PADDING AND POOLING

① DNA can be expressed as a sequence of letters from the alphabet ⟨A, C, G, T⟩ ("adenine", "cytosine", "guanine", and "thymine"), e.g.

G A T T A C A A

C A G T T A A G

A A T A A A C C

G C A T T C A G

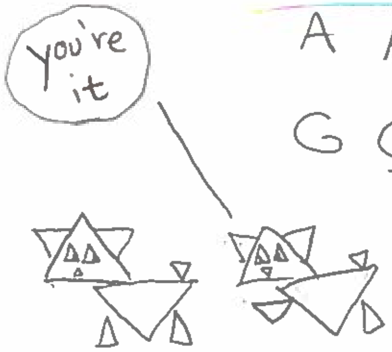
② Suppose that all DNA sequences of the form *CA*TT*AG*, where * is an arbitarily long (possibly empty) sequence, are responsible for some bodily function:

G A T T A C A A

$\underline{\text{C A}}$ G $\underline{\text{T T}}$ A $\underline{\text{A G}}$ ← positive

A A T A A A C C

G $\underline{\text{C A}}$ $\underline{\text{T T}}$ C $\underline{\text{A G}}$ ← positive



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③ We can imagine building a CNN with three convolution kernels: one to detect "CA", one to detect "TT", and one to detect "AG".

$$X: \quad \begin{array}{c|cccccccc} & C & A & G & T & T & A & A & G \\ & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow \\ A & 0 & 1 & 0 & 0 & 0 & 1 & 1 & 0 \\ C & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ G & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 1 \\ T & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 \end{array}$$

$$\vee\ \vee\ \vee\ \vee\ \vee\ \vee\ \vee$$

$$\dot{X}: \quad \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{bmatrix} \begin{array}{l} \leftarrow \text{"CA" detector} \\ \leftarrow \text{"TT" detector} \\ \leftarrow \text{"AG" detector} \end{array}$$

④ The first thing to notice is that $\dot{X}$ has one fewer column than X. This disparity will end up being rather annoying.

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⑤ We can remedy this by simply "padding" the end of the DNA sequence with a fifth letter, which we'll call "0".

$$\begin{array}{cccccccccc}
 & C & A & G & T & T & A & A & G & (0) \\
 & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow & \downarrow \\
X: & 0 & 1 & 0 & 0 & 0 & 1 & 1 & 0 & 0 \\
 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\
 & 0 & 0 & 1 & 0 & 0 & 0 & 0 & 1 & 0 \\
 & 0 & 0 & 0 & 1 & 1 & 0 & 0 & 0 & 0 \\
 & \vee & \vee & \vee & \vee & \vee & \vee & \vee & \vee &
\end{array}$$

$$\dot{X}: \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \begin{array}{l} \leftarrow \text{"CA"} \\ \leftarrow \text{"TT"} \\ \leftarrow \text{"AG"} \end{array}$$

⑥ If we run this convolution layer on other positive sequences:

$$\begin{array}{cccccccc}
G & C & A & T & T & C & A & G \\
\vee & \vee & \vee & \vee & \vee & \vee & \vee & \vee
\end{array}
\qquad
\begin{array}{cccccccc}
C & A & T & T & C & A & G & C \\
\vee & \vee & \vee & \vee & \vee & \vee & \vee & \vee
\end{array}
\qquad
\begin{array}{cccccccc}
T & T & C & A & T & T & A & G \\
\vee & \vee & \vee & \vee & \vee & \vee & \vee & \vee
\end{array}$$

$$\dot{X}: \begin{bmatrix} 0 & 1 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \quad \begin{bmatrix} 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix} \quad \begin{bmatrix} 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

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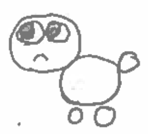
7. Observe that the next layer of the CNN is still faced with a relatively daunting task. If

$$\dot{X} = \begin{bmatrix} \dot{x}_{11} & \cdots & \dot{x}_{18} \\ \dot{x}_{21} & \cdots & \dot{x}_{28} \\ \dot{x}_{31} & \cdots & \dot{x}_{38} \end{bmatrix},$$

then we want to predict a positive response in each of the following cases:

- $\dot{x}_{11} = 1$ and $\dot{x}_{23} = 1$ and $\dot{x}_{35} = 1$
- $\dot{x}_{11} = 1$ and $\dot{x}_{23} = 1$ and $\dot{x}_{36} = 1$
- $\dot{x}_{\underline{1}1} = 1$ and $\dot{x}_{\underline{2}3} = 1$ and $\dot{x}_{3\underline{7}} = 1$
- $\dot{x}_{11} = 1$ and $\dot{x}_{24} = 1$ and $\dot{x}_{36} = 1$
- $\dot{x}_{11} = 1$ and $\dot{x}_{24} = 1$ and $\dot{x}_{37} = 1$
- $\dot{x}_{11} = 1$ and $\dot{x}_{25} = 1$ and $\dot{x}_{36} = 1$
- $\dot{x}_{12} = 1$ and $\dot{x}_{24} = 1$ and $\dot{x}_{36} = 1$
- $\dot{x}_{12} = 1$ and $\dot{x}_{24} = 1$ and $\dot{x}_{37} = 1$
- $\dot{x}_{12} = 1$ and $\dot{x}_{25} = 1$ and $\dot{x}_{37} = 1$
- $\dot{x}_{13} = 1$ and $\dot{x}_{25} = 1$ and $\dot{x}_{37} = 1$

e.g., read this line as: "CA" starts at position 1, "TT" starts at position 3, and "AG" starts at position 7



There's no way for it to generalize between these cases, so the training data would need to contain several instances of each case.

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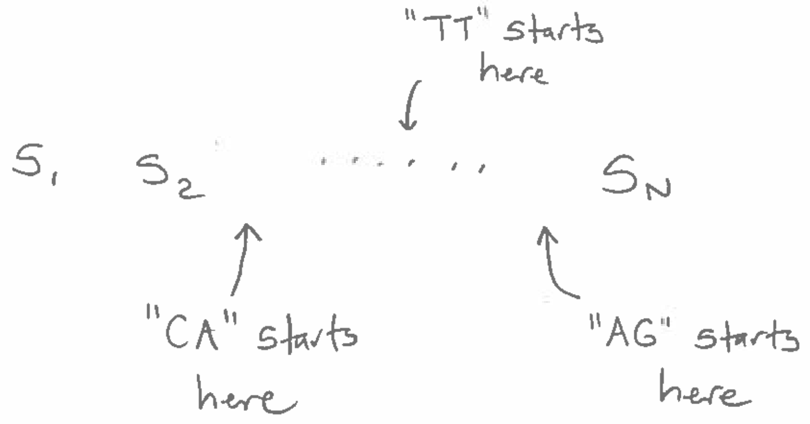
(8) This only gets worse as the length of the DNA sequence grows. If its length is N, then the number of different cases to consider is cubic in N:



(9) One way to tackle this issue is by creating a layer that summarizes the results of the detectors over subregions:

C A G T T A A G

$$\dot{X}: \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix}$$

$$\ddot{X}: \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix}$$

"AG" starts at position 7 or 8

C A T T C A G C

$$\begin{bmatrix} 1 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \end{bmatrix}$$

$$\begin{bmatrix} 1 & 0 & 1 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

e.g. "CA" starts at position 5 or position 6

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(10) This technique:

$$\dot{X}: \begin{bmatrix} \dot{x}_{11} & \dot{x}_{12} & \dot{x}_{13} & \dot{x}_{14} & \dot{x}_{15} & \dot{x}_{16} & \dot{x}_{17} & \dot{x}_{18} \\ \dot{x}_{21} & \dot{x}_{22} & \dot{x}_{23} & \dot{x}_{24} & \dot{x}_{25} & \dot{x}_{26} & \dot{x}_{27} & \dot{x}_{28} \\ \dot{x}_{31} & \dot{x}_{32} & \dot{x}_{33} & \dot{x}_{34} & \dot{x}_{35} & \dot{x}_{36} & \dot{x}_{37} & \dot{x}_{38} \end{bmatrix}$$

$$\ddot{X}: \begin{bmatrix} \max(\dot{x}_{11},\dot{x}_{12}) & \max(\dot{x}_{13},\dot{x}_{14}) & \max(\dot{x}_{15},\dot{x}_{16}) & \max(\dot{x}_{17},\dot{x}_{18}) \\ \max(\dot{x}_{21},\dot{x}_{22}) & \max(\dot{x}_{23},\dot{x}_{24}) & \max(\dot{x}_{25},\dot{x}_{26}) & \max(\dot{x}_{27},\dot{x}_{28}) \\ \max(\dot{x}_{31},\dot{x}_{32}) & \max(\dot{x}_{33},\dot{x}_{34}) & \max(\dot{x}_{35},\dot{x}_{36}) & \max(\dot{x}_{17},\dot{x}_{38}) \end{bmatrix}$$

is called <u>max-pooling</u>.

(11) Notice that max-pooling greatly simplifies the next layer of the CNN. If $\ddot{X} = \begin{bmatrix} \ddot{x}_{11} & \ddot{x}_{12} & \ddot{x}_{13} & \ddot{x}_{14} \\ \ddot{x}_{21} & \ddot{x}_{22} & \ddot{x}_{23} & \ddot{x}_{24} \\ \ddot{x}_{31} & \ddot{x}_{32} & \ddot{x}_{33} & \ddot{x}_{34} \end{bmatrix}$, then

we want to predict a positive response in these cases:

- $\ddot{x}_{11} = 1$ and $\ddot{x}_{22} = 1$ and $\ddot{x}_{33} = 1$
- $\ddot{x}_{11} = 1$ and $\ddot{x}_{22} = 1$ and $\ddot{x}_{34} = 1$
- $\ddot{x}_{11} = 1$ and $\ddot{x}_{23} = 1$ and $\ddot{x}_{34} = 1$
- $\ddot{x}_{12} = 1$ and $\ddot{x}_{23} = 1$ and $\ddot{x}_{34} = 1$

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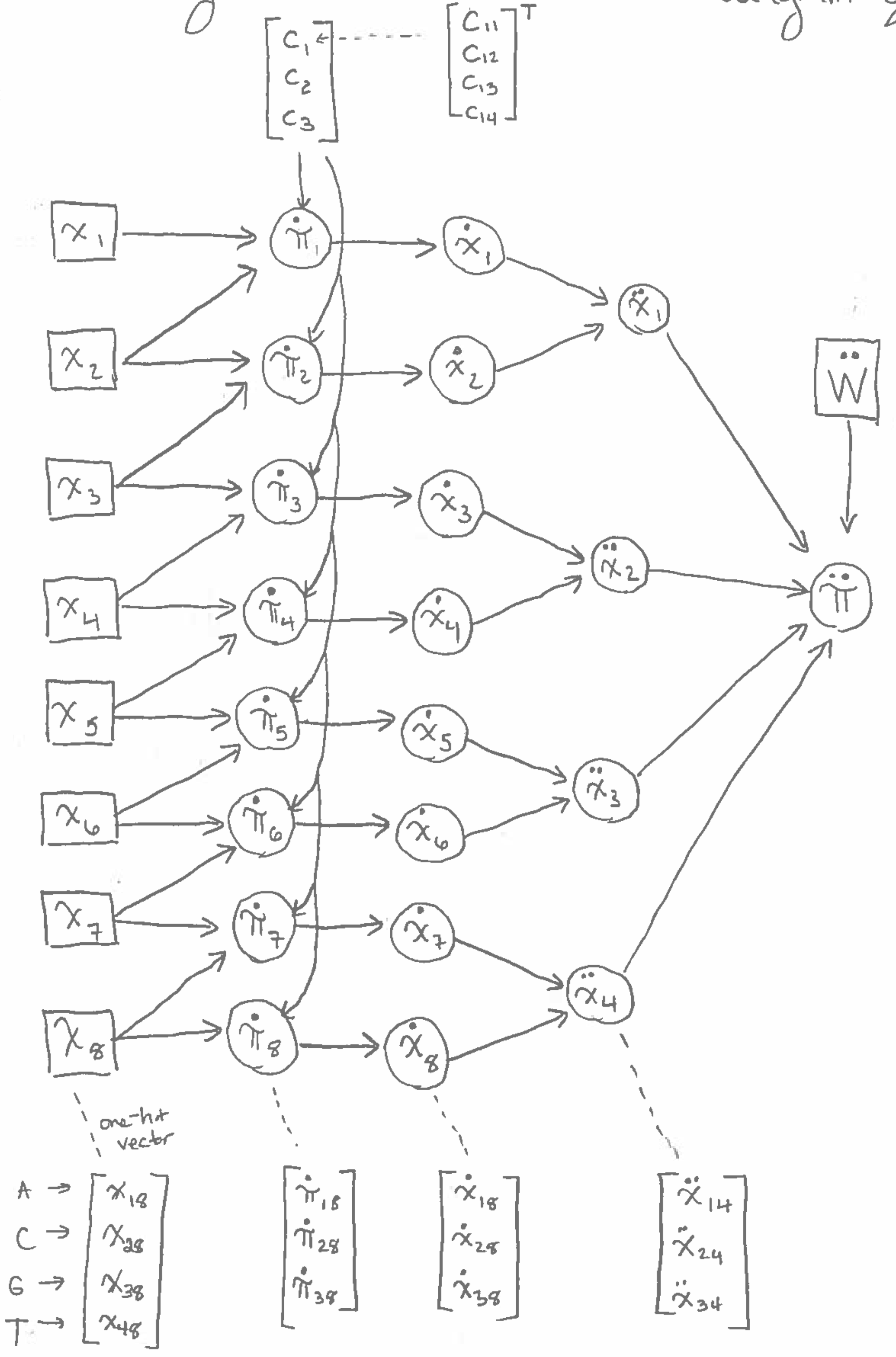
(12) Summarizing all this as a causal diagram gives us:



c_1, c_2, c_3
c_{11}, c_{12}, c_{13}, c_{14}, T
x_1, x_2, x_3, x_4, x_5, x_6, x_7, x_8
$\dot{\pi}_1$, $\dot{\pi}_2$, $\dot{\pi}_3$, $\dot{\pi}_4$, $\dot{\pi}_5$, $\dot{\pi}_6$, $\dot{\pi}_7$, $\dot{\pi}_8$
$\dot{x}_1$, $\dot{x}_2$, $\dot{x}_3$, $\dot{x}_4$, $\dot{x}_5$, $\dot{x}_6$, $\dot{x}_7$, $\dot{x}_8$
$\ddot{x}_1$, $\ddot{x}_2$, $\ddot{x}_3$, $\ddot{x}_4$
$\ddot{W}$
$\ddot{\pi}$
one-hot vector
A →, C →, G →, T →
x_{18}, x_{28}, x_{38}, x_{48}
$\dot{\pi}_{18}$, $\dot{\pi}_{28}$, $\dot{\pi}_{38}$
$\dot{x}_{18}$, $\dot{x}_{28}$, $\dot{x}_{38}$
$\ddot{x}_{14}$, $\ddot{x}_{24}$, $\ddot{x}_{34}$

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(13) How does one backpropagate through a maxpool layer? Consider the following simple example:

$$\begin{tikzcd} & x_1 \arrow[dr] & \\ w \arrow[ur] \arrow[dr] & & \dot{x} \\ & x_2 \arrow[ur] & \end{tikzcd}$$

where $\dot{x} = \max(x_1, x_2)$, and suppose we need to compute $\frac{\partial \dot{x}}{\partial w}$. Assume x_1, x_2 are scalars.

(14) From the Chain Rule:

$$\frac{\partial \dot{x}}{\partial w} = \frac{\partial \dot{x}}{\partial x_1}\frac{\partial x_1}{\partial w} + \frac{\partial \dot{x}}{\partial x_2}\frac{\partial x_2}{\partial w}$$

We know:

$$\dot{x} = \begin{cases} x_1 & \text{if } x_1 \geq x_2 \\ x_2 & \text{if } x_2 \geq x_1 \end{cases}$$

So:

$$\frac{\partial \dot{x}}{\partial x_1} = \begin{cases} 1 & \text{if } x_1 > x_2 \\ 0 & \text{if } x_2 < x_1 \\ \text{undefined} & \text{if } x_1 = x_2 \end{cases} \qquad \frac{\partial \dot{x}}{\partial x_2} = \begin{cases} 1 & \text{if } x_2 > x_1 \\ 0 & \text{if } x_1 > x_2 \\ \text{undefined} & \text{if } x_1 = x_2 \end{cases}$$

The functions are piecewise differentiable, much like ReLU:

$$\frac{d}{dz} a(z) = \begin{cases} 1 & \text{if } z > 0 \\ 0 & \text{if } z < 0 \\ \text{undefined} & \text{if } z = 0. \end{cases}$$

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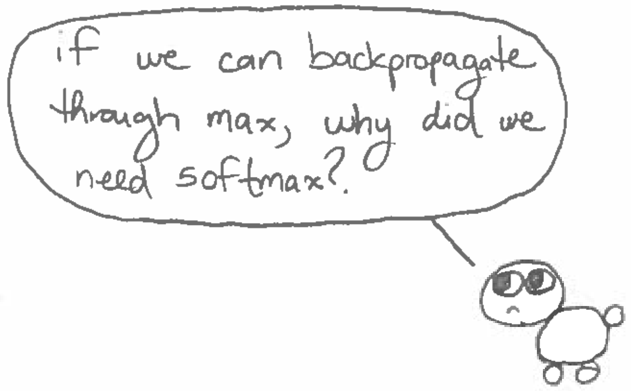
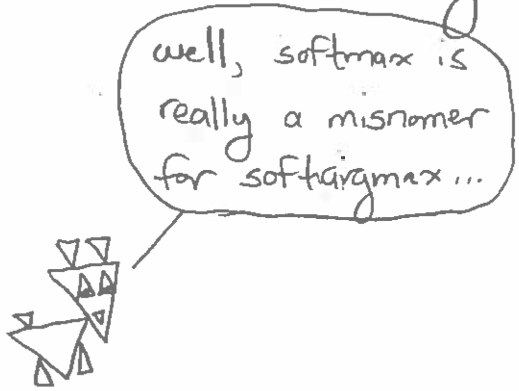
(15) As with ReLU, we just need to hope that we don't reach a place in our weight space (during gradient descent) where $x_1 = x_2$. Since they're both real numbers, chances are low.

(16) It could be asked:


if we can backpropagate through max, why did we need softmax?

The answer lies in the fact that softmax is really a misnomer for softargmax.



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(17) Recall that softmax takes a vector of reals and produces a skewed distribution of the same dimension:

e.g.

$$\begin{bmatrix} 1.6 \\ -0.2 \end{bmatrix} \longrightarrow \begin{bmatrix} .86 \\ .14 \end{bmatrix}$$

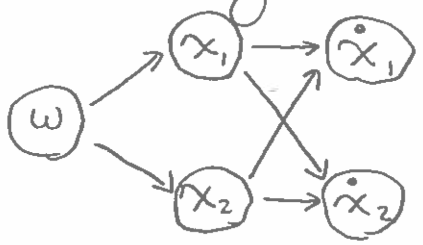
This is an approximation of an argmax function that produces a one-hot vector:

$$\begin{bmatrix} 1.6 \\ -0.2 \end{bmatrix} \longrightarrow \begin{bmatrix} 1 \\ 0 \end{bmatrix}$$

It is not an approximation of the max function:

$$\begin{bmatrix} 1.6 \\ -0.2 \end{bmatrix} \longrightarrow 1.6$$

(18) Let's try implementing this argmax function:



where: $\dot{x}_1 = \begin{cases} 1 & \text{if } x_1 \geq x_2 \\ 0 & \text{if } x_2 > x_1 \end{cases}$ $\quad \dot{x}_2 = \begin{cases} 1 & \text{if } x_2 \geq x_1 \\ 0 & \text{if } x_1 > x_2 \end{cases}$

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(19) That means:

$$\frac{\partial \dot{x}_1}{\partial x_1} = 0 \qquad \frac{\partial \dot{x}_1}{\partial x_2} = 0$$

$$\frac{\partial \dot{x}_2}{\partial x_1} = 0 \qquad \frac{\partial \dot{x}_2}{\partial x_2} = 0$$

All the derivatives are degenerate and useless.