



62% •D0

V %DEUDKDP ,QVWLWXWH &DPEULGJH &% \$7 8.

V \$OWRV /DEV &DPEULGJH ,QVWLWXWH RI 6FLHQFH &DPEULGJH &% *3 8.

Y)LUVW SXEOLVKHG	6HS	
	KWWSV GRL RUJ	I	UHVHDFK
	/DWHVW SXEOLVKHG	6HS	
	KWWSV GRL RUJ	I	UHVHDFK

\$EVWUDFW

%DFNJURXQG 5REXVW DQDO\VLV RI '1\$ VHTX|YHUVLRQ ✓ ? ?
 LQFOXGH D VHW RI TXDOLW\ FRQWURO VWHS\ 6HS YLHZ YLHZ YLHZ .FDO ELD
 NHSW WR D PLQLXP \$ PHWULF HDVLO\ REWE HDFK
 RI WKH QXFOHREDVHV IRU HDFK SRVLWLRQ DFURVV DOO VHTXHQFLOJ UHJGV
 +HUH ZH H[SORUH WKH GLIIHUHQFHV LQ QXFOHREDVH FRPSRVLWLRQV RI
 YDULRXV OLEUDU\ W\SHV SURGXFG E\ VWDQGDUGV W\SHV LPHQVDOO 5HVHDFK 3D
 PHWKRG RORJLHV b \$XVWUDOLD
 0HWKRGV :H REWDLQHG WKH FRPSRVLWLRQV RI QHDUO\ SXEOLFO\
 DYDLODEOH GDWDVHWV DQG VXEMHFWHG WKH FRPSRVLWLRQV LPHQVDOO
 \$SSUR[LPDWLRQ DQG 3URMHFWLRQ 80\$3 GLPHQVLRQDOLW\ UHGXFWRU IRU D
 WZR GLPHQVLRQDO UHSUHVHQWDWLRQ RI WKHLU FRPSRVLWLRQ FKDUFDWHULVWL
 5HVXOWV :H ILQG WKDW PRVW OLEUDU\ W\SHV UHJRO\ LQ D VSHFLILF FRPSRVLW
 SURILOH :H XVH WKLV WR JLYH DQ HVWLPDWH RI KRZ YVUROJO\ WKH
 FRPSRVLWLRQ RI D WHVW OLEUDU\ UHVHPEOHV WKH SURILOHV RI SUHYLRXVO\
 SXEOLVKHG OLEUDULHV DQG KRZ OLNHO\ WKH W\SHV FRPSOH LV WR EH RI D
 SDUWLFXODU W\SH :H LQWURGXFH /LEUDULDQ D XVHU IULHQGO\ ZHE
 DSSOLFDWLRQ DQG FRPPDQG OLQH WRRO ZKLFK HQDEOHV FKHFNLQJ EDVH
 FRPSRVLWLRQV RI WHVW OLEUDULHV DJDLQV W\SHV DQDORJDOO UHJRO\ WKH HQG RI
 &RQFOXVLRQV /LEUDU\ SUHSDUDWLRQ PHWKRGV VWURQJO\ LQIOXHGFH WKH SHU
 SRVLWLRQ QXFOHREDVH FRQWHQW %\ FRPSDULQJ WHVW OLEUDULHV WR D GDWD
 RI SUHYLRXVO\ SXEOLVKHG OLEUDU\ W\SHV ZH FDQ PDNH SUHGLFWLRQV

Highly enriched regions are often found in the vicinity of transcription start sites (TSS) and are associated with active enhancers and promoters. These regions are characterized by the presence of specific histone marks, such as H3K4me1 and H3K4me3, which are associated with active enhancers and promoters, respectively. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins.

Figure 14 (continued) shows the enrichment of these marks in the vicinity of TSS. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins. The enrichment of these marks is often correlated with the presence of transcription factors (TFs) and other regulatory proteins.

based on the number of reads. Each read is a sequence of 150 bp, and the sequencing depth is 100x. The sequencing data is stored in a BAM file.

The 'Peak calling' step is performed using the MACS2 software. The peak calling parameters are: --nomodel --shift=0 --keep-dup=all --qvalue=0.01. The peak calling results are stored in a BED file.

Here, we describe the analysis pipeline. The first step is to identify the peaks. The second step is to identify the motifs. The third step is to identify the clusters.

The data is available in the GEO database (GEO accession number GSE123456). The data was generated in 2018, 2019 and 2020. The data is available in the GEO database (GEO accession number GSE123456). The data was generated in 2018, 2019 and 2020. The data is available in the GEO database (GEO accession number GSE123456). The data was generated in 2018, 2019 and 2020.

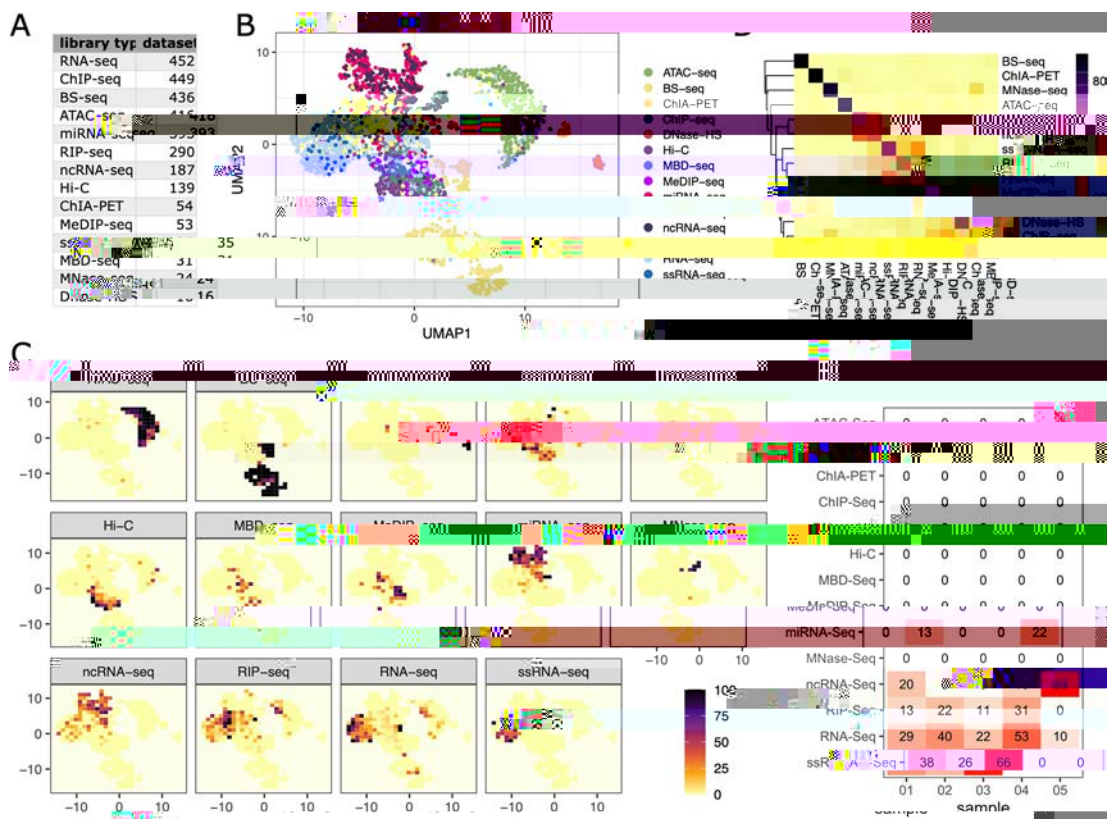


Figure 2. Library types can be distinguished by their base compositions. A) Number of samples per library type included in the analysis. B) UMAP representation of library compositions (reference map). C) Tile based probability map for each library type. Colour represents the percentage of a particular library type per tile. D) Heatmap illustrating the specificity of each library type for tiles of the reference map. All samples were assigned to a reference map tile and colour represents the average percentage of each library type for these tiles. E) Librarian tile probability

O a a e de a a a a e ba e c f e i e c g b a e hea f i e ced b a e e a d
h i gh h ch e ba a e a ed. Th f d g ca be i ed a a ea i a a i a ce f e e i e ced
i b c a a b e da a. A a e a a ch g e e e c e d c h i d a e a ed f a g a d a e i de g
ca e h i d be e g a e d be f e v g h e a a . Wh e a c i d a a e a b e
d g b a e a a , a b e a a c a e d b a - a da d e a a e a d.

Of e, a i da a b a e f i b h e d e i e c g b a e e f d a a i b e f a e h ch i e a
d f f e e b a e. Th ce i a e d b a g i f RNA- e a e h ch f a a e g f a e a h ch
e e e e c f c f ATAC- e . C e e c f a e e e a e e a a e b a e e e d ced b

2SHQ 3HHU 5HYLHZ

&XUUHQW 3HHU 5HYLHZ 6WDWXV

9HUVLF

5HYLHZHU 5HSRUWb 2FWREHU

KWWSV GRL RUJ I UHVHDFK U

k *KDUEL . 7KLV LV DQ RSHQ DFFHVV SHHU UHYLHZ UHSRUW GLVWULEXWHG
\$WWULEXWLRQ /LFHQVH ZKLFK SHUPLWV XQUHVWULFWHG XVH GLVWULEXWLRQ
RULJLQDO ZRUN LV SURSHUO\ FLWHG

.DULP *KIDJEL

7KH(DUOKDP ,QVWLWXWH 1RUZLFK 8.

,Q WKLW PDQXVFULSW 9DVKLVKWKD HW DO GHVFULEHV WKH LPSOHP
WRRO IRU QH[W JHQHUDWLRQ VHTXHQFLQJ 1*6 GDWDVHWV ZKLFK X
DORQJ VHTXHQFH UHGDV WR LQIHU WKH OLNHO\ OLEUDU\ SUHSDUDW
DXWKRUV ILUVW GHPRQVUDWH WKDW QXFOHRWLGH FRPSRVLWLRQ L
UHFRUGHG LQ WKH *(2 GDWDEDVH IRU D VHOHFWLRQ RI KXPDQ DQG F
HVWDEOLVKHG WKLW UHVXOW WKH\ LPSOHPHQWHG D SURJUDP WRRO
FRPSRVLWLRQ SURILOHV WR D FROOHFWLRQ RI UHIHQFH GDWDVHW
SURILOHV ZKLFK PD\ EH LQGLFDWLYH RI SRWHQWLDO IDLOXUH GXUL
VDPSOH GDWD PL[XSV 7KH WRRO ZKLFK LV DYDLODEOH DV D ZHE D
H[WUDFWV QXFOHRWLGH FRPSRVLWLRQ IURP XVHU VXSSOLHG)\$674 I
DJDLQVW H[LVWLQJ SURILOHV VWRUHG LQ WKH /LEUDULDQ GDWDEDV

7KH PDQXVFULSW LV ZHOO ZULWWHQ DQG WKH DXWKRUV SURYLGH V
LQIOXHQFLQJ QXFOHRWLGH FRPSRVLWLRQ LQ WKH UHGD RXWSXW ILC
WKRVLH H[SHULHQFHG ZLWK JHQHUDWLQJ DQG RU DQDO\VLQJ GLYHUV
ZHOFRPH GRFXPHQDWLRQ DQG TXDQWLILFDWLRQ RI WKHVH SDWWH
WR EHFRPH DQ LPSRUWDQW VWHS LQ WKH 4& RI 1*6 GDWD DORQJVL
DV)DVW4& DQG KHOS GHWHFW TXDOLW\ LVVXH HDUO\ LQ GDWD SU
DERXW WKH OLPLDWLRQV RI WKH VRIWZDUH DV FXUUHQWO\ LPSOHP
GLVFXVVHG LQ WKH PDQXVFULSW DQG FRXOG FDXVH VLJQLILFDQW FI
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0DMRU FRPPHQWV

3OHDVH FRPPHQW RQ WKH DSSOLFDELOLW\ RI /LEUDULDQ WR GDWD
WKDQ ,OOXPLOD ,I QRW WHVWHG RU QRW DSSOLFDEOH WKLW VKRXC

3OHDVH SURYLGH D UDWLRQDOH IRU WULPPLQJ UHGDV WR EDVHV
WKH GDWDEDVH RI QXFOHRWLGH FRPSRVLWLRQ SURILOHV L H ZK\

QXFOHRWLGH FRPSRVLWLRQ RI HDFK OLEUDU\ W\SH 6RPH PHWKRGV
H J ; *HQRPLFV ZLWK GLIIHUHQW QXFOHRWLGH FRPSRVLWLRQV
FDQ EH GLDJQRVWLF RI WKH OLEUDU\ W\SH b

7KH VHOHFWLRQ RI *(2 GDWDVHWV WR EXLOG UHIHUHQFH SURILOHV
3OHDVH FDQ \RX SURYLGH HYLGHQFH WKDW /LEUDULDQ LV DSSOLFDE
HVSHFLDOO\ VSHFLHV ZLWK GLYHUJHQW *& FRQWHQW

7KH GDWH UDQJH ILOWHU LV DOVR OLNHO\ WR K
OLEUDU\ W\SHV WR EH H[FOXGHG IURP WKH DQDO\VLV DQG WKHUHIR
OLEUDU\ W\SHV DUH KLJKO\ SRSXODU EXW VXUSULVLQJO\ DEVHQW
PLVVHG WRR b

7UDQVSRVRQ EDVHG OLEUDU\ SUHSDUDWLRQ LV LQFUHDVLQJO\ SRS
OLEUDU\ W\SHV LQFOXGLQJ VLQJOH FHOO 51\$ DQG '1\$ VHTXHQLQJ
VHT HQULFKPHQW FDSWXUH HWF 7KH DXWKRUV EULHIO\ DFNQRZOH
WR EH D PDMRU OLPLWDWLRQ RI WKH WRRO L H WUDQVSRVRQ LQV
OLNHO\ REVFXUH WKH XQGHUO\LQJ OLEUDU\ W\SH FDXVLQJ PRVW W
WRJHWKHU 7KLV VKRXOG EH H[SOLFLWO\ GRFXPHQWHG DQG LQYHVW

ORUH JHQHUDOO\ VSHDNLQJ , ZRXOG VWURQJO\ HQFRXUDJH WKH D
W\SHV DQG VSHFLHV VXSSRUWHG E\ /LEUDULDQ LQGLFDWLQJ WKDW
DQG RU VSHFLHV PD\ UHVXOW LQ LQFRQFOXVLYH RU SRWHQWLDOO\ N
VRIWZDUH ZLOO DFFHSW DQ\)\$674 ILOH

0LQRU FRPPHQWV bb bbb b

3OHDVH EULHIO\ FRPPHQW RQ WKH REVHUYHG SDWWHUQ IRU &K,\$ 3
WKHVH H[SHFWHG DQG FRQVLVWHQW ZLWK WKH OLEUDU\ PHWKRQ &K
PHWKRQ \$ VKRUW GHVFULSWLRQ VKRXOG EH LQFOXGHG LQ WKH WH

3OHDVH DGG OHJHQG WR)LJXUH ZLWK NH\ PDWFKLQJ FRORXUH G

, ZRXOG VXJJHVW PHWD DQDO\VLV RI SXEOLF GDWDVHWV DV DQRWH
H J DV D FOHDQ XS WRRO SULRU WR PHWD DQDO\VLV RU LGHQWLI\L
VXEW\SHV b

3OHDVH FODULI\ ZKHWKHU /LEUDULDQ FDQ ZH EH VHW XS ZLWK D O
DJDLQVW DQ RQOLQH GDWDEDVH YLD WKH ZHE DSS RU FRPPDQG OLQ

7KH WDEXODU GDWD LQ ILJXUH \$ VKRZV OLEUDU\ W\SHV ZLWK IHZH
FODVVLILHG DV XQGHU UHSUHVHQWHG OLEUDULHV DQG H[FOXGHG IU

2YHUDOO , EHOLHYH WKDW WKH SUHPLVH RI /LEUDULDQ LV D YHU\ J
HIIRUWV LQ UHOHDVLQJ WKH SURJUDP DV D SXEOLFO\ DYDLODEOH W
UHVSRQVHV DQG IXWXUH LWHUDWLRQV RI WKH VRIWZDUH DGGUHVVL

,V WKH UDWLRQDOH IRU GHYHORSQJ WKH QHZ VRIWZDUH WRRO FOH

<HV

,V WKH GHVFULSWLRQ RI WKH VRIWZDUH WRRO WHFKQLFDOO\ VRXQG
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UHSOLFDFWLRQ RI WKH VRIWZDUH GHYHORSPHQW DQG LWV XVH E\ RW
<HV

,V VXIILFLHQW LQIRUPDWLRQ SURYLGHG WR DOORZ LQWHUSUHWDWLR
DQG DQ\ UHVXOWV JHQHUDWHG XVLQJ WKH WRRO"
3DUWO\

\$UH WKH FRQFOXVLRQV DERXW WKH WRRO DQG LWV SHUIRUPDQFH D
ILQGLQJV SUHVHQWHG LQ WKH DUWLFOH"
3DUWO\

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, FRQILUP WKDW , KDYH UHDG WKLV VXEPLVVLRQ DQG EHOLHYH WKD
H[SHUWLHV WR FRQILUP WKDW LW LV RI DQ DFFHSWDEOH VFLHQWLIL
VLJQLILFDQW UHVHUYDWLRQV DV RXWOLQHG DERYH

5HYLHZHU 5HSRUWb

2FWREHU

KWWSV GRL RUJ I UHVHDFK U

k 2NRQHFKQLNRY . 7KLV LV DQ RSHQ DFFHVV SHU UHYLHZ ~~UHSRUW~~ GLVWUL
&RPPRQV \$WWULEXWLRQ /LFHQVH ZKLFK SHUPLWV XQUHVWULFWHG XVH GLVWUL
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.RQVWDQWLQ 2NR^DHFKQLNRY

*HUPDQ &DQFHU 5HVHDFK &HQWHU +HLGHOEHUJ *HUPDQ\

7KH PDQXVFULSW GHVFULEHV WKH TXDOLW\ FRQWURO 4& WRRO /LE
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,QLWLDOO\ IRU WKLV SXUSRVH WKH FRPSRVLWLRQ RI QXFOHRWLGH
DV LQSXW WR FUHDWH D ODUJH UHIHQFH FRQWURO FRKRUW IURP
WKHVH PHUJHG QXFOHRWLGH SURILOHV YLD 80\$3 DOORZV WR REVHU
GDWD W\SH RI D GDWDVHW 1RYHO VDP SOH FKHFN LV D SURMHFWLRQ
RQOLQH WRRO FRQILUPHG LWV XVHIXOQHVV IURP LQVSHFWLRQ RI R
GLVWLQJXLVKHG FRUHFQWV 6XFK SURMHFWLRQ RI D QRYHO GDWDV
VWHS IRU DQ\ VHTXHQLQJ H[SHULPHQW b +RZHYHU WKH PDQXVFULS
EH LPSURYHG LQ RUGHU WR SURYLG PRUH GHWDLOV DERXW WKH W

EORFNV

◦ ,Q JHQHUDO WKH PDQXVFULSW FOHDUO\ GHVFULEHV WKH WHFKO
 OLPLWDWLRQ RI WKH PHWKRQ LV VWDWHG HIIHFW RI D FXW LQ 5
 WR \$7\$& VHT LQ 'LVFXVVLQ 0RUH YDULDQFH IDFWRUV FRXOG E
 FRQFOXVLRQV DERXW WKH DQDO\VLV UHVXOWV)RU H[DPSOH W
 IURP IUR]HQ WLVVXH))3(LV WKHUH DQ\ LPSDFW RI WKLW SUHS
 LQVSHFWLRQ WKH VWDQGDUG 51\$ VHT GDWDVHWV ZHUH GLVWLQ
 GHPRQVWUDWHG WKH FORVHVW VLPLODULW\ WR 0%3' DQG 0H',3
 DOVR LQFOXGHG KRZHYHU WKH\ YDU\ VLQFH WKH\ FRXOG EH HL
 VHJPHQW RI D JHQH &RXOG WKLW KDYH DQ LPSDFW RQ UHDO

b

◦ 7KH UHDOGV VHOHFWLRQ LV SHUIRUPHG ZLWK . VXEVDPSOLQJ
 :KDW LV WKH HIIHFW RI WKH WRWDO QXPEHU RI UHDOGV" ,V LW VX
 WKHP" ,Q WKLW FDVH ZKDW LV WKH VXJJHVWHG OLPLW"

b

◦ \$OVR ES UHDO VHJPHQW LV XVHG DV WKH UHIHUHQFH EXW KF
 &XUUHQWO\ WKH PDLQ VWDQGDUG IRU VHTXHQFLQJ LV ES
 XVH D ODUJHU VHJPHQW RI WKH UHDO IRU UHIHUHQFH JHQHUDWL
 UHDOGV KDYH D QHJDWLYH LPSDFW"

b

◦ +RZ VWURQJ LV WKH VSHFLHV HIIHFW" \$UH WKHUH YDULDQFHV R
 PDWHULDQV LQ IXOO 80\$3 H J FOXVWHUV IRUPDWLRQ" 'RHV LW
 IRU VXFK D SURFHGXUH HVSHFLDOO\ ZKHQ ZRUNLQJ RQ RWKHU V

)XUWKHU DGGLWLRQDO FRPPHQWV FRXOG KHOS WR LPSURYH WKH PD

◦ ,Q)LJXUH WKH QXFOHRWLGH W\SH FRORU OHJHQG LV PLVVLQJ
 WH[W GLUHFWO\ E\ VXIL[D E F G)LJXUH D GHPRQVWUDWHV &
 LQFOXGHG VLQFH LW V QRW VWDWHG LQ WKH PDQXVFULSW WH[W

b

◦)LJXUH D \$UH WKH DPRXQWV RI PLFH DQG KXPQV PL[HG" :KDW

b

◦)LJXUH F 6HYHUDO HQULFKPHQW 80\$3 ORFDWLRQV IRU FHUWDLQ
 RWKHU H J 51\$ VHT +RZ WR LQWHUSUHW WKLW" &RXOG LW EH F
 WKH GDWDVHW W\SHV"

b

◦ :KHQ GRZQORDGLQJ H[DPSOH GDWDVHWV VDPH)\$674 ILOHV
 \$OVR WKHUH LV QR GRFXPHQWDWLRQ DYDLODEOH UHJDUGLQJ L
 QRW DOORZHG WR EH J]LSSHG LW V QRW FOHDU ZLWKRXW WHVW

b

◦ *LWKXE GRFXPHQWDWLRQ RQ WKH HVWDEOLVKPHQW ODXQFK ODF
 H[WHQG LW HVSHFLDOO\ WR VWDWH ZKDW DUH WKH V\WHP HQY
 LQVWDOODWLRQ

,V WKH UDWLRQDOH IRU GHYHORSLQJ WKH QHZ VRIWZDUH WRRO FOH
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<HV

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3DUWO\

,V VXIILFLHQW LQIRUPDWLRQ SURYLGHG WR DOORZ LQWHUSUHWDWL
DQG DQ\ UHVXOWV JHQHUDWHG XVLQJ WKH WRRO"
1R

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, FRQILUP WKDW , KDYH UHGD WKLW VXEPLVVLRQ DQG EHOLHYH WKD
H[SHUWLPH WR FRQILUP WKDW LW LV RI DQ DFFHSWDEOH VFLHQWLIL
VLJQLILFDQW UHVHUYDWLRQV DV RXWOLQHG DERYH

5HYLHZHU 5HSRUWb

2FWREHU

KWWSV GRL RUJ I UHVHDFK U

k .HQLUV\$LV LV DQ RSHQ DFFHVV SHHU UHYLHZ UHSRUW GLVWULEXWHG XQG
\$WWULEXWLRQ /LFHQVH ZKLFK SHUPLWV XQUHVWULFWHG XVH GLVWULEXWLRQ
RULJLQDO ZRUN LV SURSHUO\ FLWHG

\$QGUHZ .HidLU\
0ROHFXODU 0HGLFLQH 'LYLVLRQ :DOWHU DQG (OLJD +DOO ,QVWLWXV
\$XVWUDOLD

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LGHQWL\ LQFRUUHFV OLEUDULHV HDUO\ LQ DQDO\VLV SLSHOLQHV D
WKLW WHVW 6XFK DQ DQDO\VLV FRXOG FHUWDLQO\ EH XVHIXO DQG I
KH S4& VW DØFK DQP0p°@p0p 0 p€ u Àp 3 LQ DQ p€ pÀ0A0@ €<À S0L

WKLW SHUKDSV HQULFKPHQW WHFKQLTXHV RU GHYHORSPPHQWDO
b

, P QRW VXUH RI WKH ORJLVWLFV RI WKLW EXW /LEUDULDQ PD\ E
DV DQ RSWLRQ ZLWKLQ WKH DOUHDG\ ZLGHQ\ XVHG IDVWTF

b
\$Q H[DPSOH RI WKH /LEUDULDQ RXWSXW ZRXOG EH EHQHILFLDO

b
7KH WHUPV UHIHUHQFH PDS DQG FRPSRVLWLRQV PDS VHHP W
VLPSOLFV\ RQH WHUP VKRXOG EH XVHG WKURXJKRXW

b
)LJ \$ VKRZV WKH EDVH FRPSRVLWLRQ RI &K,\$ SHW GDWD \$V WK
LW ZRXOG EH EHQHILFLDO WR KDYH DQ H[SODQDWRQ RI WKH ED

b
)LJ LV PLVVLRQ D OHJHQG H[SODLQLQJ ZKLFK EDVH HDFK FROR

b
, P QRW FHUWDLQ ZKDW)LJ (LV VKRZLQJ &RXOG WKH DXWKRUV
OHJHQG" 7KHUH LV DOVR QR UHIHUHQFH WR WKLW ILJXUH LQ WKH

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, FRQILUP WKDW , KDYH UHGD WKLW VXEPLVVLRQ DQG EHOLHYH WKDW
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