

,QYLDWL HW DO - \*D VWURLQWH  
'2, ;

5HVHDFK \$UWLFOH 2SHQ \$F

6LOYLD 'L \*LRYDQQL 5REHUWR \*XOOR 'RPHQLFCHGFKLQDQR 3DRQDD \*DQSDHAWMORWWD DQG 6H  
D -D@p0\*0 p`0 @`0 P€@p€P0p°@ 0@p0P@`€δÀ €0@ p0\*0 €€à`0°00 00 00p0@ p000 00 00P0P€`0€`pÀ•€δÀÀ

&RQFOXVLRQV 7KLV VWXG\ GHPRQVWUDWHV WKDW VWLPXODWLRQ RI WKH SRVWHULRU  
SURFHGXUH IRU WKH WUHDWPHQW RI ,), 7KH VWLPXODWLRQ RI WKH SRVWHULRU WLELDO  
&&), VFRUH LQ WKH VKRUW WHUP DQG FWWLQJLPSURYHHPHQW LV PDLQWDLQHG DIWHU \HDO  
FRPPRQO\ LPSOLFDWHG LQ ), LQ ZRPHQ > @ +RZHYHU PRVW ZRPHQ  
ZKR VXVWDLQ DQDO VSKLQFWHU LQMXU\ GXULQJ YDJLQDO GHOLYHU\ GR QRW JR R  
WR GHYHORS ), ORUHRYHU LW LV XQFOHDU ZK\ ZRPHQ ZKR JHQHUDOO\  
VXVWDLQ REVHWWULF WUDXPD LQ WKH VHFRRG WR WKLUG GHFDGH GHYHORS ),  
VHYHUDO CHHDOOHU REVHUYDWLRQV DQG RWKHU REMHFWLYH  
DV

SDWKRSK\VLRRJ\ XVSXDWLHGWWRZGWHK ), P  
H[D#UDWHG RU UHGXFHG UHFWDQ VHQV  
VSKLQFWHU UHOD[DWLRQ > @ ,WV PDQD  
WUHDWPHQW VXFK DV PHGLFDO WUHDWPHQ  
LQYDVLYH VXUJHU\ LQMHFWRQ RI EXONL  
LPSODQWDWLRQ RI D QHRVSKLQFWHU \$O  
EH KHOSIXO D FRQVLGHUDEOH QXPEHU R  
WUHDWPHQW 2ZLQJ WR WKH IUHTXHQQW  
DUWL\SLQD FWHU LPSODQWDWLRQ WKH W  
KDV EHHQ GHYHORSHG GXULQJ WKH ODVW  
610 KDV DFKLHYHG VXFFHVU UDWHV RI  
FRPSOLFDWLRQV DQG DOVR UHTXLUHV WKH  
SXOVH JHQHUDWRU ORUH UHFHQWO\ SR  
3716 KDV EHHQ GHYHORSHG DV D VLPSON  
DOWHUQDWLYH WR 610 > @ ,W KDV EHHQ  
DGHTXDWH VXFFHVU UDWHV WKH WUHDWP  
VWXGLHV KDYH PRVWO\ UHSRUWHG RLGWW  
WXG\ LV WR HYDOXDWH WKH PLG WHUP  
VWLPXODWLRQ LQ SDWLHQWV ZLWK LGLRSI

0DWHULDOV DQG 0HWKRGV

%HIRUH VWDUWLQJ HWKLFDO DSSURYDO  
3DOHUPR )URP -DQXDU\ WR 6HSWHP

VHVPHQWV RI DQRUHFWDQ IXQFWLRQGLRSDVHKLW WKDWIHPDQHUHQGVN RDOWRP  
DQG RU GLVWXUEDQFHV RI DQRUHFWDQIXQFWLRQZHUFRQVLSXHWLWH\WKHFU

3DOHUPRdV 'LJHVWLYH ORWUOWWULBSRUWEGOWVLRQ  
ZHUH DJH EHWZHHQ DQG \HDUV VHYHUH ) ZLWK D JHOH YERIH RI  
RU KLJKHU PRUH WKDQ HSLVRGHV RI IDHFDQ HULRG RI  
GD\ DV UHFRUGHG E\ WKH SDWLHQW LQ D GL RQJHU WKDQ  
PRQWKV IDLOXUH RI FRQVHUYDWLYH WUHDV GEDFN RU  
EXONLQJ DJHQWV DQG LQWHJULW\ DQDWRPLF DQDO VSKLQF  
(\$6 DQG LQWHUQDO DQDO VSKLQFWHU )\$6 B RXQG  
FULWHULD IRU H[FOXVLRQ ZHUH VHYHUH FDU VH OHVLRQ  
WKH WLELDO SRVWHULRU QHUYH XQGHUOLC VRUGHUV H  
PXOWLSOH VFOHURVLV ELSGORRNHGHQGMXU  
YHQR QVXYFRHQWKH ORZHU DQDWRPLF QHUYH GLVHDVH  
GLDEHWHV FDUGLDF SDFHPONHEULRODWRPLF  
LPPXQRVXSSUHVVBEVDQDODEVFHVV SUHYLR  
RU SHOYLF VXUJHU\ DQG SUHJQDQF\ (QGRDQ  
QHUYH ODWHQF\ ZHUH SHUIRUPHG LQ DOO SDV SXGHQGDQ  
VSKLQFWHU DQGHQWV SDMXHUQWV KDYH D S [FOXGH DQDO  
LQFRQLQHQFH ZLWKRXW DQ DQDO VSKLQFWH HDWPHQW S  
3716 DOO SDWLHQWV ZHUH JLYHQ D && ) VF K  
SHUIHFV FRQLQHQFH DQG HLVRPUSHOZHUHQ  
UHYLVHG UDWVZFWN\WHO\PRQWKV DQG \HDU IU  
3716 F\FOH )LJXUH \$QRUHFWDQ PDQRPHV  
GHWHUPLQH DQDO UHVWLQJ DQG VTXHH]H SU B DOVR  
ZHNV DQG PRQWKV SRVW 3716 5HFWDQ VH PDWHG E\  
WKH SDWLHQWV SHUFHSWLRQ RI GLVWHQVLRQ RQ LQWURGX  
WKURXJK WKH DQXV SUH 3716 DQG ZHNV D 16  
\$QDO PDQRPHWU\ ZDV SHUIRUPHG XVLQJ D KURXJK  
WHFKQLTXH ZLWK 1DUFV %LR 6\WHP 006 P VLRQDO  
%LRPHGLFDO ,QF \$XVWLQ 7H[DV HTXLSSHG Z RQQHFWHG  
WR DQ ,QWHUQDWRQDO %LRPHGLFDO ORGH LQDO  
%LRPHGLFDO ,QF \$XVWLQ 7H[DV SQHXPRKV LQIXVLRQ  
V\WHP ZLWK SHUIXVLRQDO FDKQQHOV %( /  
SUREHV %LRHQJLQHHULQJ /DERUDWRULHV 6S LQ YDULRXV  
FRPELQDWRQV ZLWK DQ RSHQ HQG WLS SURY VLGH KROHV  
VDFHG DW FP IURPDQXHQW WKH GHWHUPLQ  
SUHVXUH 053 PP+J SUHVXUH PD[LXP Y  
SUHVXUH 63 PP+J DQG UHFWDQ JHQDWRQ  
VHQVDWRQ DQG GHVLUH HWBUBHGHKRDWZDV  
VWDQGDUGL3716 ZDV SHUIRUPHG XVLQJ WKH 8UJHQW 3&  
1HXURPRGXODWRQ 6\WHP 8URSODVWXUHQZHQDUMHWKHUODQG  
6WLPXODWRQ ZDV GHOLYHUHG XQLODWHUDOO\ XVLQJ D SHUFXWDQHRXV HOHFV  
ZLWK WKH SDWLHQW LQ WKH VXSLQH SRVWLRQ \$ JDXJH VWDLQOHVV VWHH  
QHGHQD ZDV LQVHUWHG WKURXJK WKH VNLQ DSSURILPDWHQV FP DERYH WKH  
PHGLDO PDOOHROXV EHWZHHQ WKH SRVWHULRU PDUJLQ RI WKH WLELD DQG WK  
VROHXV PXVFOH WHQGRQ \$Q DGKHVLYH HDUWK HOHFWRGH ZDV SDFHG RQ WK  
VDPH OHJ QHDU WKH DUFK RI WKH IRRV 6WROOHUdV 7HFKQLTXH %RWK QHGHQ  
DQG HOHFWRGH ZHUH FRQQHFWHG WR D VWLPXODWRU ZLWK DQ DGMXVWDEOH S  
LQWHQVLRW\ a P\$ )L[HG SDUDPHWHUV LQFOXGHG D SXOVH ZLGWK RI ,V  
DQG D IUHTXHQFV WLPXODWRU FRQWHLQHG D 9 EDWWHU\  
DPSOLWXGH ZDV VORZO~HQFRQVXVHG DQWLOVSDQWDU  
IDQQLQJ RI WKH RWKHU WRHV RFFXUUHG ,Q PRVW SDWLHQWV WKH PRWRU  
UHVSRQVH ZDV DFFRPSDQLHG E\ D VHQVRU\ UHVSRQVH IHOW DV D UDGLDWLQJ  
VHQVDWRQ VSUHDGLQJ WKURXJKWKHWRQ RI WKH IRRV  
VWLPXODWRQ ZDV VHW DW D OHYHO WKDW ZDV ZHOO WROHUDWHG

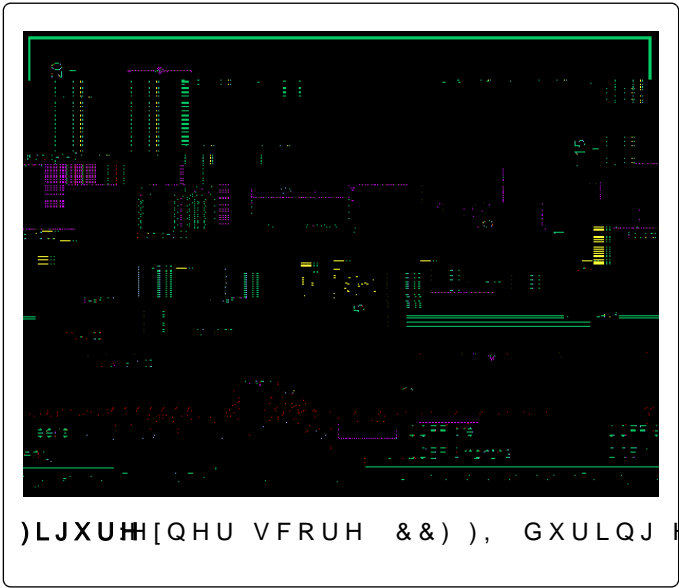
(OHYDWLRQ RI WKH OHYHO RI LQWHQVLRW\ RI VWLPXODWRQ ZDV DOORZHG  
ZKHQHYHU WKH VHQVDWRQ IDGMCHBZLPHQWR DGDSWDWRQ  
SURWRFRO FRQLVWHG RI VHVLRQV WZLFH SHU ZHNV ZLWK HDFK VHVLRQ  
ODVWLQJ PLQXWHV

IXQFWLRQDO RI WKH LQWHUQDO VSKLQFWHU UHVWLQJ SUHVXUH 053 DQG WK  
H[WHUQDO VSKLQFWHU VTXHH]H SUHVXUH 63 DW PRQKV ERSDUHC WR  
ZHHNV DQG WKH EDVHOLQH E\ 3716 053  
ZHHNV DQG EDVHOLQH PHGLDQ UHVSHF  
LQWHUTXDULOH DQG UG LQWHUTXDULOH  
PP+J YV S ,Q IDFV DW W  
RQO\ RI SDWLHQWV KDG D 053DZHHNV  
PRQKV RI WUHDWPHQW WKH KDG  
63 DW PRQKV ZDV JUHDWHU WKDQ  
UHVSHFWLYHO\ DQG LQWHUTXDULOH  
PP+J YV UG LQWHUTXDULOH DQG  
)LJXUH

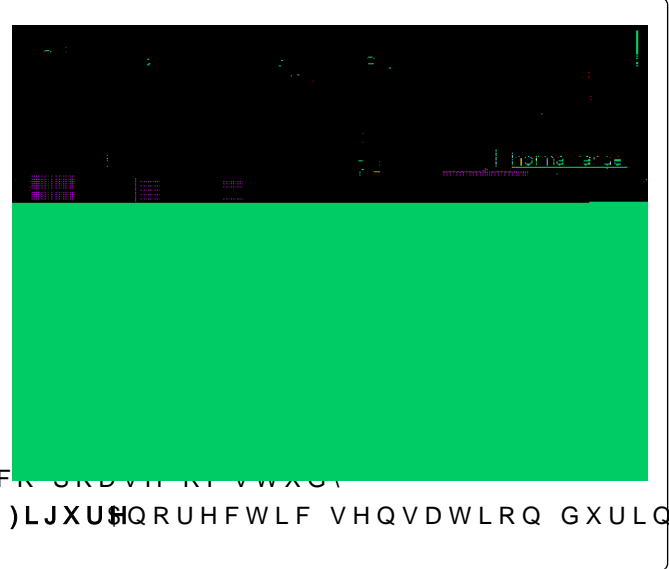


HUZHUH QR VWDWLYHEDVHOLQH VQRUH  
VHQVDWLRQ DW EDVHOLQH ZHHNV DQ  
VHQVDWLRQ LPSURYHG DW PRQKV LQ  
DW EDVHOLQH DQG ZHHNV )LJXUH

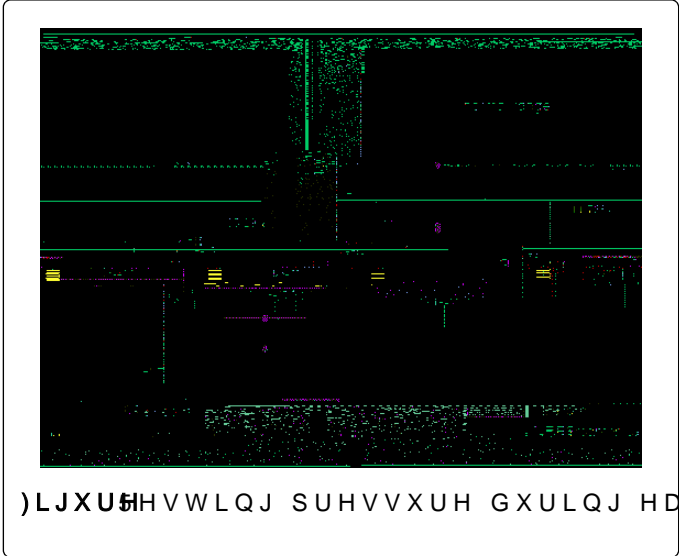
)LJXUH TXHH]H SUHVXUH GXULQJ HDFK SK



)LJXUH [QHU VFRUH && ) , GXULQJ HDFK SKDVH RI VWXG\



)LJXUH QRUHFVLF VHQVDWLRQ GXULQJ HDFK



)LJXUH UHVWLQJ SUHVXUH GXULQJ HDFK SKDVH RI VWXG\

0HGLDQ 6WDQGDUG 'HYLDFVLRQXH

\$JH “  
&& ) , “  
3UH  
&& ) , “  
ZHHNV  
&& ) , “  
PRQKV  
&& ) , “  
\HDU

3UH  
53 “



