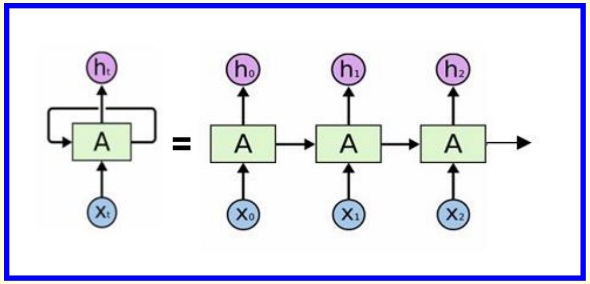
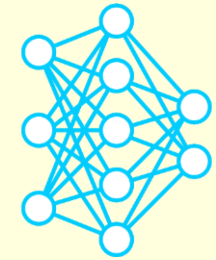
Deep Learning by Example on Biowulf

Class #2: Recurrent and 1D-Convolutional neural networks and their application to prediction of the function of non-coding DNA

Gennady Denisov, PhD



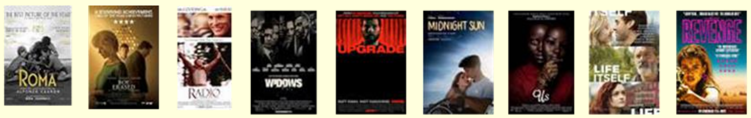
Class #2 Goals



DL networks to be discussed:
- Recurrent Neural Networks **(RNNs)**
- 1D Convolutional Neural Networks **(1D-CNNs)**

Purpose: process sequences of values

Standard non-bio RNN benchmark:
IMDB movie review sentiment prediction:

…  …

(Text) (Text) (Text) (Text) (Text) (Text) (Text) (Text) (Text)

1 0 1 0 0 1 0 1 1

Popular non-bio applications:
- natural language processing
- text document classification
- time series classification, comparison and forecasting
- …

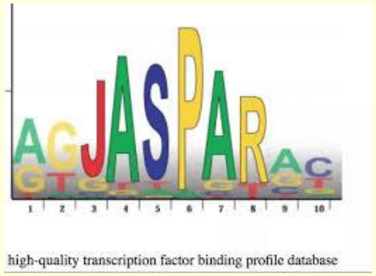
Bio example #2:
predicting the function of non-coding DNA

ATTCCCGTAATCTACGATTAAGTCACAACCAAACC

[01001101010011101 0…110]

Motif: **short**, recurring pattern in DNA that is presumed to have a certain biological function.

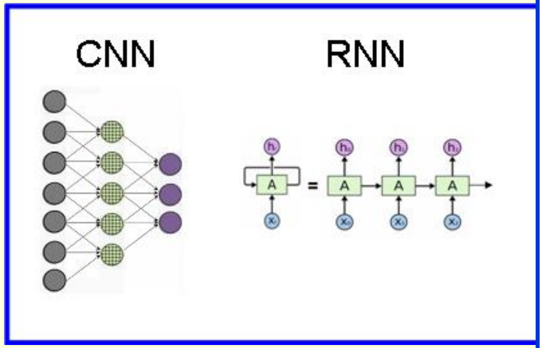
Motif database



Distinctive features of the biological example:
1) a **vector of binary labels** is assigned to each data sample
2) identification of the **motif sequences**
3) exploration of the **long-range dependencies** between motifs/different parts of fragments

Examples summary

Class #	1	2	3	4	5	6	7
Bio app	Bioimage segmentation / fly brain connectome	Genomics / prediction of function of non-coding DNA	Genomics / reduction of dimensionality of cancer transcriptome	Bioimage synthesis / developmental biology	Drug molecule design	Genomics / classification of cancer types	Drug molecule property prediction
Neural network type	Convolutional	Recurrent or 1D-Convolutional	Autoencoder	Generative Adversarial	Reinforcement Learning	Graph Convolutional	Message Passing
ML type	Supervised	Supervised	Unsupervised	Unsupervised	Reinforcement	Supervised	Supervised



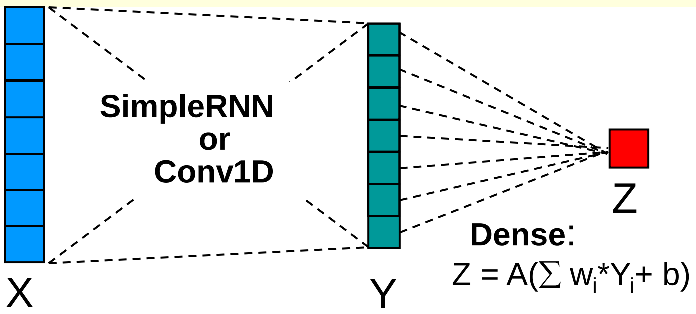
1) RNNs process **sequences of values,** while CNNs - grid values
2) both RNNs and CNNs **share parameters** between different parts of a model, unlike MLP, where each weight is unique
3) RNNs **allow cyclic connections**, unlike CNNs or MLP / Dense networks, which are feedforward / have no cycles
4) both examples #1 and #2 **take a supervised ML approach**,
5) yet are complementary in the way their training is performed:
   #1: limited ground truth **data** ⇒ augmentation, fit_generator
   #2: plenty of ground truth **data** ⇒ no augmentation, fit

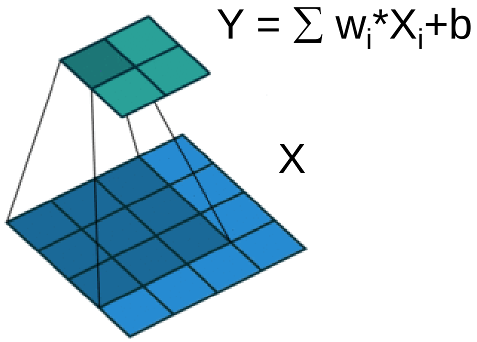
Motif detection: a prototype example #1

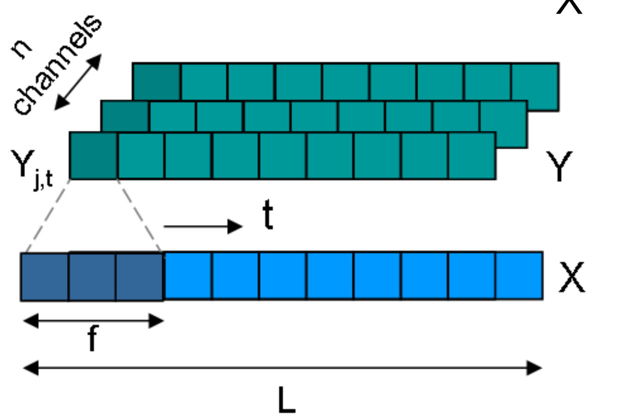
tensors, layers, parameters, hyperparameters, Dense, SimpleRNN, Conv1D, RNN memory

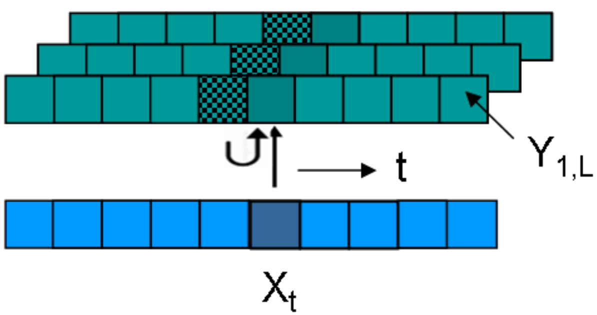
Input: a set of training **sequences** of 0's and 1's and **binary labels** assigned to each sequence, depending on whether or not a certain **(unknown) motif** is present in the sequence.
Task: train the model on the data, so that it could automatically predict labels for new sequences.
Example: 010$\boxed{111}$00101

Model:









$$Y_{j,t} = A(b_j + w_{X1,j}\cdot X_{t-1} + w_{X2,j}\cdot X_t + w_{X3,j}\cdot X_{t+1})$$

j=1,…,n

$$Y_{j,t} = A(b_j + w_{XY,j}\cdot X_t + \sum_{k=1}^{n} w_{YY,j,k}\cdot Y_{k,t-1})$$

Conv2D

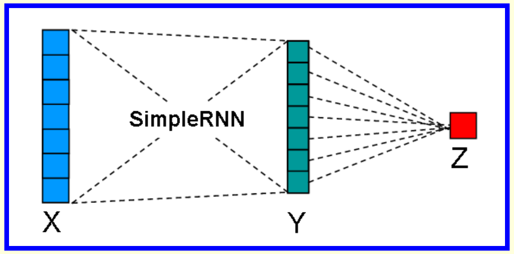
- parameters: w_i, b
- hyperparameters:
  f = filter/kernel size (=3),
  padding (= "valid")

Conv1D

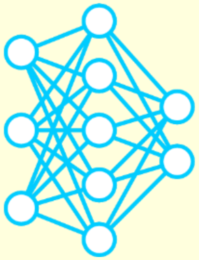
- parallelizable
- memoryless
- independent channels
- output: all the channel elements
- output shape: (n, L-f+1)
- # params = (f+1)*n

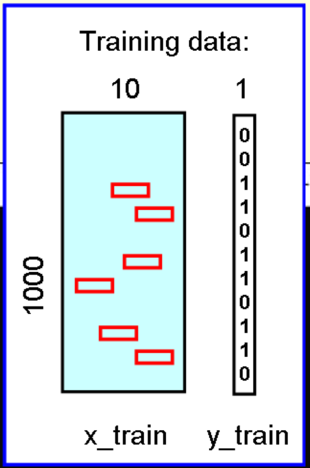
SimpleRNN

- sequential
- has memory
- interacting channels
- output: only last elements $Y_{1,L}, \ldots, Y_{n,L}$
- output shape: (n, 1)
- # params = n + n + n*n = 2n + n^2



SimpleRNN-based code for motif detection





Header:
- general Python imports
- Dense, SimpleRNN
- Sequential

Get data
- a motif to search for
- generate synthetic data:
  x_train, y_train
  x_test, y_test

Define a model
- Sequential construct approach
- compile, loss, optimizer

Run the model
- fit, checkpoint, epoch, callbacks
- predict

denisovga@biowulf:/usr/local/apps/DLBio/class2/bin

```
#!/usr/bin/env python

# Imports
import re, random, string
import numpy as np
from keras.models import Sequential
from keras.layers import SimpleRNN, Flatten, Dense
from keras.callbacks import ModelCheckpoint
from keras import metrics

# Get data
n_train,n_test,s_len,n_channels,n_epochs,motif = 1000,40,10,2,500,"111"
np.random.seed(7)
x_train_str = [''.join([random.choice('01') for i in range(s_len)]) \
                                            for j in range(n_train)]
x_test_str  = [''.join([random.choice('01') for i in range(s_len)]) \
                                            for j in range(n_test)]
x_train = np.reshape(np.array([[int(c) for c in x_train_str[j]] \
                     for j in range(n_train)]), [n_train,s_len,1])
x_test  = np.reshape(np.array([[int(c) for c in x_test_str[j]] \
                     for j in range(n_test )]), [n_test, s_len,1])
y_train = np.array([np.where(re.search(motif, x_train_str[i]), 1, 0) \
                    for i in range(n_train)])
y_test  = np.array([np.where(re.search(motif, x_test_str[i]), 1, 0) \
                    for i in range(n_test)])
# Define a model
model = Sequential()
model.add(SimpleRNN(n_channels, return_sequences=True, input_shape=(s_len, 1)))
model.add(Flatten())
model.add(Dense(1, activation='sigmoid'))
model.compile(loss='binary_crossentropy', optimizer='sgd')

# Run the model on the data
checkpoint_file = "mdet_simplernn.h5"
if 0: model.load_weights(checkpoint_file)
checkpointer = ModelCheckpoint(filepath = checkpoint_file)
model.fit(x_train, y_train, epochs=n_epochs, callbacks=[checkpointer])
y = model.predict(x_test)
for i in range(0,n_test):
    print("y, y_test=", int(round(y[i][0])), y_test[i])
                                                          12,55         All
```

Motif discovery: a prototype example #2

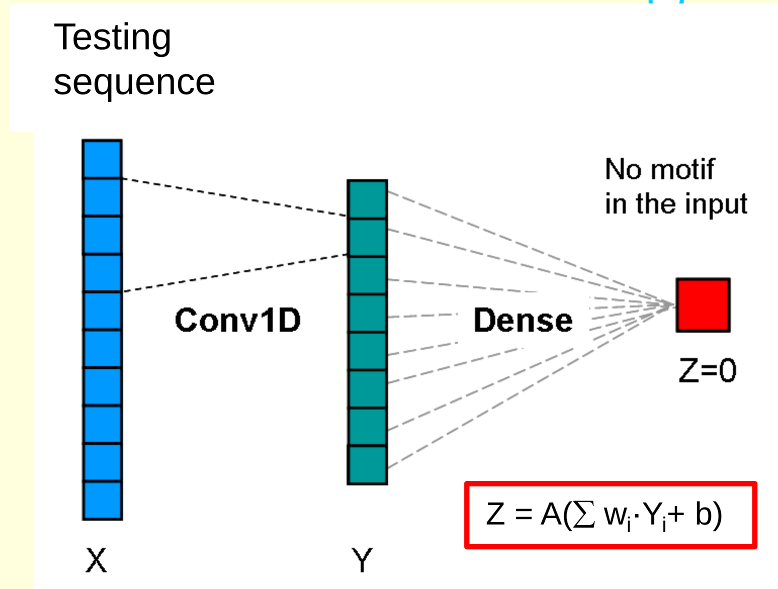
PWMs: G.D.Stormo et al, NAR 1982

Y.Ding et al, bioRxiv 2019; doi: https://doi.org/10.1101/163220

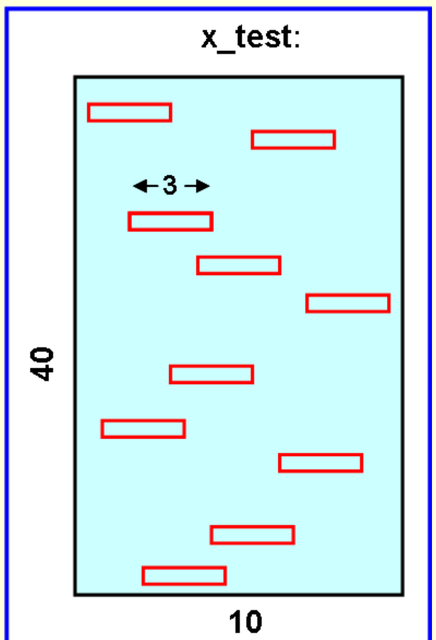
Input: 1) **pre-trained weights** from the previous example, but **using Conv1D** instead of SimpleRNN
2) a set of **testing sequences** of 0's and 1's similar to the previous example

Task: determine the **motif sequence**

Example: 010111 00101



Testing data:



(Implicit) Assumptions of the heuristic approach:

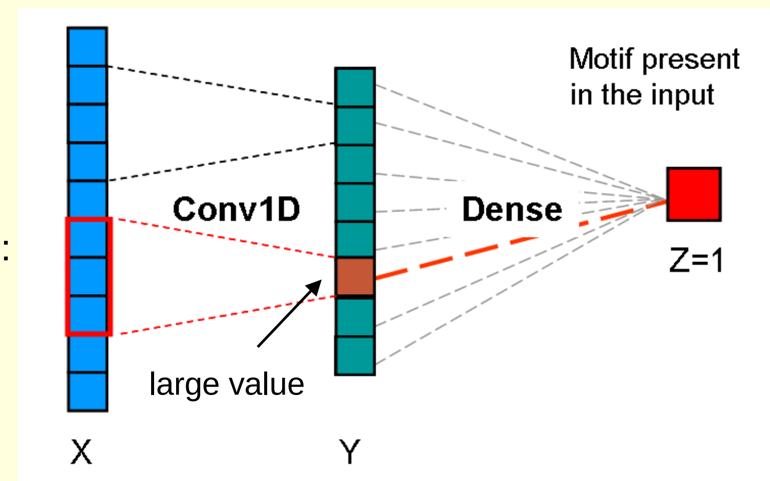
1) All the **weights** of the Dense layer are **positive**
2) The **upper bound** of the motif size is (approximately) **known**

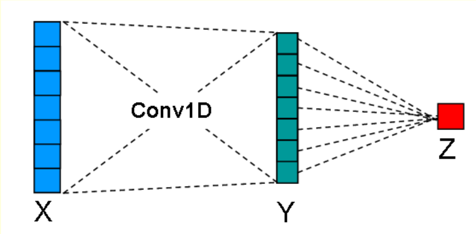
Algorithm:

1) Determine an "optimal" position of a filter in each "good" testing sequence:

$$\boxed{X_{opt} = argmax(Conv1D(X))}$$

2) Determine the motif as PWM / consensus sequence over the vicinities of X_{opt} in the test sequences





Conv1D-based code for motif discovery

Header.

Get data.

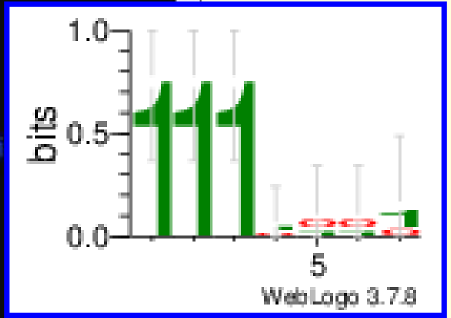
Define a model

Run the model:

- load weights
- extract the testig data with motif
- determine an "optimal" position in test sequence
- extract instances
- compute PWM and the motif sequence

@biowulf:/usr/local/apps/DLBio/class2/bin

```
#!/usr/bin/env python

# Imports
import numpy as np
from keras.models import Sequential
from keras.layers import Conv1D, Dense, Flatten
from keras import backend as K
from Bio import motifs
from Bio.Seq import Seq

# Get data
n_seq,s_len,f_size,w_size,n_filt,thresh,instances = 40,10,3,7,2,0.8,[]
np.random.seed(1)
x_test = np.round(np.random.uniform(0, 1, (n_seq, s_len, 1)))

# Define a model
model = Sequential()
model.add(Conv1D(n_filt,f_size,input_shape=(s_len,1),activation='relu'))
model.add(Flatten())
model.add(Dense(1, activation='sigmoid'))
model.compile(loss='binary_crossentropy', optimizer='sgd')

# Run the model on the data
def call(x,y,t): return "1" if x>t else ("0" if y < 1-t else "N")
model.load_weights("mdet_conv1d.h5")
z = [int(np.round(model.predict(x_test)[i,0])) for i in range(n_seq)]
x_test = np.delete(x_test,[k==0 for k in z],axis=0) # keep only data wi
output = model.layers[0].get_output_at(0)
func = K.function([model.input], [K.argmax(output, axis=1), \
                                  K.max(    output, axis=1)])
y = func([x_test])
pos = np.array([y[0][i][0] for i in range(x_test.shape[0])])
x_test = np.squeeze(x_test, axis=2).tolist()
alignment = open("01_conv1d.fa", "w")
for i in range(len(x_test)):
    pos_left, pos_right = max(0, pos[i]), min(pos[i]+w_size, s_len)
    seq = "".join([str(int(x)) for x in x_test[i][ pos_left:pos_right]])
    if len(seq) == w_size:
        instances.append(Seq(seq))
        alignment .write(">" + str(i+1) + "\n")
        alignment .write(seq + "\n")
alignment .close()
pwm = motifs.create(instances,alphabet='01').counts.normalize()
print("\nmotif=", "".join([call(x, 1-x, thresh) for x in pwm[1,:]]))
                                                                44,70          All
```



Stochastic Gradient Descent optimizer

gradient descent (GD), mini-batch GD

```
keras.optimizers.SGD(learning_rate =0.01, momentum=0.0, nesterov=False, …)
```

denisovga@biowulf:/usr/local/apps/DLBio/class2/bin

```
model.compile(loss='binary_crossentropy', optimizer='sgd', ...))
model.fit(x_train, y_train, epochs=1000)
                                                  2,42          Top
```

Using SGD with defalt options

$$\boxed{w_{t+1} = w_t - \gamma \cdot \nabla_w J(w_t)}$$

- basic gradient descent formula for updating weights

w = vector of weights

t = iteration #

γ = learning rate

$\nabla_w J$ = gradient of loss with respect to weights

(Mini-batch) Stochastic Gradient Descent:

- use the $\nabla_w J(w_t\,;\, x, y)$ <u>**averaged over a mini-batch of samples**</u> (= data items x, labels y)
- N / **batch_size** iterations per epoch (N = total number of samples, **batch_size** =32 by default)

denisovga@biowulf:/usr/local/apps/DLBio/class2/bin

```
customized_sgd = keras.optimizers.SGD(learning_rate =1.e-4,
                                      momentum = 0.9,
                                      nesterov = True)
model.compile(loss       = 'binary_crossentropy',
              optimizer = customized_sgd , ...)
model.fit(x_train, y_train, epochs=1000, batch_size = 10)
                                                  11,59         Bot
```

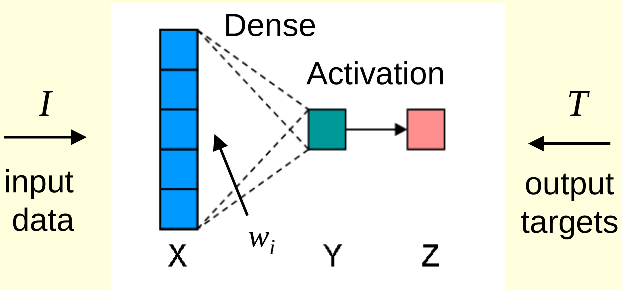
Using SGD with customized options

(To be continued on a backup slide)

Training a feedforward network

backpropagation, chain rule, vanishing gradient

Perceptron

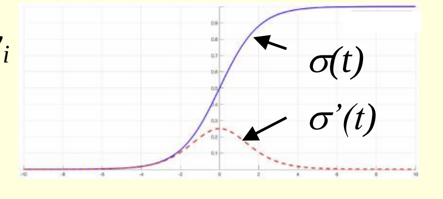


Backpropagation purpose: compute the gradient of loss

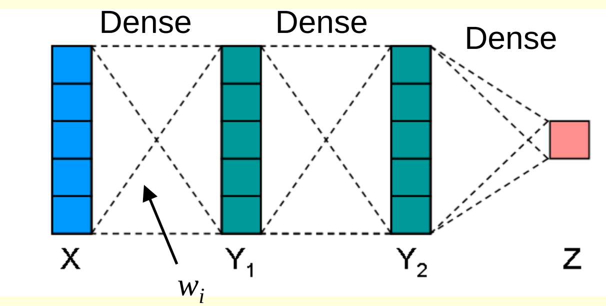
$Z(w) = \sigma(w\cdot X + b)$ (mse) loss $J = \frac{1}{2}(Z(w) - T)^2$ $\Delta J \Rightarrow \Delta w$

$$\Delta J_i = (\partial J / \partial w_i) \cdot \Delta w_i = (Z-T)\cdot(\partial Z/\partial w_i)\cdot\Delta w_i$$

$$= \underbrace{\boxed{(Z-T)\cdot \sigma'(w\cdot I + b)\cdot I_i}}_{\text{(the component of) the gradient of loss}} \cdot \Delta w_i$$



Multi-layer perceptron (MLP)

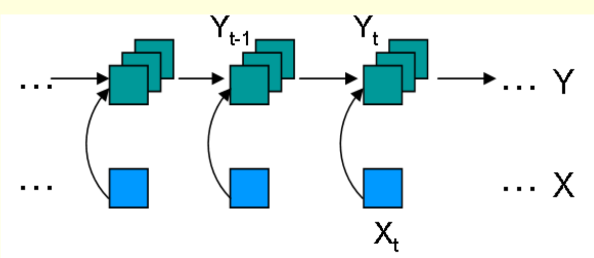


Backpropagation for MLP:

$Z = \sigma(W_3\cdot Y_2 + b_3)$ $Y_2 = \sigma(W_2\cdot Y_1 + B_2)$ $Y_1 = \sigma(W_1\cdot X + B_1)$

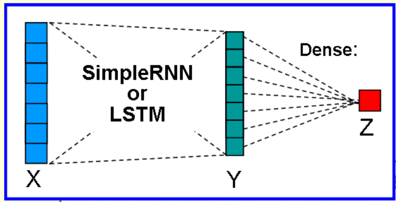
$$\Delta J_i = \underbrace{\boxed{(Z - T)\cdot\sigma'(W_3\cdot Y_2 + B_3)\cdot W_3\cdot\sigma'(W_2\cdot Y_1 + B_1)\cdot W_2\cdot\sigma'(W_1\cdot X + B_1)\cdot X_i}}_{\text{(the component of) the gradient of loss}} \cdot \Delta w_i$$

Unfolded SimpleRNN



- similar to the **very deep** feedforward network:
  $Y^t = \sigma(W_X\cdot X^t + W_Y\cdot Y^{t-1} + B)$
- **weights are shared** across the (time) layers

The deeper the network is, the more likely that the vanishing gradients issue will occur



Vanishing gradients: a prototype example #3

A.Joulin and T.Mikolov . arXiv:1503.01007v4 (2015)

```
#!/usr/bin/env python

import re, random, string, numpy as np, tqdm
import keras
from keras.models import Input, Model
from keras.layers import Dense, Flatten, Dropout, LSTM, SimpleRNN

# Get data
n_seq,seq_len,n_train,pred_len,max_len_pattern,n_epochs = 200,1000,150,100,20,700
data, x_train, y_train, x_test, y_test = [], [], [], [], []
np.random.seed(7)
for i in tqdm.tqdm(range(n_seq)):
    seq = []
    while len(seq) < seq_len:
        n = np.random.randint(1,high=max_len_pattern)
        seq += ['0']*n + ['1']*n
    data.append(''.join(seq[:seq_len]))
    start = False; prev_char = ''
    for j in range(pred_len, seq_len):
        seq_in, c_out  = data[i][(j-pred_len):j], data[i][ j]
        if start and (c_out=='1' or (c_out=='0' and prev_char=='1')):
            if i < n_train: x_train.append([int(c) for c in seq_in]); \
                            y_train.append( int(c_out))
            else:           x_test.append( [int(c) for c in seq_in]); \
                            y_test.append(  int(c_out))
        if prev_char == '0' and c_out == '1': start = True
        prev_char = c_out

# Define a model
X = Input((pred_len,1,))
if 1: Y = SimpleRNN(1, return_sequences=True)(X)
else: Y =      LSTM(1, return_sequences=True)(X)
Y = Dropout(0.2)(Y)
Y = Flatten()(Y)
Z = Dense(1, activation='sigmoid')(Y)
model = Model(inputs = X, outputs = Z)
model.compile(loss='mse', optimizer="adam", metrics=['acc'])

#Run the model on the data
expand_dims = lambda x, y: np.expand_dims(np.array(x), axis=y)
bsize, checkpoint_file = 1000, "vgrad_rnn.h5"
checkpointer = keras.callbacks.ModelCheckpoint(filepath=checkpoint_file)
if 0: model.load_weights(checkpoint_file)
if 1: model.fit(expand_dims(x_train,2), np.array(y_train), batch_size=bsize,
                shuffle=True, epochs=n_epochs, callbacks=[checkpointer])
scores = model.evaluate(expand_dims(x_test,2), np.array(y_test), verbose=0)
print("\n%s: %.2f%%" % (model.metrics_names[1],np.array(scores[1])*100))
                                                          47,76
```

Input: a **sequence of** consecutive **palindromes**
$X = \{0^n 1^n\}$ **for random** $n = 1, \ldots, N$
$N = 20$

Example: $\underbrace{000111}_{n=3}\underbrace{0011}_{n=2}\underbrace{0000011111}_{n=5}\ldots$

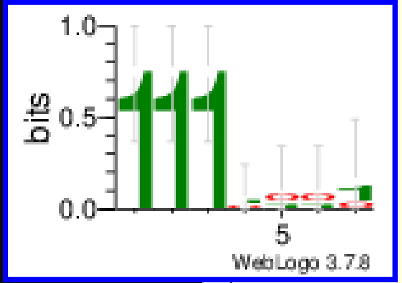
Task: predict next character in the **deterministic** part of the sequence

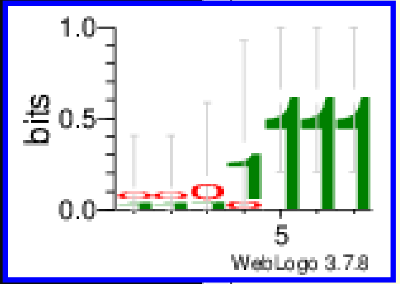
# training epochs	predict. acc
SimpleRNN	
100	91.81%
300	91.89%
500	**92.90%**
700	**92.94%**
LSTM	
100	97.92%
300	98.84%
500	**98.99%**
700	**99.05%**

How to run the prototype examples on Biowulf?

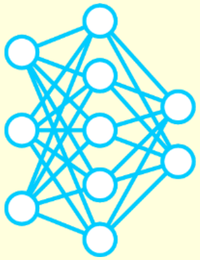
denisovga@biowulf:/data/denisovga/1_DL_Course/0_Intro

```
[user@biowulf] sinteractive

[user@cn0858] module load DLBio/class2
...
[+] Loading DLByExample class2  ...

[user@cn0858]$ ls $DLBIO_BIN
mdet_conv1d.py      mdisc_conv1d.py       vgrad_rnn.py
mdet_simplernn.py   mdisc_simplernn.py

Using TensorFlow backend.
...
Epoch 1/500
32/32 [==============================] - 1s 2ms/step - loss: 0.7808
...
Epoch 500/500
32/32 [==============================] - 0s 2ms/step - loss: 0.1024
...
[user@cn0858]$ mdet_conv1d.py
...
[user@cn0858]$ mdisc_conv1d.py
...
motif= 111NNNN
[user@cn0858]$ weblogo -f 01_conv1d.fa    -F png -o 01_conv1d.png  \
                       -a '01' -C green 1 '1' -C red 0 '0'
...
[user@cn0858]$ mdisc_simplernn.py
...
motif= NNNN111
[user@cn0858]$ weblogo -f 01_simplernn.fa -F png -o 01_simplernn.png \
                       -a '01' -C green 1 '1' -C red 0 '0'
...
[user@cn0858]$ vgrad_rnn.py
...
...
Epoch 700/700
74/74 [==============================] - 4s 53ms/step - loss: 0.0543 - acc: 0.9318

acc: 92.94%
                                                              8,39          Top
```





Biological example #2: Predicting the function of noncoding DNA *de novo* from sequence with DanQ and DeepSEA

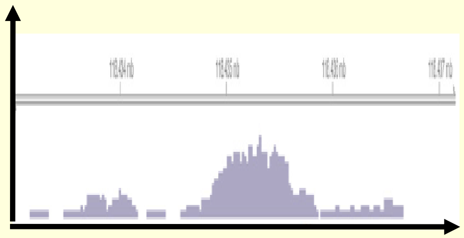


DanQ: D.Quang, X.Xie, Nucl. Acids Res. (2016)
DeepSEA: J.Zhou, O.G.Troyanovskaya, Nature Methods (2015)
Review: G.Eraslan et al., Nature Reviews Genetics (2019)

Task:
predict the targets directly from DNA sequence

Events ("targets"; total = 919 types):
- **transcription factor binding sites (690 types)**
- **DNase I hypersensitivity sites (125 types)**
- **histone marks (104 types)**

NGS →



Call peaks → **Narrow peak format** → One-hot encode → **DeepSEA data**

Models:
DanQ (2016) – Keras,
DeepSEA (2015) – Torch (reimplemented in Keras),
DeepBind (2015), Basset (2016) – Torch,
FIDDLE (2016), DeepMotif (2016),
Basenji (2017) – Tensorflow, DeepCpG (2017), …

DL frameworks:
Keras,
Torch,
Tensorflow,
…

Network types:
RNN,
1D-CNN

Overview of the training code
(only the main function is shown)

Imports statements, other function definitions

Header
- parse the command line options

Get data
- training, testing and validation data

Define a model
- DeepSEA model
- DanQ model
- MaxPooling1D, Flatten, Dropout
- LSTM and BLSTM
- compile, loss
- optimizer

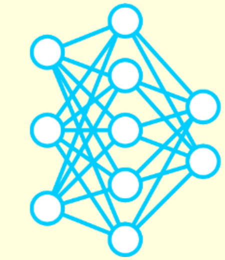
Run the model
- fit

denisovga@biowulf:/data/denisovga/1_DL_Course/2_RNNs

```
if __name__ == "__main__":

    # Parse command line argumants
    opt, checkpoint_name, input_weights_file, Optimizer \
        = parse_command_line_arguments("train")
    os.environ['CUDA_VISIBLE_DEVICES'] = "0,1,2,3"

    # Get data
    X_train, y_train, X_valid, y_valid = load_data(opt)
    print("\nX_train.shape=", X_train.shape, " y_train.shape=", y_train.shape)
    print("\nX_valid.shape=", X_valid.shape, " y_valid.shape=", y_valid.shape)

    # Define a model
    strategy = tf.distribute.MirroredStrategy()
    with strategy.scope():
        model = get_model(opt)
        custom_checkpointer = MyCustomCallback(model, checkpoint_name,
                                   verbose=opt.verbose, save_best_only=True)
        custom_val_loss = MyCustomValidationCallback(model, [X_valid, X_valid],
                                                            [y_valid, y_valid])
        model.compile(loss      = "binary_crossentropy",
                      optimizer = Optimizer,
                      metrics   = ['acc'])
        if opt.load_weights:
            model.load_weights(opt.checkpoint_file)
        model.summary()

    # Run the model
    callbacks_list = [custom_checkpointer]
    if opt.lr_schedule:
        global_lr = opt.learning_rate
        callbacks_list.append(LearningRateScheduler(step_decay))
    model.fit(X_train, y_train, batch_size=opt.batch_size, shuffle=True,
        epochs=opt.num_epochs, validation_data = (X_valid, y_valid),
        callbacks=callbacks_list, workers=opt.num_gpus)

                                                   122,9          Bot
```

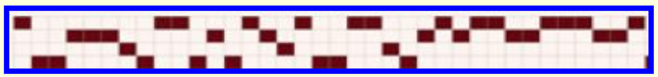
Available data

one-hot encoding; training, validation, and testing data

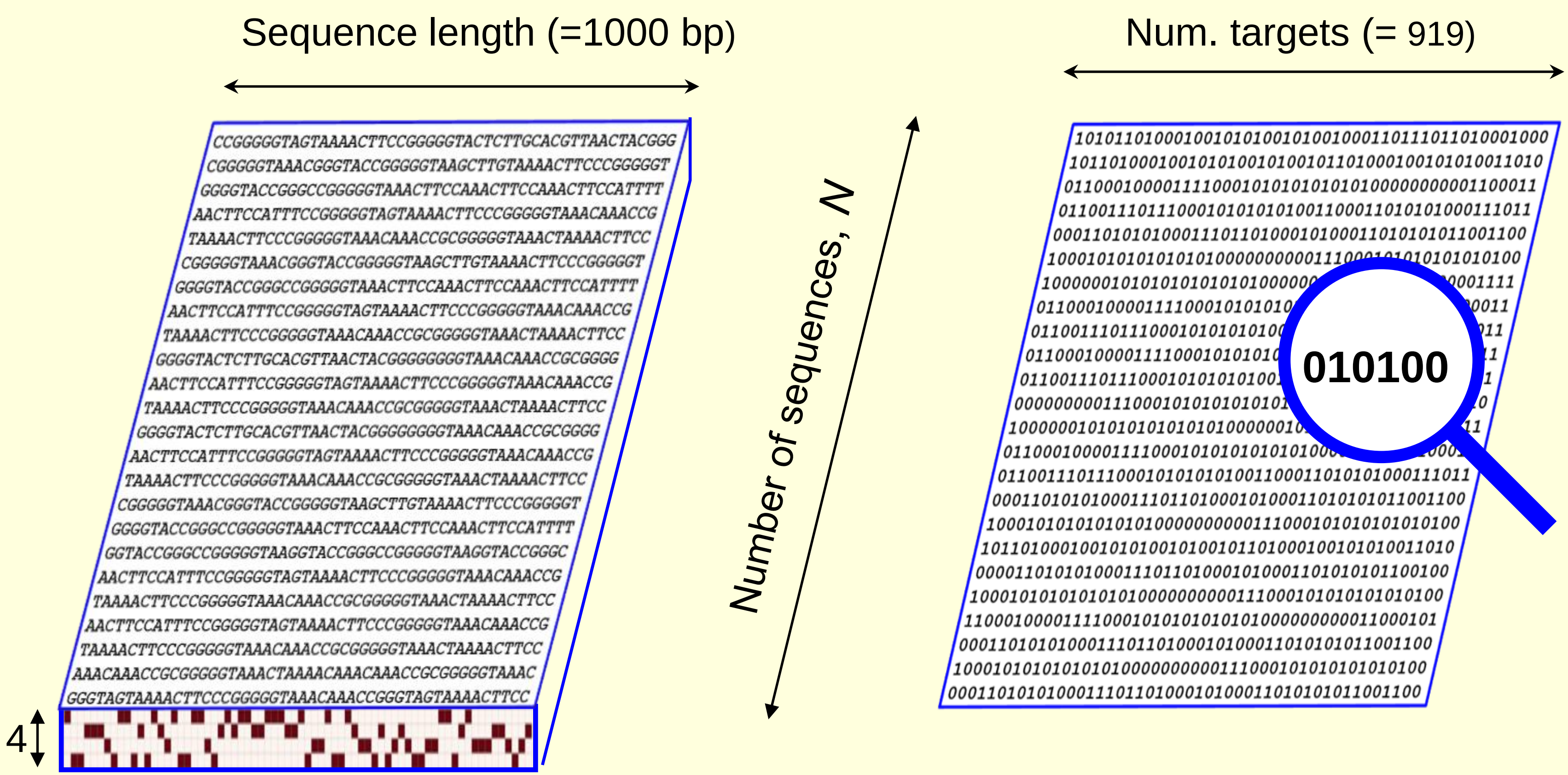


One-hot encoding:

ATTCCCGTAATCTACGATTAAGTCACAACCAAACC



Training data: N = 4.4 M => **fit: adjust <u>parameters</u>**
Validation data: N = 8 K => **fit: tune <u>hyperparameters</u>**
Testing data: N = 455 K => **predict**: **test <u>predictions</u>**

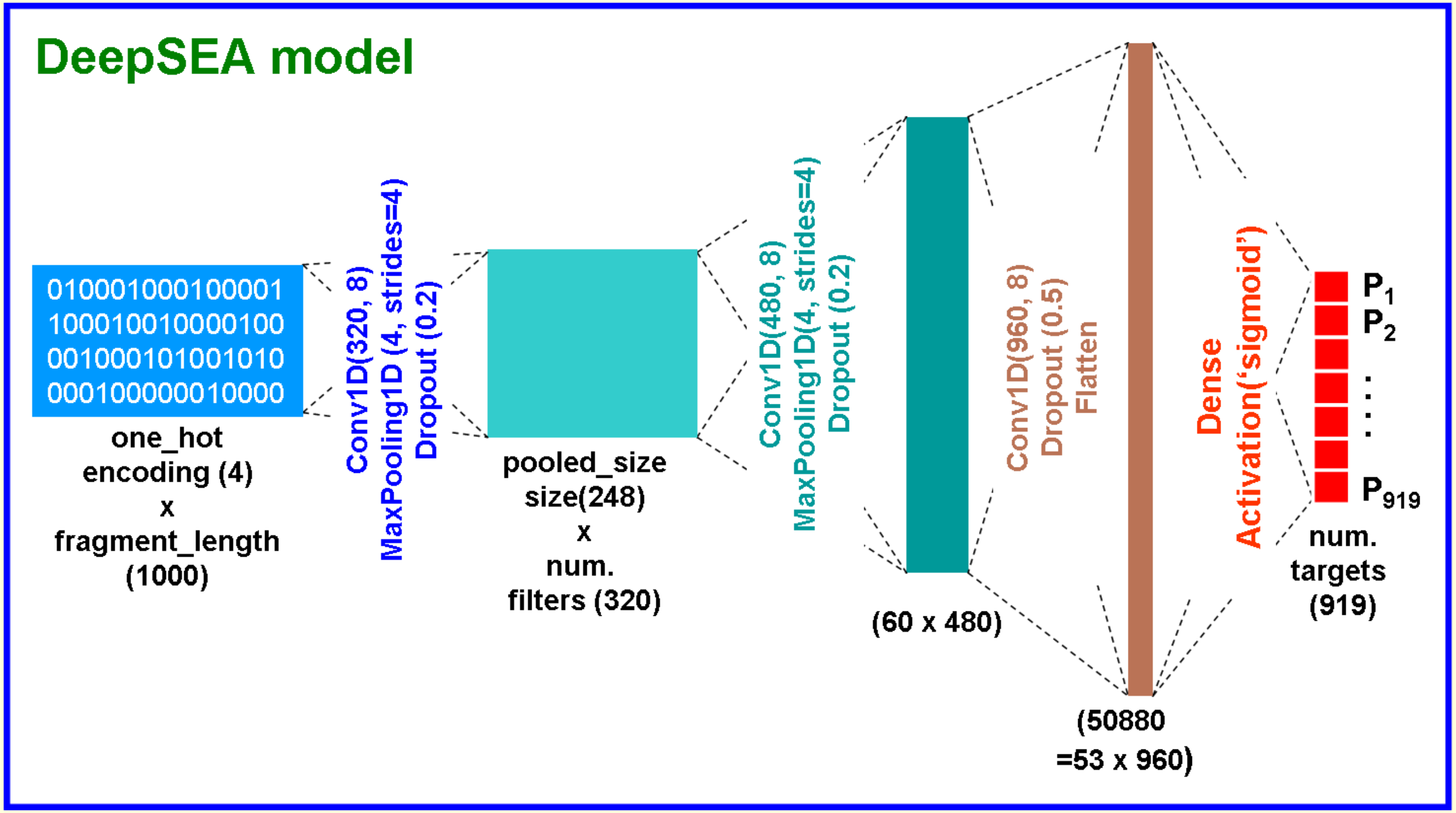


X (data) : N x 1000 x 4

y (labels): N x 919

The DeepSEA model

J.Zhou, O.G.Troyanskaya, Nature Methods (2015)



Layers: Conv1D, Dense,
MaxPooling1D, Dropout,
Flatten

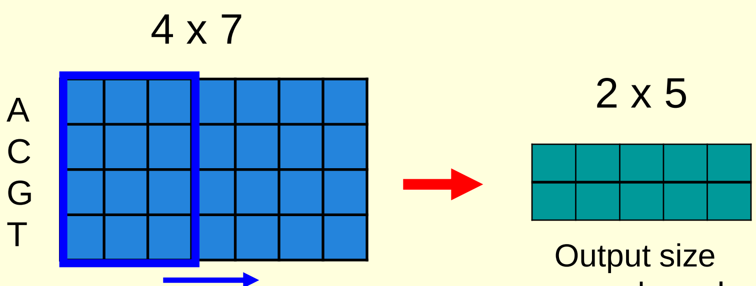
First Conv1D layer: capture the sequence motifs**.**

Second Conv1D and **third Conv1D:** produce higher level representation of the data output by previous layer

Dense: linearly combine outputs and produce target probs.

Conv1D, MaxPooling1D, Dropout and Flatten layers

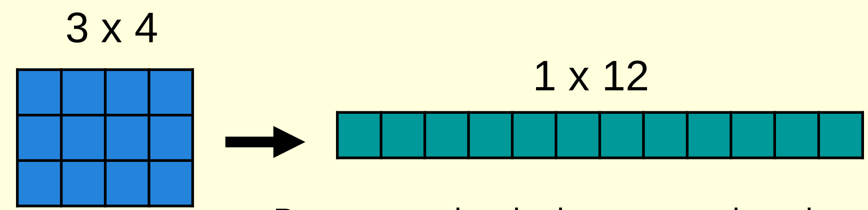
Conv1D(2, kernel_size = 3)



Rectangular window
of size = 4 x kernel_size

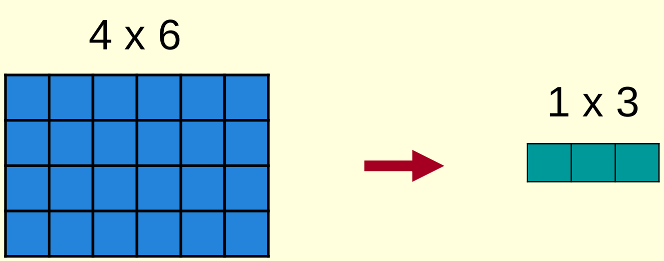
Output size
= num_kernels
x num_kernel_positions

Flatten()



Purpose: resize the input tensor in order
to make the output acceptable
by Dense layer

MaxPooling1D(pool_size = 2)

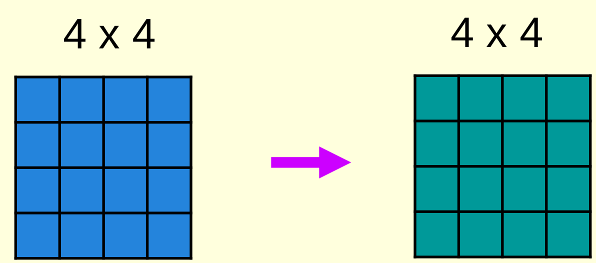


2.0	3.0	0.0	5.0	2.5	0.0
2.0	1.0	5.0	0.0	4.0	1.5
3.0	5.0	6.0	3.0	2.0	0.0
4.0	4.0	0.5	1.5	1.0	2.0

5.0	6.0	4.0

Purpose: prevent the model from overfitting

Dropout (0.5)



3.0	2.5	1.5	2.0
4.0	3.0	5.0	7.0
6.0	5.0	7.0	2.0
2.5	5.0	2.0	2.0

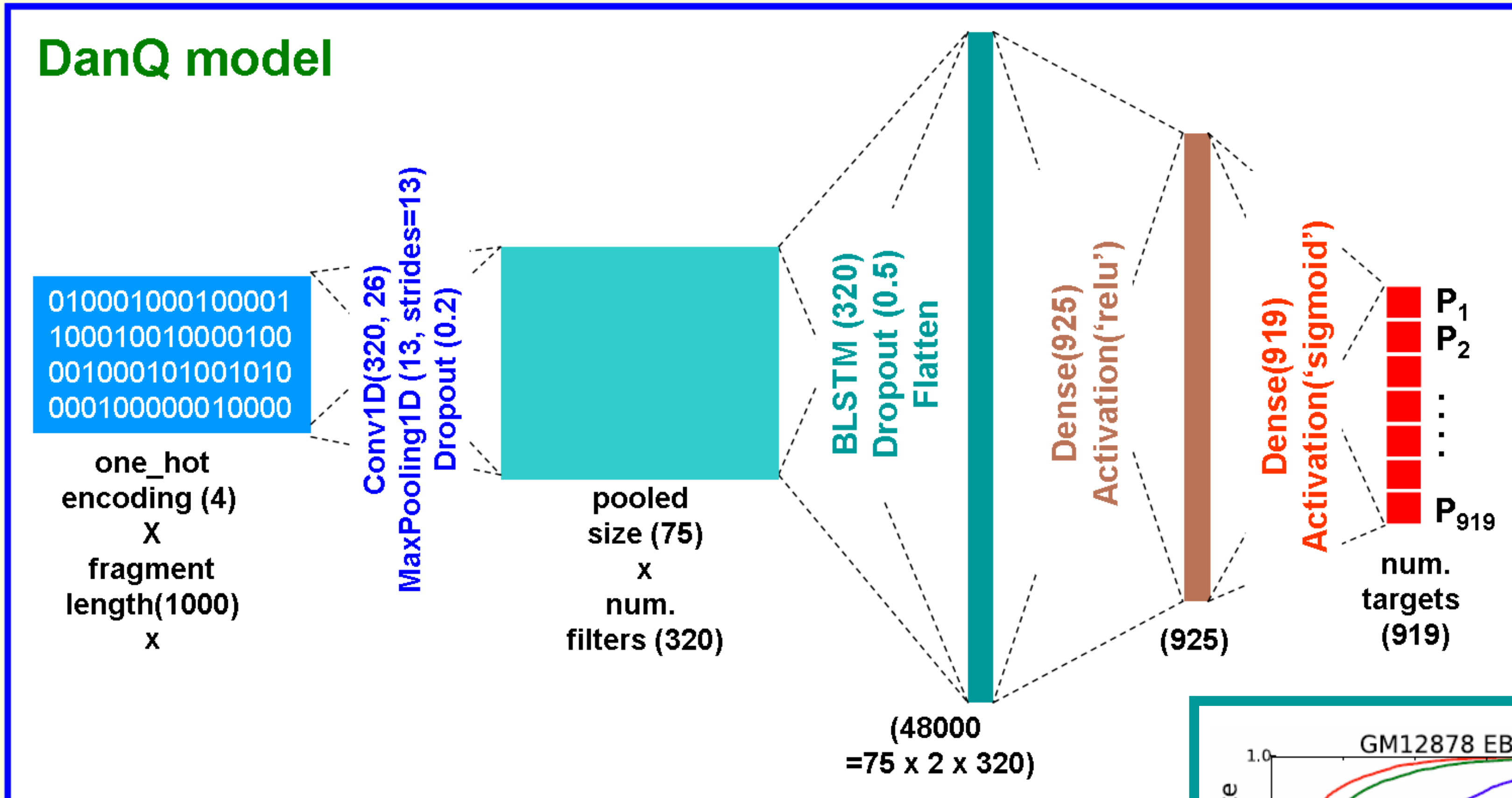
3.0	0.0	1.5	2.0
0.0	3.0	0.0	7.0
0.0	5.0	7.0	0.0
0.0	5.0	0.0	0.0

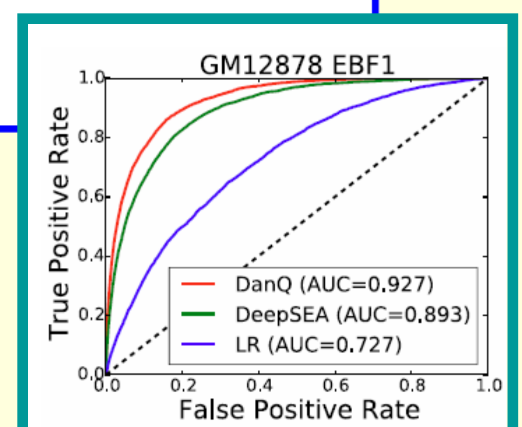
Purpose: prevent the model from overfitting

The DanQ model

LSTM, BLSTM, MaxPooling1D, Dropout, Flatten

D.Quang, X.Xie, Nucl. Acids Res. (2016)





Conv1D: # params = 33,600;
purpose: discover motif sequences

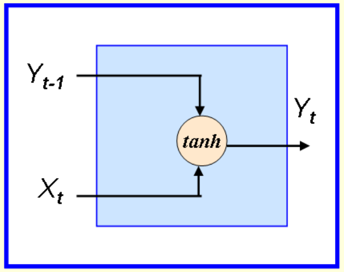
BLSTM: # params = 1,640,960;
purpose: capture the long-range dependencies
between motifs / different parts o fragments

Long Short-Term Memory (LSTM) cell

Orig. study: S Hochreiter, J Schmidhuber, Neural computation 9, p.1735 (1997)
Tutorial: https://adventuresinmachinelearning.com/keras-lstm-tutorial

SimpleRNN:

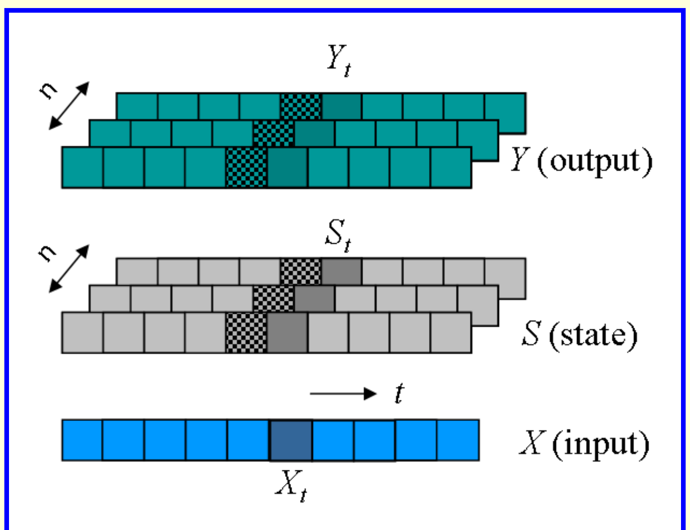
1) $X_t, Y_{t-1} \Rightarrow Y_t$

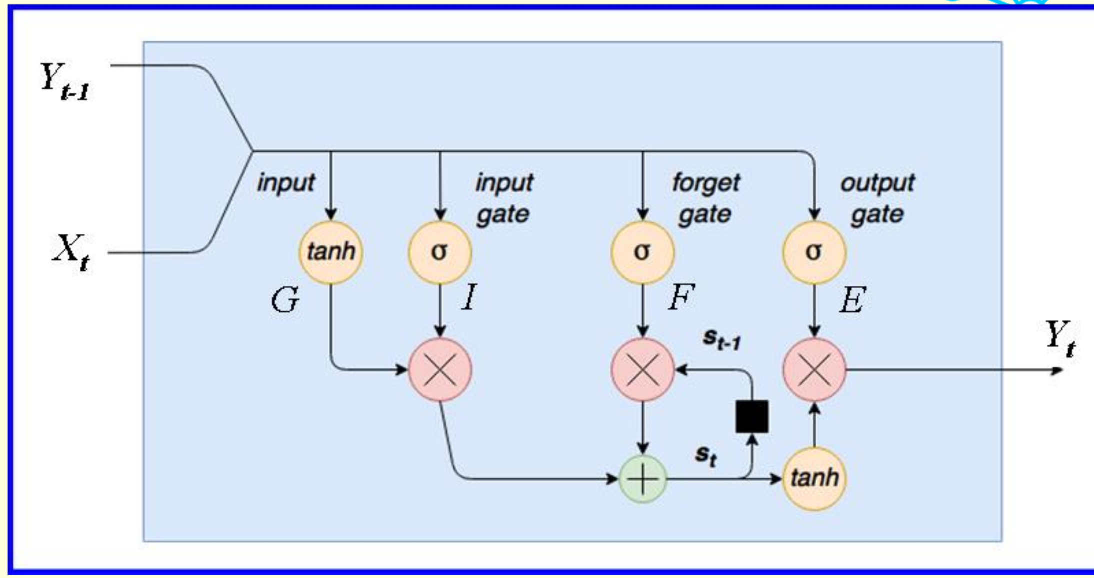


$$Y_t = tanh(b + w_{XY} \cdot X_t + w_{YY} \cdot Y_{t-1})$$

LSTM:

1) $X_t, Y_{t-1}, S_{t-1} \Rightarrow S_t$
2) $X_t, Y_{t-1}, S_t \Rightarrow Y_t$





1) $\boldsymbol{S_t = S_{t-1} \otimes F(X_t, Y_{t-1}) + G(X_t, Y_{t-1}) \otimes I(X_t, Y_{t-1})}$
2) $\boldsymbol{Y_t = tanh(S_t) \otimes E(X_t, Y_{t-1})}$

$$G(X_t, Y_{t-1}) = tanh(b_G + w_{XG} \cdot X_t + w_{YG} \cdot Y_{t-1})$$
$$I(X_t, Y_{t-1}) = \sigma(b_I + w_{XI} \cdot X_t + w_{YI} \cdot Y_{t-1})$$
$$F(X_t, Y_{t-1}) = \sigma(b_F + w_{XF} \cdot X_t + w_{YF} \cdot Y_{t-1})$$
$$E(X_t, Y_{t-1}) = \sigma(b_E + w_{XE} \cdot X_t + w_{YE} \cdot Y_{t-1})$$

$\otimes$ = elementwise multiplication; σ = sigmoid activation

parameters = $4*(2n + n^2)$

How to run the DanQ code on Biowulf?

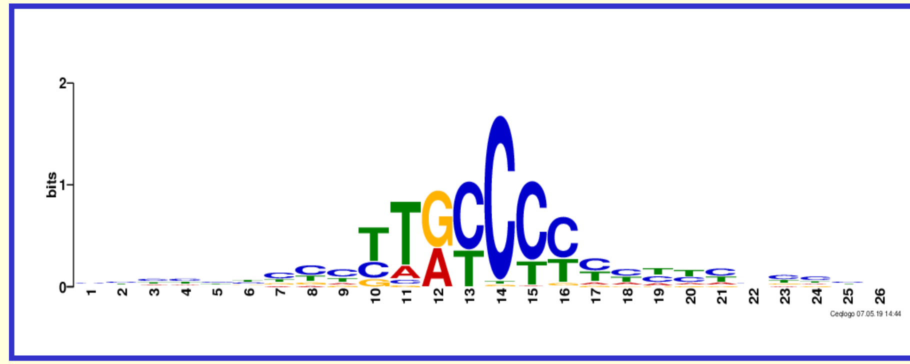
https://hpc.nih.gov/apps/DanQ.html

Using a single GPU:

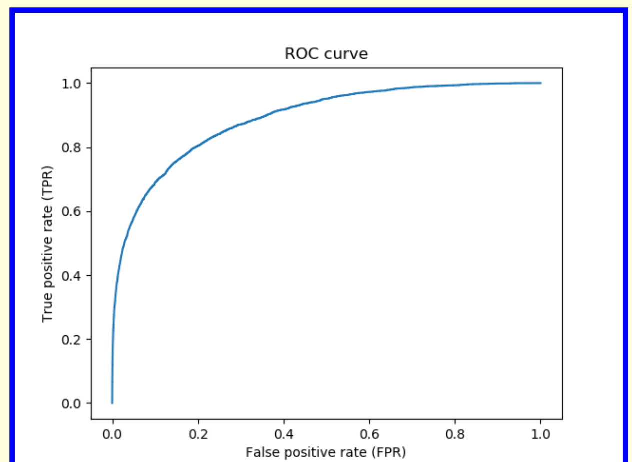
denisovga@biowulf:/usr/local/apps/danq/20210407/src

```
sinteractive  --mem=64g --gres=gpu:v100:1,lscratch:100 \
              --cpus-per-task=14

module load danq

ls $DANQ_SRC
models.py  options.py  predict.py  train.py  visualize.py

cp -r $DANQ_DATA/* .

train.py -d data  [ other options ]

predict.py -d data [ other options ]

visualize.py -t <target_id> [ other options ]
                                          15,48          Top
```

Discovered motif sequence logo:



ROC curve:



Using 4 GPUs:

denisovga@biowulf:/data/denisovga/1_DL_Course/2_RNNs

```
sinteractive  --mem=64g --gres=gpu:v100:4,lscratch:100 \
              --cpus-per-task=14

module load danq

ls $DANQ_SRC
models.py  options.py  predict.py  train.py  visualize.py

cp -r $DANQ_DATA/*  .

train.py -d data -g 4 [ other options ]
                                      11,42          Top
```

Summary

1) Further intro using simple examples
   - SimpleRNN vs Conv1D layers/transformations
   - the notion of the RNN network memory and interacting channels
   - motif detection and discovery
   - the SGD optimizer
   - backpropagation, long-range sequence dependencies and vanishing gradients

2) Predicting the function of a non-coding DNA
   - the DeepSEA and DanQ models
   - MaxPooling1D, Dropout, Flatten and (Bidirectional) LSTM layers
   - how to run the DanQ code on Biowulf

BACKUP SLIDES

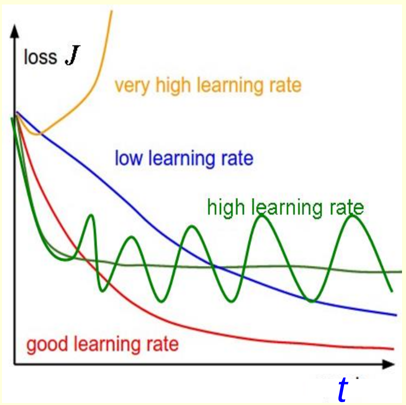
Stochastic Gradient Descent optimizer (cont.)

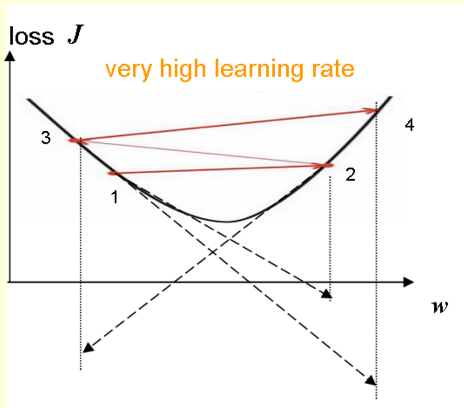
learning rate, momentum, Nesterov accelerated gradient

$$\Delta w_t = -\gamma \cdot \nabla_w J(w_t) \quad ; \quad \Delta w_t = w_{t+1} - w_t$$

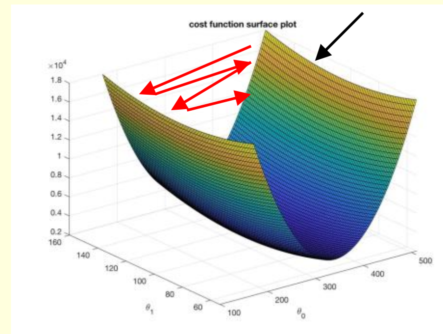
- the basic gradient descent formula re-written

1) learning_rate γ

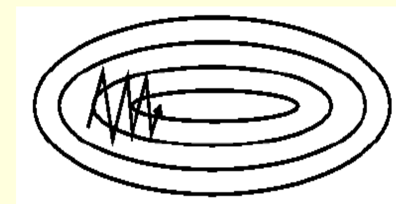




loss J



view from above



- small $\gamma \rightarrow$ slow convergence along the valley
- larger $\gamma \rightarrow$ oscillations in the perpendicular dir.

2) momentum > 0

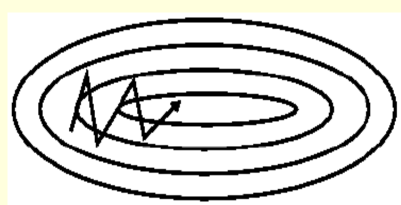
$$\Delta w_t = \mu \cdot \Delta w_{t-1} - \gamma \cdot \nabla_w J(w_t)$$

- gradient descent formula with momentum μ (usually, = 0.9)

3) nesterov = True

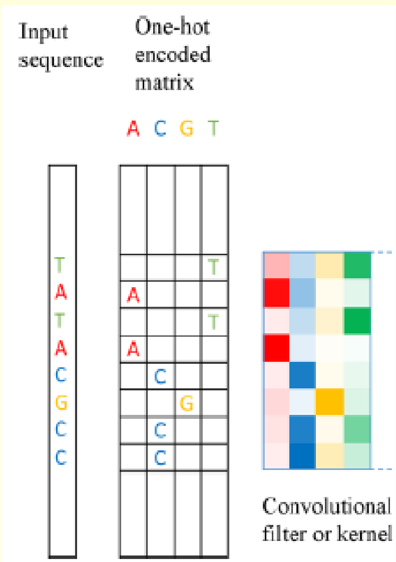
$$\Delta w_t = \mu \cdot \Delta w_{t-1} - \gamma \cdot \nabla_w J(w_t - \mu \cdot \Delta w_{t-1})$$

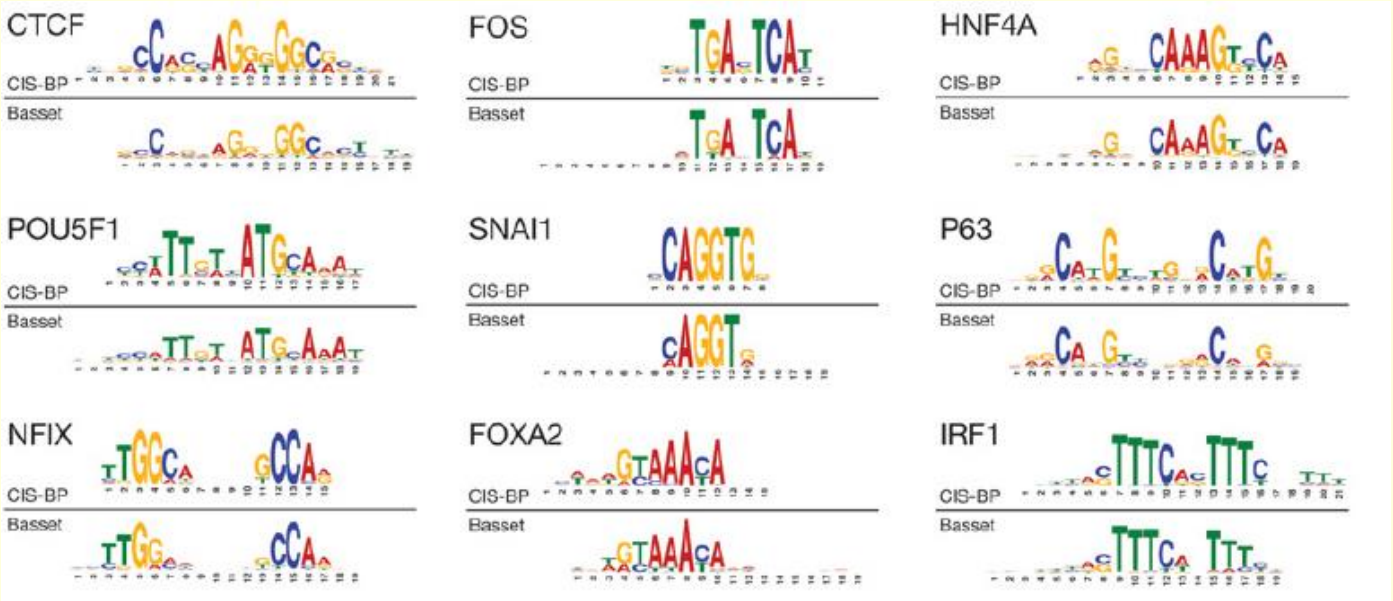
- gradient descent formula with momentum μ and Nesterov accelerated gradient



Predicting motifs

David R. Kelley et al - Basset: …, Genome Res , 2016, 26:990–999





Overall, 45% of filters could be annotated