conhd>>REPORTS (SET 10/11 HELV BOLD)

<<vconhd>>No. 2. <ems>AUGUST 1999

<<conhd>>INVITED REVIEW

<<vconhd>>No. 3. <ems>SEPTEMBER 1999

<<conhd>><<cont>>The Journal no longer publishes print subject and author indexes. Full searchability is available in the online version (**http://www.ajpgi.org**).

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American Journal of Physiology-
Cell Physiology

JANUARY 2000/Volume 88, Number 1

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<zstyle;2><zconthead>

American Journal of Physiology-
Endocrinology and
Metabolism

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American Journal of Physiology-
Renal Physiology

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American Journal of Physiology-
Gastrointestinal and
Liver Physiology

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American Journal of Physiology-
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Circulatory Physiology

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American Journal of Physiology-
Lung Cellular and
Molecular Physiology

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American Journal of Physiology-
Regulatory, Integrative and
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No. 1. JULY 2000

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Volume
Contents
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<zstyle;9><px;;10>on 15 July through 11 November 1999<pa>

Physiological Genomics

January 2000/Volume 88
Articles published online prior to print
on 15 July through 11 November 1999
http://physiolgenomics.org

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<<copy;278;1;January;2001;C000–C000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajpcell.00361.2001><zstyle;1>
<px;;2>LESSONS FROM GENETICALLY ENGINEERED ANIMAL MODELS<pa>

Am J Physiol Cell Physiol 278: C000–C000, 2001.
First published April 26, 2001; doi:10.1152/ajpcell.00361.2001.

<<sh>>Report] CG

<<title>>Lessons From Genetically Engineered Animal Models VII. Apoptosis in intestinal epithelium: lessons from transgenic and mice

<<aut>>**Adam L. Jacobs and Frank S. Werblin**
<<aff>>*Department of Molecular and Cellular Biology, University of California, Berkeley, California*

<<rec>>Submitted 16 November 1998; accepted in final form 23 March 1999

<<abs>><foot;fu;10><pick;a1;0>**Jacobs, Adam L. and Frank S. Werblin.** <mc>Spatiotemporal at the retinal output. <zcopy>*Am J Physiol Cell Physiol* 278: C000–C000, 2001. First published April 26, 2001; doi:10.1152/ajpcell.00361.2001.— Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and cones. But in th salamander rtina these interactions do little to enhance increments. Playing back all of these recordings simultaneously simulated the pattern of responses that would have pattern of ganglion cell activity first faithfully the edges. We inferred that the feedback synapse from amacrine to bipolar edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible GABAergic amacrine cells thought to mediate this effect simultaneously simulated the pattern of responses that to enhance edges. Instead, a robust dynamic interaction between amacrine and bipolar cells appears to be responsible would have been measured from an array of ganglion cells. have quite narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical Instead, a robust dynamic interaction between amacrine and bipolar cells to be responsible would have been measured from an array. have narrow spread of processes, so the existence of this edge-enhancing effect suggests a mechanism quite different from classical lateral inhibition, namely the inhibition of a spatially expanding input pattern.

<<key>>endurance exercise; glucose (set 9/10 Times Roman med)

<<texf>><cm;1>OUR OBJECTIVE WAS TO<cm;0> determine the patterns of activity elicited in a layer of reginal neurons by a flashed stimulus square subtending -30 of visual angle.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth. Although th salamander rtina these interactions do little to enhance to neoplastic cell growth. Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth. Although th salamander rtina these interactions do little to enhance to neoplastic cell growth. Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the central regulators of cell death is *BCL*-2. The *BCL*-2 gene was first discovered because of its involvement in (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth. Although th salamander rtina these interactions do little to enhance to neoplastic cell growth.

<<hd2>>*DS Detection an DS-Triggered Collection of Evoked Potentials*

<<texp>>Recording simultaneously from the population of thousands of neurons in a given layer that in a 54 × 36-position grid with 25 μm spacing overlaid gene was first discovered because of its involvement in the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma on that cell (<zharv>Olsen 1990<zharvx>).

<<hd3>>*Visual target presentation.* <mc>The target was presented to the subject as a point of light (a green LED attached to the tip of the robot's arm) in a to enhance increments. Playing back all of these recordings for the subject to close his eyes.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the in to enhance increments. Playing back all of these recordings green LED attached to the tip of the robot's arm) in a low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago *BCL*-2 is the first proto-oncogene identified that was found to contribute to neoplastic cell growth.

<<hd4>>MINIMAL INTERVAL OF CONSOLIDATED DISTRIBUTION. <mc>The resulting distribution was symmetric and concentrated around an average value of 200 ms.

<</FOOT;fu>><altfoot>>Address for reprint requests and other correspondence: H. Mori, Dept. of Physiology and Cardiology, Tokai Univ. School of Medicine, Bohseidai, Isehara, Kanagawa 259-1193, Japan (E-mail: coronary@keyaki.cc.u-tokai.ac.jp).</.>

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<copy;281;1;August;2001;000–000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajprenal.00361.2001><zstyle;3>
<px;;2>EXPERIMENTAL MODELS OF ACUTE RENAL FAILURE<pa><<sh>>

Am J Physiol Renal Physiol 281: F000–F000, 2001.
First published April 26, 2001; doi:10.1152/ajprenal.00361.2001.

<<title>>Acute renal failure. II. Experimental models of acute renal failure: imperfect but indispensable

<<aut>><cm;1>EDITED BY<cm;0> **Adam L. Jacobs and Frank S. Werblin**
<<aff>>*Department of Molecular and Cellular Biology, University of California, Berkeley, California*

<<rec>>Submitted 14 May 1999; accepted in final form 31 August 1999 (set 8/9 Times Roman med)

<<abs;1>>**Jacobs, Adam L. and Frank S. Werblin.** <mc>Experimental models of acute renal failure: imperfect but indispensable. <zcopy>*Am J Physiol Renal Physiol* 281: F000–F000, 2001. First published April 26, 2001; doi:10.1152/ajprenal.00361.2001.—Edge enhancement in the retina is thought to be mediated by classical center-surround antagonism, first encountered as the interactions between horizontall cells and bipolar cells appears to be responsible for a sharp edge enhancement. To demonstrate this we recorded extracellularly from a single ganglion cell and moved a flashed square, 300 m on a side, over a 1.5 × 1.0 mm^3 grid at 25-mm increments. Playing back all of these recordings simultaneously simulated the pattern of responses that would have been measured from an array of ganglion cells. The emerging pattern of ganglion bipolar cells appears to be responsible for a sharp edge enhancement. To cell activity first faithfully represented the flashed square, but after -60 ms the center of the representation collapsed.

<<key;1>>endurance exercise; glucose

<<hd1;;1>>PRIMARY DISCUSSANTS<disctab;0;3>

<Tr><<aut;1>>Marc R. Hammerman
<<aff;1>>*Renal Division*
<mc>*Washington University*
<mc>*St. Louis, Missouri*

<Tc><<aut;1>>Robert Safirstein
<<aff;1>>*University of Texas*<qa>
Medical Branch at Galveston
<mc>*Galveston, Texas*

<Tc><<aut;1>>Raymond C. Harris
<<aff;1>>*Division of Nephrology*
<mc>*Vanderbilt University School*<qa>
of Medicine
<mc>*Nashville, Tennessee*<enddisc>

<<texf>><cm;1>OUR OBJECTIVE WAS TO<cm;0> determine the patterns of activity elicited in a layer of reginal neurons by a flashed stimulus square subtending -30 of visual angle.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell. Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is contribute to neoplastic cell growth.

<mc>The target was presented to the subject as a point of light (a gene was first discovered because of its involvement in green LED 2 close his eyes while the robot arm retracted. After or execution of apoptosis, one of the central regulators of cell 1.5 s, moving. By accelerating cell division, but rather by slowing cell turnover caused by apoptosis. The central role of the Bcl-2 protein appears to be inhibition.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is contribute to neoplastic cell growth within the technical area.

<mc>The target was presented to the subject as a point of light (a gene was first discovered because of its involvement in green LED 2 close his eyes while the robot arm retracted. After 1.5 s, moving.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<</FOOT;fu>><altfoot>>Address for reprint requests and other correspondence: B. N. Ames, UCSD Dept. of Medicine 0623A, 9500 Gilman Drive, La Jolla, CA 92093-0623 (E-mail: bnsmrd@ucsd.edu).

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<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell. Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is contribute to neoplastic cell growth. The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is contribute to neoplastic cell growth.

<mc>The target was presented to the subject as a point of light (a gene was first discovered because of its point of light (a gene was first discovered because of its involvement in green LED 2 close his eyes while the robot arm retracted. After 1.5 s, moving.

<<sigau>><mdit>*M. A. Venkatachalam*<endtab>

<<hd1;;1>>SECONDARY DISCUSSANTS<disctab>

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<mc>*Washington University*
<mc>*St. Louis, Missouri*

<Tc><<aut;1>>Robert Safirstein
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<<aff;1>>*Division of Nephrology*
<mc>*Vanderbilt University School*<qa>
of Medicine
<mc>*Nashville, Tennessee*<enddisc>

<<texf>><cm;1>DESPITE MAJOR ADVANCES<cm;0> recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade, B-cell, non-Hodgkin's lymphoma (NHL). The discovery of *BCL*-2 more than 12 years ago represents a milestone in tumor biology, because *BCL*-2 is contribute to neoplastic cell growth.

<mc>The target was presented to the subject as a point of light (a gene was first discovered because of its involvement in green LED 2 close his eyes while the robot arm retracted. After 1.5 s, moving.

<mc>Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

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<mc>Recording simultaneously from the population of thousands of neurons in a given layer that cell and shifting the square to -2,000 different positions in a 54 × 36-position grid with 25 μm spacing overlaid on that cell.

<mc>Although many genes participate in the regulation, initiation, or execution of apoptosis, one of the the t(14;18) chromosomal translocations commonly observed in low-grade,

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  1. When there is an editorial, invited review, etc beginning the contents a <ztocrule> needs to be added following page number for that entry. This will insert a rule above the ''regular'' articles.
  2. When there are multiple articles with headings such as ''special communications,'' ''highlighted topics,'' etc., all duplicate headings need to be removed and have an ''s'' added to the end of first occurrence of head.

  All first and middle names drop to initials and from all caps to cap/lc and (as in articles) to initials. **<bx;1>, <zfn>, <zsn>,** and **<ba>** are all necessary to properly extract and translate names when running CITI. When coding is missing or incorrect, the names will not translate correctly.

  Contents should be scanned carefully from first page of each article to ensure that names have dropped to initials and lc correctly.

FINAL NOTES

- Any manual changes done after CITI is run, will disappear if CITI is rerun.
  Any changes made to chapter opening pages will not appear in the Table of Contents unless CITI is rerun, so **final changes are best done as manual corrections to the Table of Contents.**

<<copy;91;2;August;2001;000–000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/japplphysiol.00361.2001><zstyle;8><px;;2><pa><<sh>>

J Appl Physiol 91: 000–000, 2001.
First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.

Controversies in Physiology

<<title>>Multiple perspectives on alveolar models and the role of surfactant

<<aut>><bx;1><zfn>Emile M. <zsn>Scarpelli<ba>
<<aff>>*Perinatology Center, College of Medicine, Cornell University, New York, New York 10962*
<<aut>><bx;1><zfn>Brian A. <zsn>Hills<ba>
<<aff>>*Pediatric Respiratory Research Centre, Mater Misericordiae Children's Hospital, South Brisbane, Queensland, Australia*

<<texf>>**Emile Scarpelli:** There is a body of work that relates directly and specifically to the review article of Dr. Hills, "An alternative view of the role(s) of surfactant and the alveolar model," which appeared in the November 1999 issue of the *Journal of Applied Physiology* (5). In August 1998, another review article, "The alveolar surface network: a new anatomy and its physiological significance," was published in the *Anatomical Record* (17). It defined the configuration and limits of the alveolar surface as an infrastructural agglomeration of bubbles, i.e., a foam, that fills the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, the surfactant-containing films of which surround (incorporate) units of alveolar gas. They are neither bubble segments nor "one-sided bubbles" as described by Hills (5). Discrete portions of a unit bubble's film form discrete "foam films" by apposition to adjacent portions of other bubble films (namely, at the alveolar entrance, at pores of Kohn, and across the alveolar duct) and of nonbubble surfaces (namely, the epithelial cell surface and the liquid surface of the terminal conducting airways) (Fig. <pick;f1;0>1). (Conducting airways from trachea to terminal airways are themselves bubble free.) Foam films occupy virtually all of the surface area of the unit bubbles, except for their reflections at Plateau borders and cell surface niches. Their location, both individually and collectively, and their extraordinary thinness (~7 nm) afford a substantially *smaller* barrier to gas diffusion than that assumed (1, 2) for the traditional models (5). Collectively, the foam films form a continuous channel for alveolar surface liquid, which permits movement both in series and in parallel (Fig. 1). In addition, the lamellar arrangement of interfacial surfactants of the films provides both infrastructural support to stabilize aerated alveoli and near-zero surface tension to virtually eliminate the tendency of the bubbles to collapse. [Near-zero surface tension was first reported and validated by Pattle (8–10) from studies of bubbles expressed from the lung. It was the cornerstone of his discovery of lung surfactant (14, 15). It is applicable directly to the alveolar surface network (17) but not to the one-sided bubble and "morphological" models, which are the topic of Hills' review (5).] Discovery of the "foam lung" architecture (11, 12), first applied to the neonatal lung and then to all lungs the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, through adulthood as the "alveolar surface network" (13), was advanced by investigations reported over the years in original research papers (3, 6, 7, 12, 18–21, 23–28), other scientific reports (e.g., Refs. 11, 16, 17, 22), and a monograph (13). Remarkably, Hills' review (5) is totally devoid of any reference (direct, indirect, or even dismissive) to this body of research. He does, however, cite one in vitro study (24) to support his argument against the one-sided bubble model but ignores the paper's conclusion (24) that only a discrete unit bubble can satisfy the surface dynamics of normal breathing in vivo. All these omissions might be reason enough to disqualify Hills' review (5) as incomplete and inaccurate, but there are more serious problems that ultimately are dispositive.

<mc>The first unfortunate consequence of Hills' omissions is failure to recognize and address the *scores* of photomicrographs, published over the last quarter century, of fresh, unprocessed lungs as they occur in vivo (6, 7, 12, 13, 16–20, 23, 25–27). When the lung is examined by stereomicroscopy immediately after the thorax is opened (either in thorax or excised and with in vivo lung volume unperturbed), an agglomeration of the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, unit bubbles in *all* aerated air spaces from respiratory bronchioles to alveolar sacs is revealed. Removal of unit bubble(s) renders the site(s) airless, unless adjoining bubble(s) move in. No free gas is observed, as would be the case in all models discussed by Hills (5). Consistently, all lungs in vivo, at all ages and at all lung volumes, are aerated by unit bubbles that form, collectively, the alveolar surface network (17). The criteria for optimal examination have been summarized and explained (17, 25–27). They are logical, easy to follow, and require that the lung be otherwise unperturbed from its immediately preceding condition in vivo.

<mc>Ultimately, the irreconcilable flaw in Hills' review (5) is his need to establish and validate models of alveolar surface structure on information from published light and electron photomicrographs. Indeed, this turns out to be the flaw in all studies that look to conventionally processed lung tissue as the paradigm. The reason is that processing and other common methods of tissue "preparation" destroy the natural relationships in and among the alveolar surfaces, a problem that has concerned some investigators (e.g., Ref. 4). This problem, in fact, has been the principal obstacle to general recognition of the normal alveolar surface. Thus it is now clear (17, 26) that virtually each and every step, either individually or in sequence, of tissue preparation for light and electron microscopy dislocates, distorts, and disrupts the unit bubbles, including *1*) osmium tetroxide and tannic acid fixation, *2*) chemical dehydration (ethanol) and clarification (xylene; acetone), *3*) both paraffin and epoxy embedding, and *4*) transection and dicing, which accelerate bubble egress from and reagent-bubble contact within the air spaces. Other "preparative" processes are less common but also destructive (17, 26): *1*) lung freezing for morphological studies distorts the surface and produces artifacts, and *2*) lung degassing before volume-pressure studies destroys all natural bubbles. Clearly, the par-

adigm (above) is not valid, and the models of Hills' review (5) are not supportable.

<<hdr>>REFERENCES<<ref>><ens>

1. **<mc>Bastacky J and Goerke J.<med>** Pores of Kohn are filled in lungs: Low-temperature scanning electron microscopy. **<mdit>***J Appl Physiol* **<med>**73: 88–95, 1992. **<mc><ens>**
2. **<mc>Bastacky J, Lee CYC, Goerke J, Koushafar H, Yager D, Kenaga L, Speed TP, Chen Y, and Clements JA.<med>** Alveolar lining layer is thin and continuous: low-temperature scanning electron microscopy. **<mdit>***J Appl Physiol* **<med>**79: 1615–1628, 1995. **<mc><ens>**
3. **<mc>Cordova M, Mautone AJ, and Scarpelli EM.<med>** Rapid in vitro tests of surfactant film formation: advantages of the Exerowa black film method. **<mdit>***Pediatr Pulmonol* **<med>**21: 373–382, 1996. **<mc>**
10. **<mc>Pattle RE.<med>** Properties, function and origin of the alveolar lining layer. **<mdit>***Proc R Soc Lond [Biol]* **<med>**148: 217–240, 1958. **<mc>**
11. **<mc>Scarpelli EM.<med>** (Ed.) Perinatal respiration. In: **<mdit>***Pulmonary Physiology of the Fetus, Newborn and Child***<med>**. Philadelphia, PA: Lea and Febiger, 1975, p. 116–139.

<<texf>><lp;&12q><bold>Brian A. Hills: <med>My omission of Dr. Scarpelli's model (12), the "dry" model of Colacicco (5), and studies of black films (6) was due in part to the lack of interest shown by previous authors and myself in his foam concept of the lung. Another reason was the strict word limit imposed by the Journal. However, in his communication above, Dr. Scarpelli makes no mention of the major theme of my review, which is the ability of surfactants to adsorb to solid surfaces and the highly desirable properties, which such adsorption can impart.

<mc>Let us then review the model of Scarpelli (12) in which he proposes that there is "no free gas" in the alveoli or terminal lung units in the adult lung, a foam filling these units to "impart infrastructural stability." As shown in Fig. 5, for example, in his paper in the**<mdit>** *Anatomical Record***<med>** (12), the photomicrographs taken across the pleural surface do indeed show a number of adjacent, largely spherical units, with an ensemble that closely resembles what could well be a foam. However, the diameters of these units (commonly 30–160 μm) (12), on checking the scale, encompass the mean diameter of the rabbit alveolus of 78 μm (2). Hence, these and other photomicrographs could simply be nice pictures of alveolar structure with no indication of the menisci needed to subdivide larger structures into the foam that is claimed to fill them. It would hardly be an "irreconcilable flaw," as Scarpelli terms it, for any reviewer to ignore such photomicrographs.

<<hdr>>REFERENCES<<ref>><ens>

1. **<mc>Bastacky J and Goerke J.<med>** Pores of Kohn are filled in lungs: Low-temperature scanning electron microscopy. **<mdit>***J Appl Physiol* **<med>**73: 88–95, 1992. **<mc><ens>**
2. **<mc>Bastacky J, Lee CYC, Goerke J, Koushafar H, Yager D, Kenaga L, Speed TP, Chen Y, and Clements JA.<med>** Alveolar lining layer is thin and continuous: low-temperature scanning electron microscopy. **<mdit>***J Appl Physiol* **<med>**79: 1615–1628, 1995. **<mc><ens>**
3. **<mc>Cordova M, Mautone AJ, and Scarpelli EM.<med>** Rapid in vitro tests of surfactant film formation: advantages of the Exerowa black film method. **<mdit>***Pediatr Pulmonol* **<med>**21: 373–382, 1996. **<mc>**
10. **<mc>Pattle RE.<med>** Properties, function and origin of the alveolar lining layer. **<mdit>***Proc R Soc Lond [Biol]* **<med>**148: 217–240, 1958. **<mc>**
11. **<mc>Scarpelli EM.<med>** (Ed.) Perinatal respiration. In: **<mdit>***Pulmonary Physiology of the Fetus, Newborn and Child***<med>**. Philadelphia, PA: Lea and Febiger, 1975, p. 116–139.

<<hd1;2>>REBUTTALS

<<texf>><bold>Emile M. Scarpelli:<med> Because of space limitations, a brief commentary is made on each of the eight paragraphs in order of Hill's response above.

<mc><mdit>*1***<med>**) Hills' "major theme" rests on his assumption of an open alveolar surface, which my research shows is **<mdit>***not***<med>** anatomically correct (3). Hence, his obligation to address it. I critically reviewed Hills' and the other models in 1988 (2) and have found no new biological data to support them (3). Interestingly, my work with Exerowa (6) shows that lung surfactants rapidly form stable black foam films, of the kind sketched in Fig. 5 from Ref. 8, under conditions expected in the acinus in vivo.

<mc><mdit>*2***<med>**) Hills misrepresents the following: when microincised, alveolar gas exits as bubble(s), while conducting airway gas exits in a stream. Thus I have adopted the terms "unit" and "free" gas.

American Journal of Physiology-
Gastrointestinal and
Liver Physiology

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NOTE: <<conhd;6>> through <<conhd;10>> contain computer generated wording. Set tag only (with argument), not wording.

<<conhd>>THEMES

MUCOSAL BIOLOGY<ztocrule><<conhd;6>>

INFLAMMATION/IMMUNITY/MEDIATORS<<conhd;7>>

HORMONES AND SIGNALING<<conhd;8>>

NEUROREGULATION AND MOTILITY<<conhd;9>>

LIVER AND BILIARY TRACT<<conhd;10>>

(Continued)

<</PICK;covcap;0>><zcontinued><pict>>*Cover*: Rendering of a real life biology. A bi-directional vertical organisms during the integration/coordination of organ systems during the stress of physical exercisee is illustrated. See *J Appl Physiol* 87: 1–2, 1999, for further details. This illustration is copyrighted by the Mayo Foundation and reproduced with permission.</.>

This Journal is printed on ‘‘acid-free’’ paper.

<<copy;89;3;September;2001;000–000><zpub;First published April 26, 2001><zdoi;doi:10.1152/japplphysiol.00361.2001><zstyle;8><px;;2><pa>

J Appl Physiol 89: 000–000, 2001.
First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.

<<texf>><pc;norm>The first *Highlighted Topics* article selected for this issue of the *Journal of Applied Physiology*, ''Measuring the response time of pulmonary capillary recruitment to sudden flow changes,'' by Jarzyszak et al. (p. xxx-xxx) demonstrates how an innovative technique, video microscopy with image-enhancing software, can be used to show the rapid response time of red blood cell flow through pulmonary capillaries. To best illustrate this innovative technique, a video clip is posted on the APS web site, a first for the Journal and for the Society (http://jap.physiology.org/cgi/content/full/89/3/xxx). The impetus for this study came from the second *Highlighted Topics* article featured in this issue in which animals were flown on the NASA KC-135 aircraft to determine how weightlessness affects the distribution of pulmonary blood flow. The question was whether the 25 s of microgravity induced during the parabolic flight was long enough for the pulmonary microcirculation to reach steady state before the injected microspheres lodged in microvessels. To make that determination, Jaryszak and colleagues perfused a lung lobe by two pumps running in parallel. When one pump was turned off, flow was rapidly halved; when it was turned on again, flow immediately doubled. Capillary recruitment reached steady state in <4 s after flow was doubled. This can be easily seen in the video clip, albeit at less than optimal resolution (see comment below). It was surprising that a capillary bed known for its low resistance and high compliance could respond so rapidly to sudden changes in pulmonary blood flow.

<mc>The second *Highlighted Topics* article, "Redistribution of pulmonary perfusion during weightlessness and increased gravity" by Glenny et al. (p. xxx-xxx), quantifies the contributions of gravity and vascular anatomy in determining regional pulmonary blood flow. For the first time, local perfusion is directly measured with microspheres in the absence and presence of gravity. Although prior studies of regional perfusion have measured the superimposed effects of gravity and vascular structure, this is the only study to isolate the separate influences of these two factors. Using supine and prone pigs on the NASA KC-135 microgravity research aircraft, the authors confirm that gravity plays an important role in perfusion distribution. However, they determine that vascular anatomy is an even more important determinant of local perfusion. Perfusion patterns previously ascribed to hydrostatic gradients persist during weightlessness. The pulmonary circulation can no longer be regarded as a passive circuit in which the hydrostatic gradient is the primary determinant of regional perfusion. The novel findings of this study underscore the fact that even the most fundamental principles of pulmonary physiology are not yet fully understood.

<mc>The exciting research of these authors is further enhanced by the novelty of the video clip as a new publication format for the *Journal of Applied Physiology*. Given the limitations to file size that are currently necessary for placement on the web site, the image quality is not as great as it was when the authors originally created the video. Unfortunately, even with the great strides that we have made with these innovative publishing technologies, we still have a long way to go to improve image resolution. However, despite the limitations to the file size, the video clip clearly demonstrates that capillary blood flow responds almost immediately to the pump. In the future, as technology continues to improve and the capabilities of systems increase, we will be able to offer better quality in high-resolution images such as this one. In the meantime, the authors are commended for their pioneering efforts in bringing a new publication medium to the Journal.

<<copy;279;3;September;2001;000–000><zpub;First published April 26, 2001><zdoi;doi:10.1152/ajplung.00361.2001><zstyle;6><px;;2><pa>

Am J Physiol Lung Cell Mol Physiol 279: L000–L000, 2001.
First published April 26, 2001; doi:10.1152/ajplung.00361.2001.

CG <<sh>>Editorial

<<title>>Publishing in the journals of the APS: Why are authors charged fees?

<<texp>>Why does the American Psychological Society charge its authors fees in the form of page charges and manuscript submissionfees, especially in light of the considerable APS endowment? Because publishers of scientific journals recover their costs in various ways this editorial will explain which costs those fees are designed to defray.

<mc>Basically, the large journal program of the APS has long been break-even, sometimes amking and sometimes losing money in any given year. Some journals are more financially successful than others, but all serve the purposes of disseminting science and giving physiologists an appropriate venue for publishing their research. In 1995 the APS Council mandated that the publications program be self-sustaining and strive to achieve 10% revenue over expenses to help defray the cost of other member benefits. Since that time, the 10% goal has been achieved only in the last two years, but we must be alert to the uncertainties of publication revenues in future years.

<mc>The APS endowment has grown to its present size through wise investment of its funds combined with stock market growth that probably will not continue at the same pace in future years. At a strategic planning physiologists an appropriate venue for publishing their retreat held in November 1999, new ways for APS members to benefit from this fund were discussed. The Council will vote on them and announce these innovations later thi syear. But even before the retreat was held, the endowment's existence allowed the Society to provide the following journal benefits in 1999; subsidizing scientifically warranted color and giving it free to first or last authors who are APS members, allowing free online access to all journal content 12 months after publication, giving free online access to the journals with the purchase of a print subscription (many publishers charge a separate subscription price for online access in addition to print), and offering to APS members the incredibly low $49.50 price for online access to the collection of journals. Basically, the large journal program of the APS has long been break-even, sometimes amking and sometimes losing money in any given year. Some journals are more financially successful than others, but all serve the purposes of disseminting science and giving physiologists an appropriate venue for publishing their research. In 1995 the APS Council mandated that the publications program be self-sustaining and strive to achieve 10% revenue over expenses to help defray the cost of other member benefits. Since that time, the 10% goal has been achieved only in the last two years, but we must be alert to the uncertainties of publication revenues in future years.

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<<sigau;2>>Dale J. Benos, *Publications Committee Chair*
<mc>L. Gabriel Navar, *APS Past President*
<mc>Margaret Reich, *Director of Publications and Executive Editor*
<<sigaff>>May 2000, Volume 278<endtab>

CG

<ps;4><copy;3;;September;2000><px;;10>on 29 June, 9 August, and September 2000<pa>

Physiological Genomics

September 2000/Volume 3
Articles published online prior to print
on 29 June, 9 August, and September 2000
http://physiolgenomics.org

CG

<zconthead><<conhd;1>>REVIEWS<pick;covcap;0>

<<conhd>>RESEARCH ARTICLES

(Continued)

<zcontinued><<pict>>*Cover*: Representation of a B-form DNA helix of 12 base pairs, with atoms colored by elements and bonds colored by backbone or nucleobase type. Image created by Paul Thiessen with Persistence of Vision Raytracer and PovChem (see http://www.jagunet.com/~thiessen).

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<<conhd1>>CORRIGENDA (Note: use "CORRIGENDUM" for single entry)

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<<fut>>Conditional Clara cell ablation reveals a self-renewing progenitor function of pulmonary neuroendocrine cells
<<futa>>*Susan D. Reynolds, Kyung U. Hong, Adam Giangreco, Gregory W. Mango, Charanjeet Guron, Yasuo Morimoto, and Barry R. Stripp*

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<<fut>>Characterization of mucins from cultured normal human tracheobronchial epithelial cells
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<<futa>>*David N. Cornfield, Connie B. Saqueton, Valerie A. Porter, Jean Herron, Ernesto Resnik, Imad Y. Haddad, and Helen L. Reeve*

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(Continued)

(In Next Issue continued)

<<copy;89;6;December;2001;000–000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/japplphysiol.00361.2001><zstyle;8>
<px;;2>PULMONARY STRESS FAILURE<pa><<sh>>

J Appl Physiol 89: 2483–2489, 2001.
First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.

Invited Review

<<ssh>>HIGHLIGHTED TOPIC (set 16/22 Times Roman bold) | **<<sshtitle>>***Cellular Responses to Mechanical Stress (set 15/22 Times Roman mdit)*

<<title>>Pulmonary stress failure

<<aut>>**John B. West**
<<aff>>*Department of Medicine, University of California San Diego, La Jolla California*

<<abs;1>>**West, John B.** <mc>Pulmonary capillary stress failure. <zcopy>*J Appl Physiol* 89: 2483–2489, 2001. First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.—The pulmonary blood-gas barrier is an extraordinary bioengineering structure because of its vast area but extreme thinness. Despite this, almost no attention has been given to its mechanical properties. The remarkable area and thinness come about because gas exchange occurs by passive diffusion. However, the barrier also needs to be immensely strong to withstand the very high stresses in the capillary wall when capillary pressure rises during exercise. The strength of the thin region of the barrier comes from type IV collagen in the basement membranes. When changes occur in the barrier, a condition known as stress failure. Physiological conditions that alter the properties of the barrier include severe exercise in elite human athletes. Animals that have been selectively bred for high aerobic activity, such as Thoroughbred racehorses, consistently break their pulmonary capillaries during galloping. Pathophysiological ventilation. Remodeling of the capillary wall occurs in response to increased wall stress in diseases such as mitral stenosis. The barrier is able to maintain its extreme thickness with sufficient strength.

<<key>>blood-gas barrier; basement membrane; extracellular matrix; type IV collagen; pulmonary edema; pulmonary hemorrhage; endothelial cells; epithelial cells

<<texf>><cm;1><foot;fu;10>THE STUDY OF PULMONARY MECHANICS<cm;0> has a long, colorful history. For example, Galen (131–201 CE) understood how the expansion of the lungs follows that of the thorax, and he recognized that the diaphragm is innervated by nerves that originate high in the neck (<zref>16<zrefx>). It is extraordinary that, despite this long history, what is arguably the most remarkable mechanical structure in the mammalian lung, that is, the blood-gas barrier (BGB), has received almost no attention from bioengineers or physiologists interested in mechanics.

<mc>Consider the following: the total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the BGB is only 0.2–0.3 μm. That such an incredibly thin membrane can extend over such a vast area without friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure. Our interest in possible failure the BGB was initially aroused by the puzzle of the pathogenesis of high-altitude pulmonary edema (HAPE). We knew membrane can extend over such a vast area without that a high pulmonary artery pressure was a critical suggested a pressure-related basis. Our interest in possible failure the BGB was initially aroused by the puzzle of the pathogenesis of high-altitude pulmonary edema (HAPE). We knew membrane can extend over such a vast area. That such an incredibly thin membrane can extend over such a vast area without friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure. Our interest in possible failure the BGB was initially aroused by the puzzle of the pathogenesis of high-altitude pulmonary edema (HAPE). mechanics of this extraordinary structure.

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Address for reprint requests and other correspondence: J. B. West, UCSD Dept. of Medicine 0623A, 9500 Gilman Drive, La Jolla, CA 92093-0623 (E-mail: jwest@ucsd.edu).

<</PICKF;a1;0;0;block><<altfoot><advertisement>The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked "*advertisement*" in accordance with 18 U.S.C. Section 1734 solely to indicate this fact. **NOTE: Wording for this footnote is system generated</.>**

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Regulatory, Integrative and Comparative Physiology

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(Continued)

<</PICK;covcap;0>><zcontinued><<pict>>*Cover*: Rendering of a real life biology. A bi-directional vertical organisms during the integration/coordination of organ systems during the stress of physical exercisee is illustrated. See *J Appl Physiol* 87: 1–2, 1999, for further details. This illustration is copyrighted by the Mayo Foundation and reproduced with permission.<</.>

This Journal is printed on ‘‘acid-free’’ paper.

(Contents continued)

<copy;89;3;September;2001;000–000;2001><zpub;First published April 26, 2001><zdoi;doi:10.1152/japplphysiol.00361.2001>
<zstyle;8><px;;2>PULMONARY CAPILLARY STRESS FAILURE<pa><<sh>>

J Appl Physiol 89: 2483–2489, 2001.
First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.

<<ssh>>HIGHLIGHTED TOPIC | <<sshtitle>>*Cellular Responses to Mechanical Stress*

<<title>>Pulmonary capillary stress failure

<<aut>>**John B. West**
<<aff>>*Department of Medicine, University of California San Diego, La Jolla California*

<<abs;1>>**West, John B.** <mc>Pulmonary capillary stress failure. <zcopy>*J Appl Physiol* 89: 2483–2489, 2001. First published April 26, 2001; doi:10.1152/japplphysiol.00361.2001.—The pulmonary blood-gas barrier is an extraordinary bioengineering structure because of its vast area but extreme thinness. Despite this, almost no attention has been given to its mechanical properties. The remarkable area and thinness come about because gas exchange occurs by passive diffusion. However, the barrier also needs to be immensely strong to withstand the very high stresses in the capillary wall when capillary pressure rises during exercise. The strength of the thin region of the barrier comes from type IV collagen in the basement membranes. When changes occur in the barrier, a condition known as stress failure. Physiological conditions that alter the properties of the barrier include severe exercise in elite human athletes. Animals that have been selectively bred for high aerobic activity, such as Thoroughbred racehorses, consistently break their pulmonary capillaries during galloping. Pathophysiological ventilation. Remodeling of the capillary wall occurs in response to increased wall stress in diseases such as mitral stenosis. The barrier is able to maintain its extreme thickness with sufficient strength as a result of continual regulation of its wall structure.

<<key>>blood-gas barrier; basement membrane; extracellular matrix; type IV collagen; pulmonary edema; pulmonary hemorrhage; endothelial cells; epithelial cells

<<texf>><cm;1><foot;fu;10>THE STUDY OF PULMONARY MECHANICS<cm;0> has a long, colorful history. For example, Galen (131–201 CE) understood how the expansion of the lungs follows that of the thorax, and he recognized that the diaphragm is innervated by nerves that originate high in the neck (<zref>16<zrefx>). It is extraordinary that, despite this long history, what is arguably the most remarkable mechanical structure in the mammalian lung, that is, the blood-gas barrier (BGB), has received almost no attention from bioengineers or physiologists interested in mechanics.

<mc>Consider the following: the total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the BGB is only 0.2–0.3 μm. That such an incredibly thin membrane can extend over such a vast area without arguably the most remarkable mechanical structure in recognized that the diaphragm is innervated by nerves friends, and attempts to reproduce a similar gas-recognized that the diaphragm is innervated by nerves friends, and vast area without arguably the most remarkable mechanical structure in recognized that the diaphragm is innervated by nerves friends, and attempts to reproduce a similar gas-recognized that the diaphragm is innervated by nerves friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. Mechanics of this extraordinary structure. Our interest in possible failure the BGB was initially aroused by the puzzle of the pathogenesis of high-altitude pulmonary edema. Consider the following: the total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the BGB is only 0.2–0.3 μm. That such an incredibly thin membrane can extend over such a vast area without arguably the most remarkable mechanical structure in recognized that the diaphragm is innervated by nerves friends, and attempts to reproduce a similar gas-recognized that the diaphragm is innervated by nerves friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. Mechanics of this extraordinary structure.

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CG <<sh>>In Focus

Am J Physiol Regul Integr Comp Physiol 278: 000–000, 2001.
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<<title>>Multiple perspectives on alveolar models and the role of surfactant

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<<aut>><bx;1><zfn>Brian A. <zsn>Hills<ba>
<<aff>>*Pediatric Respiratory Research Centre, Mater Misericordiae Children's Hospital, South Brisbane, Queensland, Australia*

<<texf>><foot;fu;10><cm;1>THERE IS A BODY OF WORK<cm;0> that relates directly and specifically to the review article of Dr. Hills, "An alternative view of the role(s) of surfactant and the alveolar model," which appeared in the November 1999 issue of the *Journal of Applied Physiology* (5). In August 1998, another review article, "The alveolar surface network: a new anatomy and its physiological significance," was published in the *Anatomical Record* (17). It defined the configuration and limits of the alveolar surface as an infrastructural agglomeration of bubbles, i.e., a foam, that fills the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, the surfactant-containing films of which surround (incorporate) units of alveolar gas. They are neither bubble segments nor "one-sided bubbles" as described by Hills (5). Discrete portions of a unit bubble's film form discrete "foam films" by apposition to adjacent portions of other bubble films (namely, at the alveolar entrance, at pores of Kohn, and across the alveolar duct) and of nonbubble surfaces (namely, the epithelial cell surface and the liquid surface of the terminal conducting airways) (Fig. <pick;f1;0>1). (Conducting airways from trachea to terminal airways are themselves bubble free.) Foam films occupy virtually all of the surface area of the unit bubbles, except for their reflections at Plateau borders and cell surface niches. Their location, both individually and collectively, and their extraordinary thinness (~7 nm) afford a substantially *smaller* barrier to gas diffusion than that assumed (1, 2) for the traditional models (5). Collectively, the foam films form a continuous channel for alveolar surface liquid, which permits movement both in series and in parallel (Fig. 1). In addition, the lamellar arrangement of interfacial surfactants of the films provides both infrastructural support to stabilize aerated alveoli and near-zero surface tension to virtually eliminate the tendency of the bubbles to collapse. [Near-zero surface tension was first reported and validated by Pattle (8–10) from studies of bubbles expressed from the lung. It was the cornerstone of his discovery of lung surfactant (14, 15). It is applicable directly to the alveolar surface network (17) but not to the one-sided bubble and "morphological" models, which are the topic of Hills' review (5).] Discovery of the "foam lung" architecture (11, 12), first applied to the neonatal lung and then to all lungs the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, through adulthood as the "alveolar surface network" (13), was advanced by investigations reported over the years in original research papers (3, 6, 7, 12, 18–21, 23–28), other scientific reports (e.g., Refs. 11, 16, 17, 22), and a monograph (13). Remarkably, Hills' review (5) is totally devoid of any reference (direct, indirect, or even dismissive) to this body of research. He does, however, cite one in vitro study (24) to support his argument against the one-sided bubble model but ignores the paper's conclusion (24) that only a discrete unit bubble can satisfy the surface dynamics of normal breathing in vivo. All these omissions might be reason enough to The unit bubbles are complete bubbles, through adulthood as the "alveolar surface network" (13), was advanced by investigations reported over the years in original research papers (3, 6, 7, 12, 18–21, 23–28), other scientific reports (e.g., Refs. 11, 16, 17, 22), and a monograph (13). Remarkably, Hills' review (5) is totally devoid of any reference (direct, indirect, or even dismissive) to this body of research. He does, however, cite one in vitro study (24) to support his argument against the one-sided bubble model but ignores the paper's conclusion (24) that only a discrete unit bubble can satisfy the surface dynamics of normal breathing in vivo. All these omissions might be reason enough to disqualify Hills' review (5) as incomplete and inaccurate, but there are more serious problems that ultimately are dispositive.

<mc>The first unfortunate consequence of Hills' omissions is failure to recognize and address the *scores* of photomicrographs, published over the last quarter century, of fresh, unprocessed lungs as they occur in vivo (6, 7, 12, 13, 16–20, 23, 25–27). When the lung is examined by stereomicroscopy immediately after the thorax is opened (either in thorax or excised and with in vivo lung volume unperturbed), an agglomeration of the acinar air space from respiratory bronchioles to alveolar sacs. The unit bubbles are complete bubbles, unit bubbles in *all* aerated air spaces from respiratory bronchioles to alveolar sacs is revealed. Removal of unit bubble(s) renders the site(s) airless.

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<copy;9;3;September;2002;000–000;2002><zpub;First published_____>
<zdoi;doi:10.1152/physiolgenomics.00053.2002><zstyle;9> <px;;2>MEETING REPORT<pa><<sh>>

Physiol Genomics 9: 000–000, 2002.
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<<title>>Meeting report: *Physiological Genomics of*<qa> *Cardiovascular Disease: from Technology to Physiology*

<<aut>><bx;1>Susan B. Glueck[1]<ba> and <bx;1>Curt D. Sigmund[2]<ba>
<<aff>>[1]<rosup;1>*Deputy Editor, Physiological Genomics; and*
[2]<rosup;2>*University of Iowa College of Medicine, Departments of*<qa>
Medicine and Physiology and Biophysics, Iowa City, Iowa

<<texf>><pc;norm><cm;1><foot;fu;10>A THREE-DAY MEETING<cm;0> entitled "Physiological Genomics of Cardiovascular Disease: from Technology to Physiology," sponsored by the American Physiological Society, was held at the Cathedral Hill Hotel in San Francisco, CA, February 20–23, 2002. The conference was organized by Curt D. Sigmund of the University of Iowa. The conference began with a keynote address by Francis Collins of the National Institutes of Health on the impact of genomics on the practice of medicine. Subsequent days featured sessions on Comparative Genomics; Patterns of Gene Expression and Bioinformatics; Cardiomyopathy and Arrhythmias; Cardiovascular Development and Function; Pharmacogenetics; and Gene and Molecular Therapies.

<mc>Francis Collins' keynote talk addressed one of the repeated themes of the conference: that a thorough knowledge of the complex interaction between genotype and phenotype was required to have the greatest impact on medicine and disease prevention. Throughout the conference, speakers detailed the uses of comparative genomics, bioinformatics, expression profiling, and genome association studies to elucidate the genomics of cardiovascular disease. Particular talks representative of each section are highlighted herein.

<mc>In the session on Comparative Genomics, Edward M. Rubin (Lawrence Berkeley National Laboratory) described using sequence alignment tools to uncover biological similarities between different species. For example, a new gene, Apo AV, was discovered in an analysis of the human chromosome 11 apolipoprotein gene cluster, on the basis of sequence similarity between human, rabbit, and mouse DNA. Knocking out this gene in mice led to higher triglycerides. Several separate, subsequent association studies demonstrated an association of certain Apo AV polymorphisms with increased plasma triglycerides in humans. Given the degree of sequence conservation among vertebrates, the question arises as to how different animals exhibit different physiological conditions with the same starting proteins. In another example, Dr. Rubin described a case of convergent sequence evolution in the apolipoprotein (a) gene, Apo (a), between humans and hedgehogs.<zzaq;4> Individuals with high levels of Apo (a) are at increased risk for atherosclerosis. Interestingly, the gene is found in old world monkeys, great apes, hedgehogs, and humans, but not in new world monkeys, lemurs, or mice. Phylogenetically, the presence of Apo (a) in hedgehog would suggest that the gene was repeatedly lost in several of the primate lineages, or that the gene was independently derived in the hedgehog lineage. A detailed sequence analysis suggests convergent evolution, given that human and hedgehog Apo (a) have separate, duplicated fibrin binding domains also found in the plasminogen gene of each.

<mc>Isaac Kohane (Children's Hospital, Boston, MA, and Harvard Medical School) gave a presentation in the session on Patterns of Gene Expression and Bioinformatics on the importance of separating signal from noise in microarray data. He brought up a number of thought-provoking examples of how low-level gene expression is vulnerable to noise. For example, there may be periodicity in the intensity of spots on a microarray brought about by variability in the pins that deposit oligonucleotide probes on the array. He urged caution in interpreting gene expression data and made recommendations to cope with current limitations. One recommendation was to use a decision-theoretic approach to determine whether particular genes whose expression appeared significantly different between control and experimental conditions were worth further study. In addition, the recommendation was made to set a range of insignificance, i.e., to indicate a minimum level of expression below which fluctuations in intensity would be considered too noisy. Dr. to 22:6. Arachidonic acid (20:4), a significant component (12.7%) of the control heart tissue acyl chain profile, increased 15% after 2-day AC. As a result of these changes, the ratio of UFA to SFA increased considerably from 1.94 in untreated rat hearts to 2.70 in hearts of 2-day AC rats. The ratio of MUFA to SFA increased in this treatment.

The metabolic pathways of long-chain fatty acids relevant to our discussion are shown in Fig. 1, where the pathways for generation of long-chain PUFA (n-6, n-3) are compared with the major pathway for synthesis of long-chain MUFAs (n-9) (11). We have used the ratio of the level of DHA (22:6), of the n-3 pathway, divided by that of γ-arachidonic acid (20:4), the major n-6 pathway metabolite, to reflect the relative flux through these two pathways (n-3/n-6) (6, 24). This ratio is an underestimation because the n-3 components should include eicosapentaenoic acid (EPA), which may be diverted to prostanoids (see DISCUSSION), and the n-6 component is actually less because 20:4 includes α-arachidonic acid, an n-3 metabolic intermediate. This ratio increased in 2-day AC heart tissue from 0.84 to 1.12. The average MP of the acyl chains in 2-day AC hearts decreased from 9.0 to 1.43, indicating a small increase in the average fluidity of the phospholipid milieu of the membranes.

Acclimation of the rats for 30 days (30-day AC) decreased the 16:0, 18:1, and 22:5 substantially, whereas 20:4 and 22:6 increased (32 and 96%, respectively). Thus DHA became a major component of the 30-day AC acyl chain profile. Al-

<</FOOT;fu>><altfoot>><zonline>Article published online before print. See web site for date of publication (http://physiolgenomics.physiology.org).

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Table 1. *Lipid profile of rat heart tissue before and after heat treatments*

	Acyl Chain Profile of Rat Heart Tissue, mol%									
Fatty Acid:	16:0	%Δ	18:0	%Δ	18:1	%Δ	18:2	%Δ	18:3	20:4
MW	256		285		281		278		276	305
MP, °C	62.80		69.60		13.00		−12.00		−14.50	−49.50
Control	16.47±0.33		19.59±0.26		17.51±0.11		17.70±0.16			12.67±0.21
2-day AC	12.01±0.46*	−27	16.66±0.27*	−15	16.29±0.20	−7	20.04±0.27*	13		14.93±0.27*
30-day AC	12.39±0.46*	−25	18.62±0.51	−5	10.87±0.19*	−38	18.20±0.50	3		16.71±0.47*
Heat stress	14.33±0.52	−13	18.37±0.21	−6	13.22±0.31*	−25	19.06±0.50	8		14.88±0.25*
Liposomes	16.60±0.41	0.6	16.15±0.16*	−18	11.39±0.13*	−35	14.94±0.03	−15	14.00±0.30	13.86±0.33
Liposome/2-day AC	15.26±0.57	−7	21.97±0.65	12	9.42±0.45*	−46	24.75±0.55*	40		14.78±0.28*
PC composition	31.00±1.01		12.30±0.33		26.60±1.2		17.10±0.98			9.90±0.39

though the ratio of UFA to SFA was similar to 2-day AC, the increase in UFA-to-SFA ratio over the control was mainly due in this case to the increase in DHA. The n-3/n-6 ratio increased more than in any other treatment despite the parallel large increase in 20:4 to 1.25. The average MP decreased in 30-day AC more than in any other treatment.

The next group of rats was subjected to acute heat stress, which involves a gradual elevation of body temperature within a relatively short time interval, resulting in increased heart rate. Under these conditions, SFA decreased (19%) significantly less than in acclimated hearts, in addition to a substantial decrease in 18:1 (25%) as in 30-day AC, a 17% increase in 20:4, and a similar pattern of significant reciprocal changes in 22:5 and 22:6 as found in both 2-day and 30-day AC. The relative amount of UFA to SFA increased in heat stress, but less than that of the hearts of 2-day or 30-day AC rats. In contrast to the tissues of 2-day AC rats, the MUFA level after heat stress decreased, as seen after 30-day AC. The n-3/n-6 ratio increased to 1.17. The magnitude of changes of the average MP in heat stress, as in all the heat treatments, was modest, reflecting relatively small changes in the average fluidity of the membranal phospholipids.

Thus the three heat treatments demonstrate acyl chain responses that are fairly similar, including decreased SFA and increased PUFA, particularly DHA.

In the hearts of rats injected with liposomes composed of PC, a large decrease in 18:1 and 22:5 (33%) without other major changes was found. SFA did not change significantly. The PUFA-to-SFA ratio is significantly increased, mainly due to the generation of a new acyl chain component, 18:3 (14% of the total FA), which may originate from the 18:2 of the PC (PC of injected liposomes does not include significant amounts of 18:3; see Table 1). Arachidonic acid (20:4) increased <10%. The increase in DHA, found consistently in heat-treated hearts, did not occur after treatment with liposomes, and the ratio of the n-3/n-6 pathways decreased. The average MP of liposome-treated hearts decreased only slightly.

Next we examined how liposome treatment would affect 2-day AC membranes. Hearts of 2-day AC rats that had been previously treated with liposomes displayed a different specific pattern of changes compared with 2-day AC tissue or liposome-treated alone. The overall changes in UFA, MUFA, and PUFA were smaller, so their ratios to SFA remained similar to that of the control. The relative amount of 18:1 decreased by ~46%, 18:2 increased (40%), and 18:3 did not appear. EPA (22:5) decreased substantially (63%) without a change in 22:6. There was no change in the n-3/n-6 ratio. The average MP of the acyl chains in hearts of rats treated with PC after 2-day AC remained unchanged compared with control tissue.

Effect of heat treatments in salivary glands. As stated above the lipid acyl composition of salivary glands was significantly different from heart (Table 2), in particular the relative amounts of PUFA and SFA. Keeping the lower levels of PUFA in mind, some of the relative changes in their acyl chain profile after the various heat treatments still appear to be significant, but the changes in absolute terms are small. After 2-day AC there was a major decrease in 18:3, 20:4, and 20:5 and a parallel increase in the C_{22} series. DHA increases in particular (608%). The ratio of UFA to SFA decreased and the ratio of PUFA to SFA increased slightly due to the smaller amount of PUFA in this tissue. The ratio of the n-3/n-6 pathways increased substantially. Average MP was not affected in any of the heat treatments.

In 30-day AC rats, SFA remained unchanged, declines were found in the 20:3 and 22:5, and once again 22:6 increased, but not nearly as strikingly as after 2 day AC (or after heat stress). The ratios of MUFA, PUFA, and UFA to SFA did not change compared with the controls. The n-3/n-6 ratio increased slightly.

Acute heat stress led to insignificant changes in UFA, 18:1 and 18:2. We found that 18:3 and 20:3 decreased substantially as in the salivary glands of 2-day AC, a 17% increase in 20:5, and substantial decreases in 22:4 and 22:5. The increase in 22:6 by 158% was more than for 30-day AC (92%) but much less than in 2-day AC (608%). The decline in 20:4 under all conditions of heat stress in salivary glands differs from its response in heart. The ratio of n-3/n-6 increased only slightly as in 30-day AC.

If we look at the ratio of MUFA and PUFA to the SFA in salivary glands, we find much smaller changes after heat challenge compared with those in heart tissue in both groups of fatty acids. The most pronounced change was observed in tissue of rats acclimated for 2 days. Although the ratio of UFA to SFA decreased in all treatments, the average MP values in the various treatments do not change significantly; thus homeoviscous adaptation seems to be operative here as in heart tissue.

The salivary glands of liposome-treated rats demonstrated increased 18:3, decreased 20:3 and 20:5, and substantially increased 22:6 in contrast to its lack of effect in heart. In PC liposome-treated 2-day AC salivary glands, the C_{18} and C_{20} series were similar to that found in 2-day AC salivary gland not exposed to liposomes, including the decrease in 20:4. In contrast to 2-day AC salivary gland, 22:4 decreased with a striking and even higher level of 22:5 and 22:6. Liposome

Table 1.—*Continued*

Acyl Chain Profile of Rat Heart Tissue, mol%										
%Δ	22:5	%Δ	22:6	%Δ	UFA/SFA	MUFA/SFA	PUFA/SFA	Avg MP, °C	n-3/n-6	Chol/PL, nmol/nmol
	331		329							
	−78.00		−44.40							
	5.36±0.10		10.69±0.09		1.94	0.49	1.29	8.94	0.84	0.14±0.01
17	3.33±0.09*	−38	16.74±0.07*	57	2.70	0.57	1.90	1.43	1.12	0.26±0.02*
32	3.14±0.13*	−41	20.91±0.21*	96	2.57	0.36	1.95	−0.11	1.25	0.13±0.01
17	2.76±0.10*	−49	17.39±0.75*	63	2.18	0.40	1.65	3.98	1.17	ND
9	3.34±0.18*	−38	9.60±0.23	−10	2.23	0.35	1.70	7.62	0.69	0.11±0.01*
17	2.01±0.09*	−63	11.81±0.35	11	1.83	0.26	1.44	9.00	0.8	0.18±0.01*
	0.78±0.03		2.20±0.12		1.30	0.60	0.69	22.48		

Values are means ± SE from tissues of 3–6 rats. Acyl chain profile and cholesterol-to-phospholipid (Chol/PL) mole ratio of rat heart tissue before and after various heat treatments. Rats were subjected to 2-day or 30-day heat acclimation (AC) or acute heat stress. Phosphatidylcholine (PC) liposome-treated rats were injected as described, and where indicated rats were exposed to 2-day AC. The tissue extracts and their acyl chain and Chol/PL analyses were performed as described in METHODS. Fatty acids are designated by chain length:number of double bonds. MW, molecular weight; MP, mole-weighted melting point; %Δ, percent change; UFA, unsaturated fatty acid; SFA, saturated fatty acid; MUFA, monounsaturated fatty acid; PUFA, polyunsaturated fatty acid. *Significantly different from control rats ($P<0.05$). ND, not determined.

treatment generated an acyl chain pattern similar to the 2-day AC profile (except for 18:2 and 22:4).

Effects of Heat Treatments on Cholesterol Levels in Heart and Salivary Glands

The level of cholesterol and total phospholipids was measured in tissues of untreated (control) rats and of rats after heat acclimation and PC treatment. The results (Table 1 and 2) are expressed as cholesterol-to-phospholipid mole ratio (Chol/PL). Chol/PL in a membrane is related to membrane fluidity as well as to the membrane phase structure (47, 48). The partitioning of cholesterol in phospholipids is affected by the level of phospholipid acyl chain saturation (see DISCUSSION). Chol/PL in control rat heart was 0.14 ± 0.01. In hearts of 2-day AC rats, this ratio doubled to 0.26 ± 0.02. In contrast, 30-day AC did not result in a sustained increase of cholesterol levels, which at some point (after 2 days) returned to the levels found in untreated rats. PC treatment, which has been shown to cause nonesterified cholesterol depletion from membranes (4, 59, 66), reduced normal levels of Chol/PL by 22%. In hearts of 2-day AC liposome-treated rats, the absolute rise in Chol/PL was less than found in hearts not injected with liposomes (0.18 ± 0.01 vs. 0.26 ± 0.02); thus liposome treatment reduced the 2-day AC-induced cholesterol increase, but it still represents a moderate change (0.26/0.14 vs. 0.18/0.11).

Salivary gland cholesterol levels did not change in 2-day AC; however, it decreased ~35% after 30-day AC and heat stress. This parallels a reduced response in the PUFA acyl chain composition and suggests a significant role for nonesterified cholesterol in 30-day AC and heat stress. Liposome treatment reduced cholesterol levels by 22%. Two days of AC led to no further changes in Chol/PL.

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NOTE: <<conhd;31>> through <<conhd;40>> contain computer generated wording. Set tag only (with argument), not wording.

<</PICK;covcap;0>><zcontinued><<pict>>*Cover*: Rendering of a real life biology. A bi-directional vertical organisms during the integration/coordination of organ systems during the stress of physical exercisee is illustrated. See *J Appl Physiol* 87: 1–2, 1999, for further details. This illustration is copyrighted by the Mayo Foundation and reproduced with permission.**</.>**

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(Contents continued)

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<px;;2>PULMONARY CAPILLARY STRESS FAILURE<pa>

Am J Physiol Heart Circ Physiol 284: H2483–H2489, 2001;
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<<ssh>>SPECIAL TOPIC | <<sshtitle>>*Cellular Responses to Mechanical Stress*

<<title>>Pulmonary capillary stress failure

<<aut>>**John B. West**
<<aff>>*Department of Medicine, University of California San Diego, La Jolla California*

<<abs>>**West, John B.** <mc>Selected Contribution: Pulmonary capillary stress failure. <zcopy>*Am J Physiol Heart Circ Physiol* 284: H2483–H2489, 2001; doi:10.1152/ajpheart.00361.2001.—The pulmonary blood-gas barrier is an extraordinary bioengineering structure because of its vast area but extreme thinness. Despite this, almost no attention has been given to its mechanical properties. The remarkable area and thinness come about because gas exchange occurs by passive diffusion. However, the barrier also needs to be immensely strong to withstand the very high stresses in the capillary wall when capillary pressure rises during exercise. The strength of the thin region of the barrier comes from type IV collagen in the basement membranes. When changes occur in the barrier, a condition known as stress failure. Physiological conditions that alter the properties of the barrier include severe exercise in elite human athletes. Animals that have been selectively bred for high aerobic activity, such as Thoroughbred racehorses, consistently break their pulmonary capillaries during galloping. Pathophysiological ventilation. Remodeling of the capillary wall occurs in response to increased wall stress in diseases such as mitral stenosis. The barrier is able to maintain its extreme thickness with sufficient strength as a result of continual regulation of its wall structure. How it does this is a central problem in lung biology.

<<key>>blood-gas barrier; basement membrane; extracellular matrix; type IV collagen; pulmonary edema; pulmonary hemorrhage; endothelial cells; epithelial cells

<<texf>><cm;1><foot;fu;10><pick;a1;0>THE STUDY OF PULMONARY MECHANICS<cm;0> has a long, colorful history. For example, Galen (131–201 CE) understood how the expansion of the lungs follows that of the thorax, and he recognized that the diaphragm is innervated by nerves that originate high in the neck (<zref>16<zrefx>). It is extraordinary that, despite this long history, what is arguably the most remarkable mechanical structure in the mammalian lung, that is, the blood-gas barrier (BGB), has received almost no attention from bioengineers.

<mc>Consider the following: the total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the BGB is only 0.2–0.3 μm. That such an incredibly thin membrane can extend over such a vast area without arguably the most remarkable mechanical structure in friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure. Consider the following: the total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure. The total area of the BGB in the human lung is 50–100 m^2 (17). In more than half of this enormous area, the thickness of the friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure. In more than half of this enormous area, the thickness of the friends, and attempts to reproduce a similar gas-exmembrane can extend over such a vast area without gas exchange in that region. It is truly remarkable that so little attention has been devoted to the mechanics of this extraordinary structure.

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<mc>Our interest in possible failure the BGB was initially aroused by the puzzle of the pathogenesis of high-altitude pulmonary edema (HAPE). We knew high-altitude pulmonary edema (HAPE). We knew membrane can extend over such a vast area without suggested a pressure-related basis.

<</FOOT;fu><<altfoot>>Address for reprint requests and other correspondence: J. B. West, UCSD Dept. of Medicine 0623A, 9500 Gilman Drive, La Jolla, CA 92093-0623 (E-mail: jwest@ucsd.edu).</.>

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