Mathematical modeling of the lambda switch

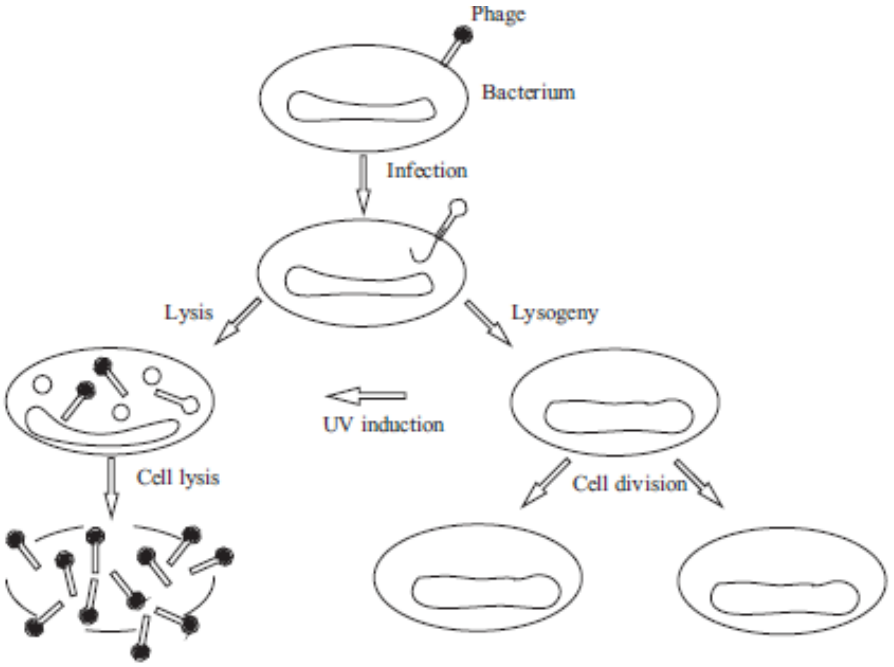
$$\dot{r} = A_r a_r(t) - d_r r(t)$$

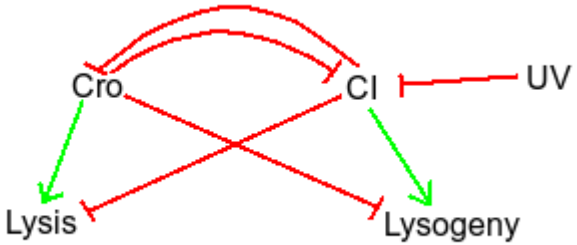
$$\dot{c} = A_c a_c(t) - d_c c(t)$$

$A_r(c)$ = *number of* $CL(Cro)$ *molecules made per transcript*

$a_r(c)$ = *transcription rates*

$d_r(c)$ = *degradation rate of* $CL(Cro)$





Rule 1. If (r *is* $medium_r$) and (c *is* low_c) then $a_r = a_1$.

Rule 2. If (r *is* low_r) and (c *is* low_c) then $a_r = a_2$.

Rule 3. If (r *is* $high_r$) or (c *is* $high_c$) then $a_r = 0$.

$$\dot{r} = A_r(rcp_1^{ij} + rp_2^{ij} + cp_3^{ij} + p_4^{ij}) - rd_r,$$
$$\dot{c} = A_c(rcp_5^{ij} + rp_6^{ij} + cp_7^{ij} + p_8^{ij}) - cd_c.$$

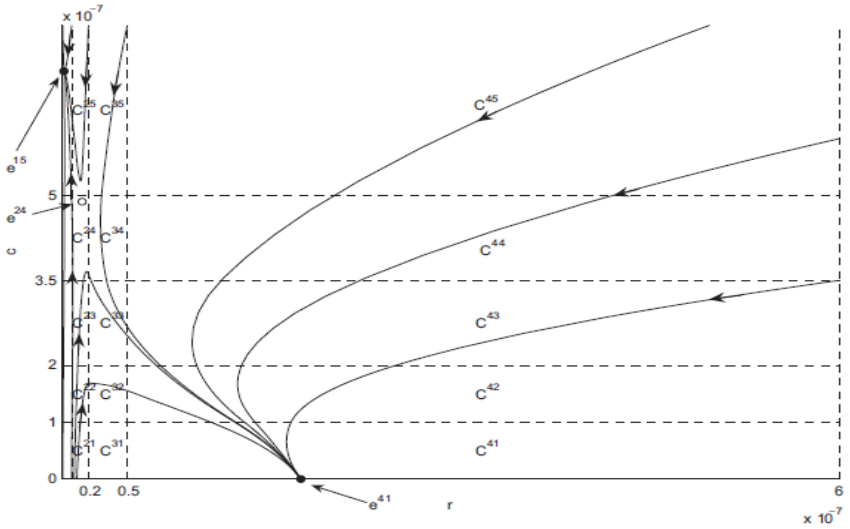


Fig. 10. Phase space trajectories for $d_r = 3.5d_n$.

- Transcription rate is modeled according to FL rules
- Rates for r and c become a piecewise-quadratic second-order DE

  System is sensitive to degradation rate

VDR signaling

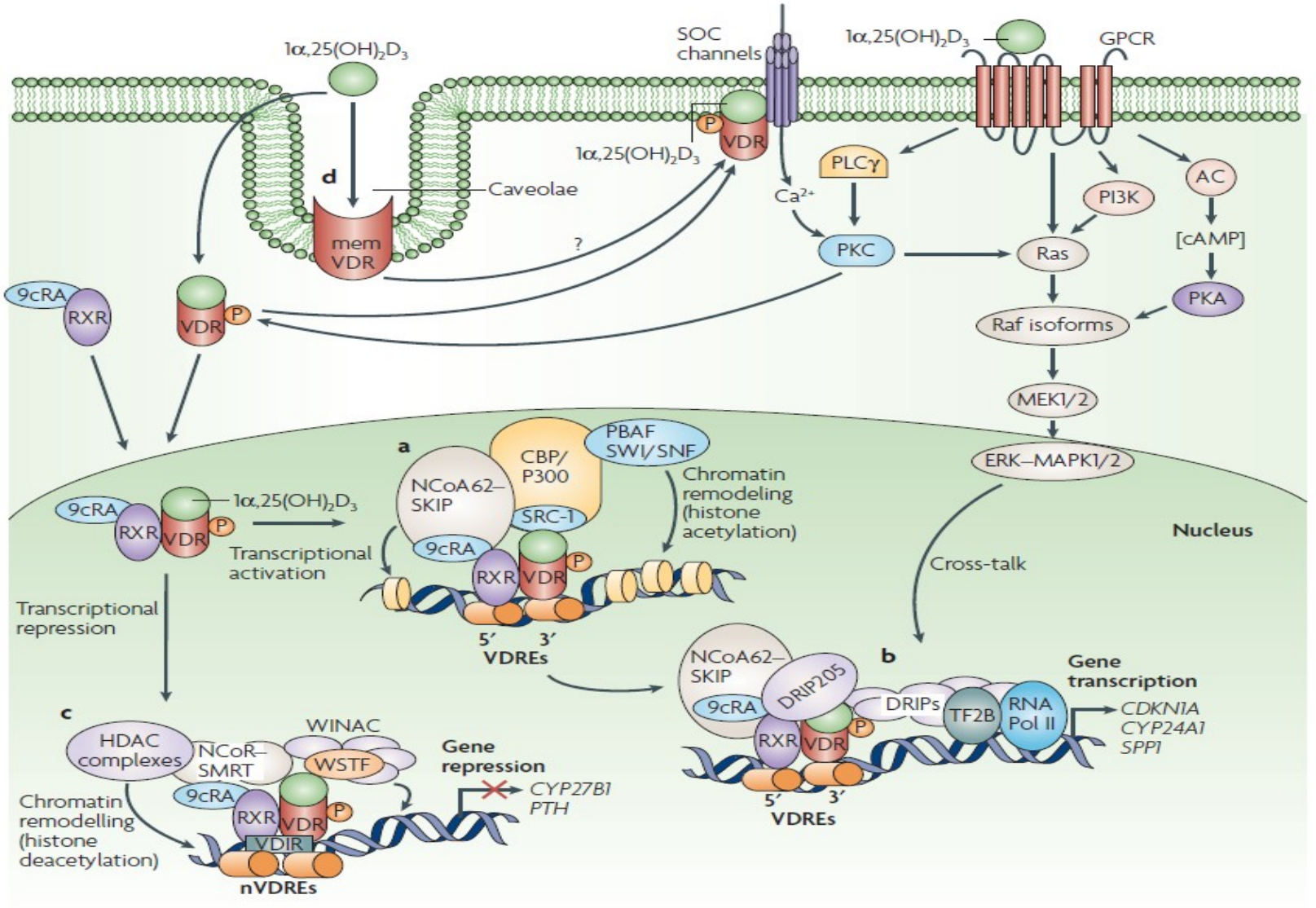


Figure 2 | 1α,25(OH)2D3-mediated transcriptional regulation. Classical action of 1α,25(OH)2D3 is mediated by

Transcriptional activation

- VitaminD receptor-interacting protein attracts VDR-RXR-NCoA62-SKIP-DRIP205
- CDKN1A, SPP1, CYP24A1 are transcribed

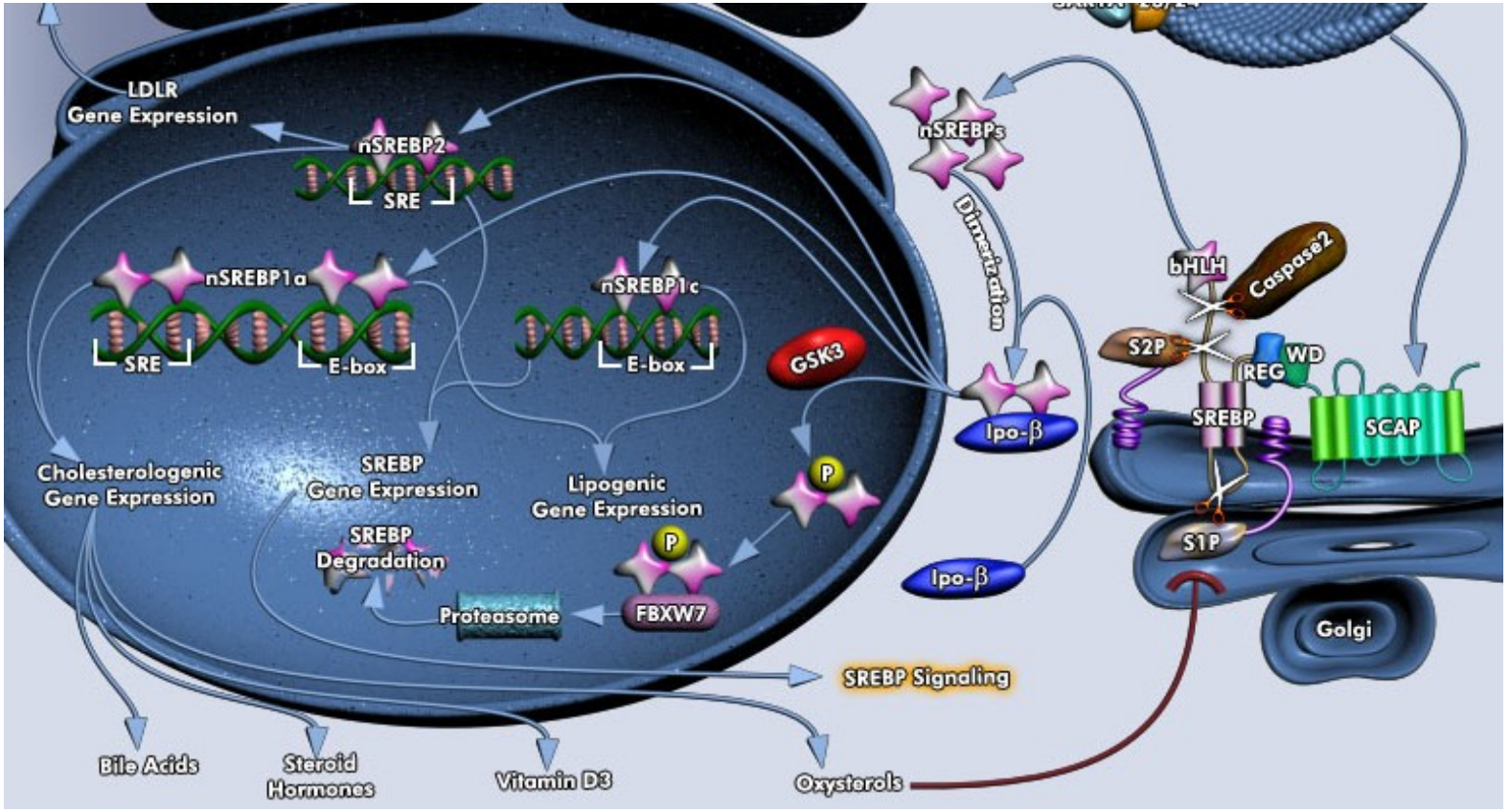
Transcriptional repression

- VDR-RXR interact with VDIR
- Repression of CYP27B1, PTH (encodes parathyroid hormone)

Non-genomic signaling

- Activation MAPK – ERK ½ pathway through phosphorylation of PKC/ Ca2+ influx through SOC channels

SREBP signaling



- SREBP is cleaved when sterol is absent – dimerized SREBP is imported into the nucleus with importin-β
- SREBP binds also to Vitamin-D receptor-interacting protein