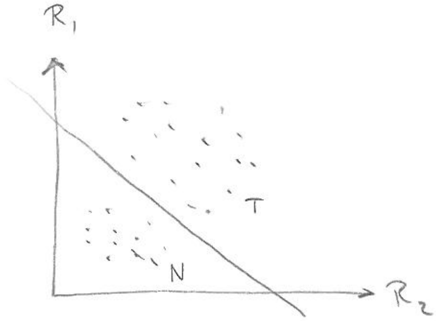
11/15

LINEAR CLASSIFIER FOR MULTI-ANALYTE DETECTION:



$$K = \sum_i \alpha_i [R_i]$$

EXAMPLE:

$$4nM = 5[R_1] - 3[R_2]$$

$R_1 \dots R_N$: RNA WITH ARBITRARY SEQ.

FOR MOLECULAR IMPLEMENTATION, USE NUCLEIC ACID TRANSLATOR + AMPLIFIERS:

$\alpha_i > 0$: $1 R_i \longrightarrow \alpha_1 S_A$

$\alpha_i < 0$: $1 R_i \longrightarrow |\alpha_i| S_B$

$K > 0$: ADD K S_A TO SOLUTION

$K < 0$: K S_B

COMPARE $[S_A]$ TO $[S_B]$

SAMPLE 1: $1R_1, 1R_2$: $4[S_A] + 5[S_A] > 3[S_B] \Rightarrow T$

FIXED GAIN AMPLIFIER:

$I + G \xrightarrow{k} O + W$ (HERE O: S_A, S_B. I: R_i)

$I + T \xrightarrow{q} W$

$$O(t) = G_0 - G_0 \left(\frac{1 - I_0/T_0}{1 - \frac{I_0}{T_0} e^{q(I_0 - T_0)t}} \right)$$

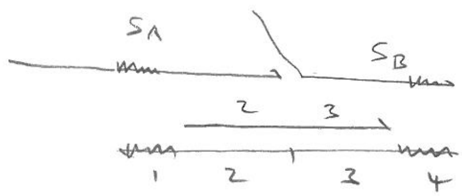
$$\lim_{t \to \infty} O(t) = G_0 \begin{cases} 1 & I_0 > T_0 \\ 1 - (1 - I_0/T_0)^{k/q} & I_0 < T_0 \end{cases}$$

$k = q: \; O(t \to \infty) = I_0 \underbrace{(G_0/T_0)}_{\alpha} = \alpha I_0$

USE SAME TOEHOLD ON G AND T TO GET $k = q$

ADJUST G_0/T_0 RATIO TO GET DESIRED α.

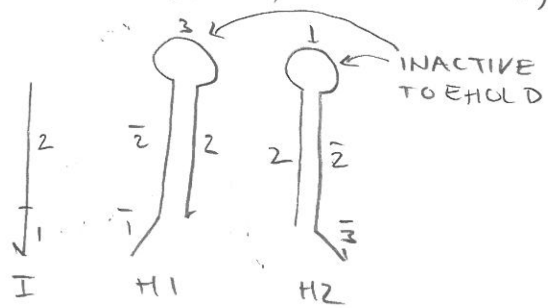
HOW CAN WE COMPARE $[S_A]$ TO $[S_B]^2$?



⇒ 2 —— 2 → IS RELEASED ONLY IF BOTH INPUTS ARE PRESENT.

POLYMERIZATION

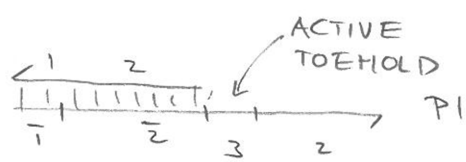
(DIRKS + PIERCE, PNAS 2004; VENKATARAMAN ET AL. PNAS 2010)



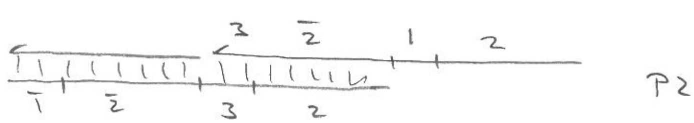
1, 3: 4nt

2: 14nt

I + H1:



P1 + H2:



P2 + H1: ...

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11/19

THERAPEUTIC APPLICATION:

DETECT DELETION IN mRNA

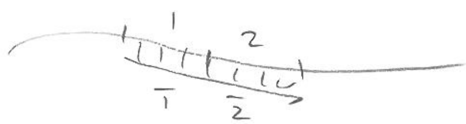
NORMAL mRNA:

CANCER mRNA

THERAPEUTIC MECHANISME:

PKR (PROTEIN KINASE R) BINDS dsRNA $\gtrsim$ 30bp ⇒ APOPTOSIS

SHIR + LEVITSKI (2004): TARGET DELETION WITH ASO



1,2: 20nt

⇒ FULL DUPLEX 40bp

⇒ PKR ACTIVATION

VENKATARAMAN 2010: