



imagia

Applications: Séries temporelles

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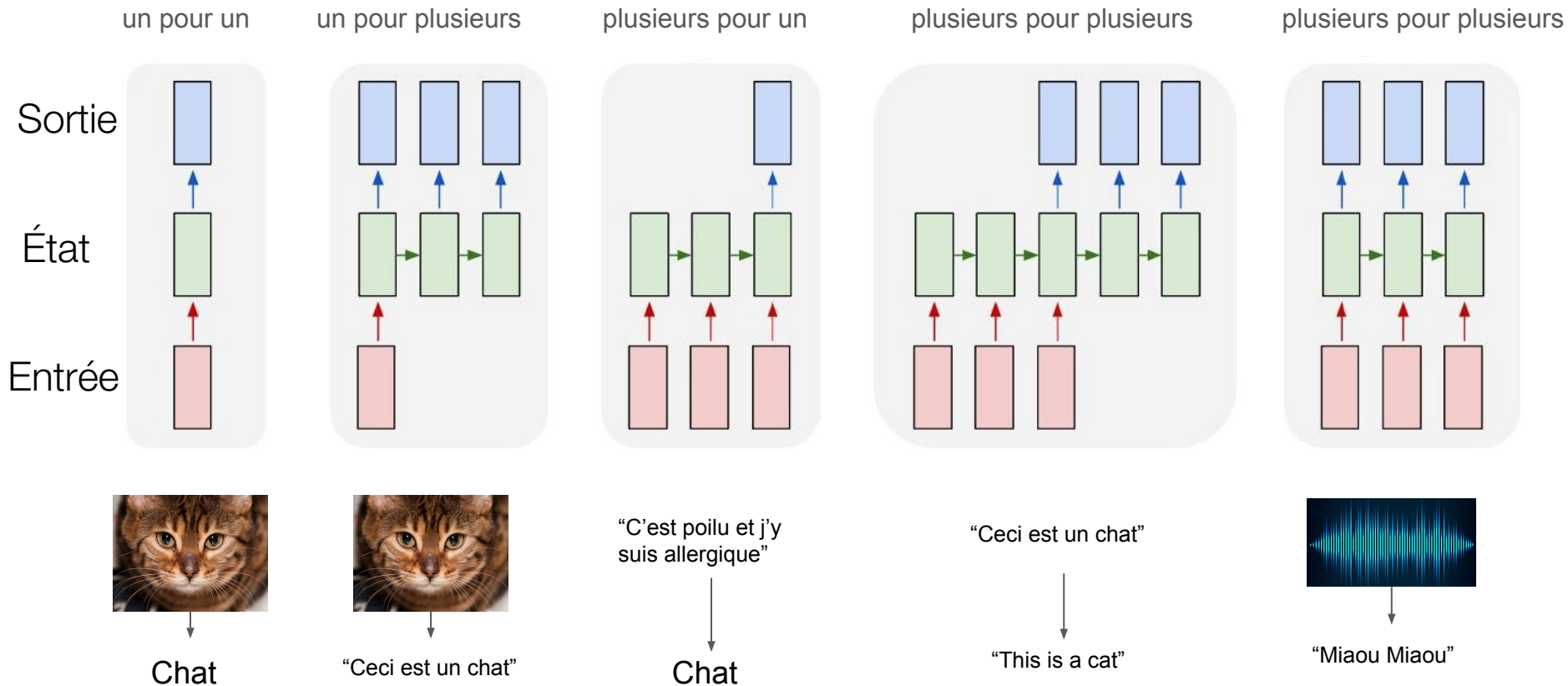
Plan

1. Introduction aux réseaux de neurones récurrents
2. Données médicales
3. Diverses applications

Plan

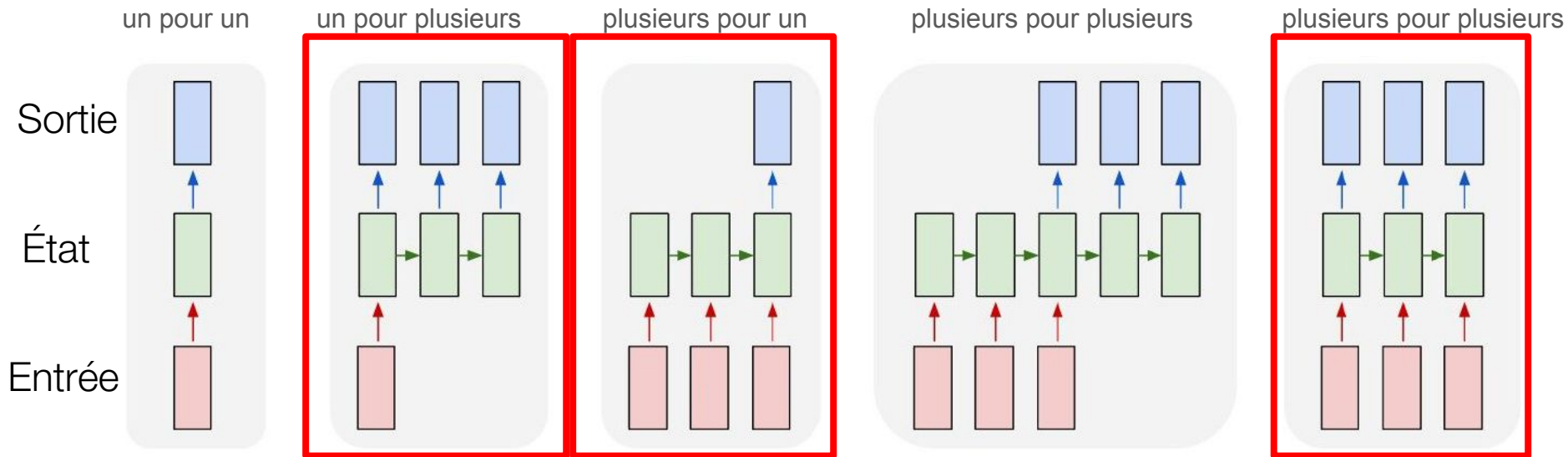
- 1. Introduction aux réseaux de neurones récurrents**
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Rappel: type de tâches avec les séries temporelles



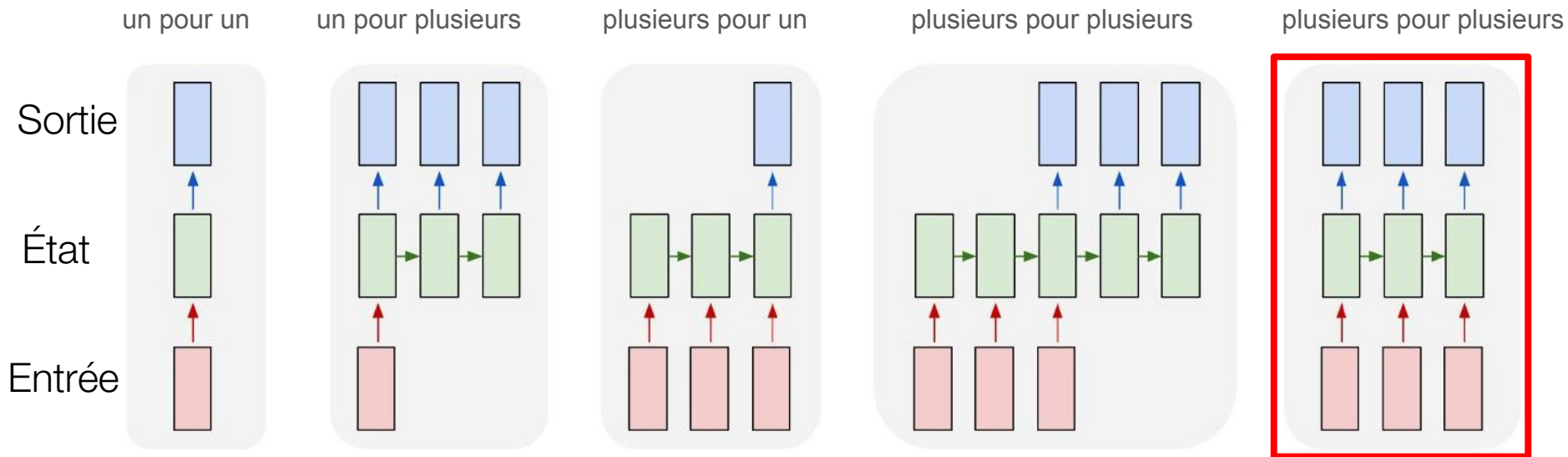
Rappel: type de tâches avec les séries temporelles

Dans cette présentation



Rappel: type de tâches avec les séries temporelles

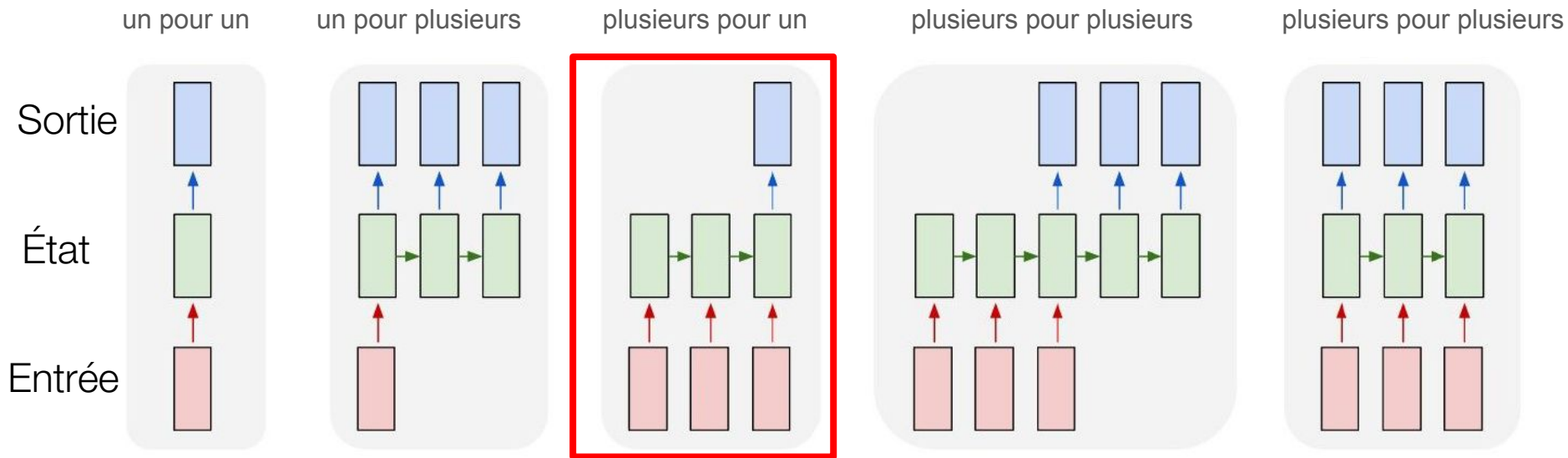
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Suivi de patient

Rappel: type de tâches avec les séries temporelles

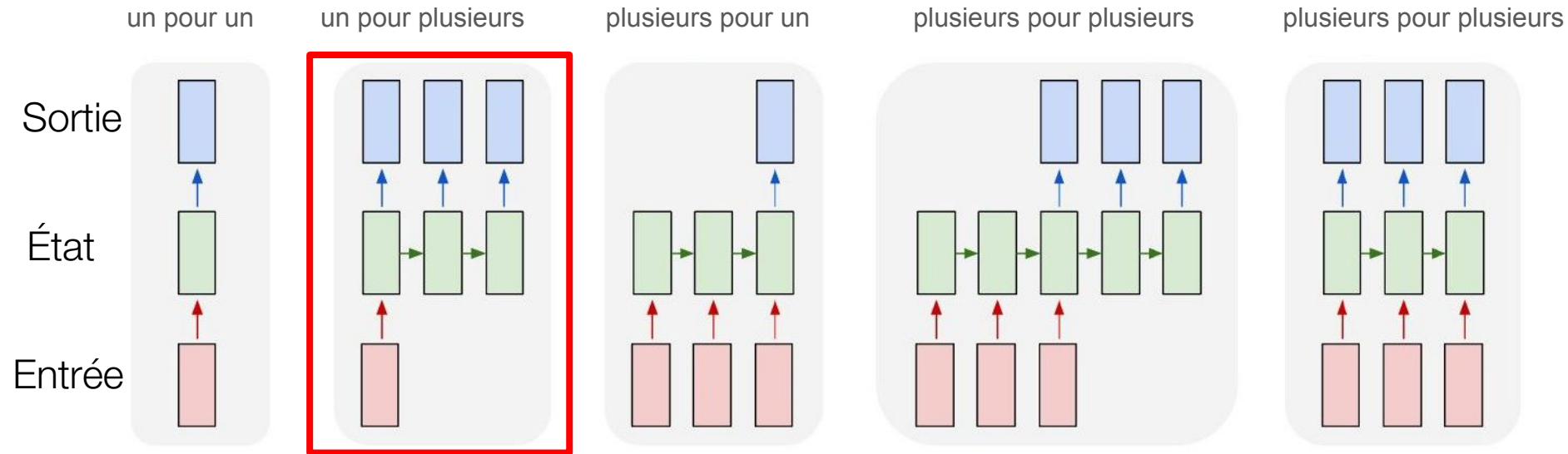
Dans cette présentation



Diagnostic d'un épisode

Rappel: type de tâches avec les séries temporelles

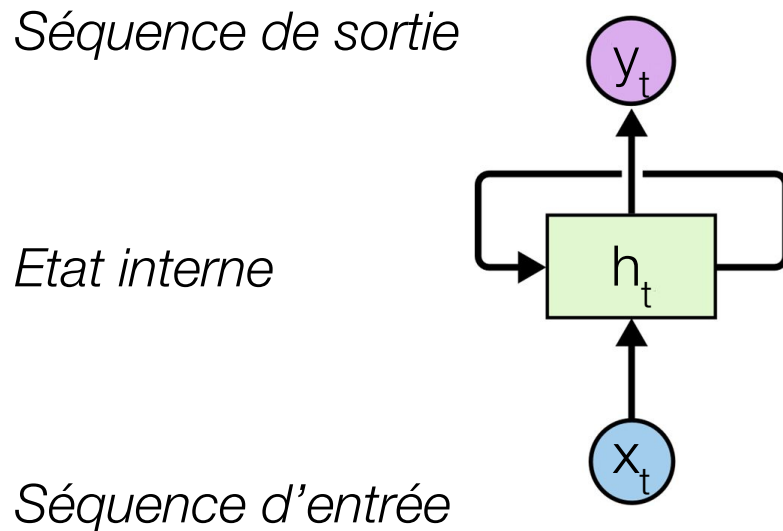
Dans cette présentation



Génération de note clinique
à partir d'image

Réseaux de neurones récurrents

Un RNN applique une fonction à une **séquence d'entrée** $[x_1, x_2, \dots, x_T]$, pour produire une **séquence de sortie** $[y_1, y_2, \dots, y_T]$, en maintenant un **état interne** $[h_1, h_2, \dots, h_T]$.



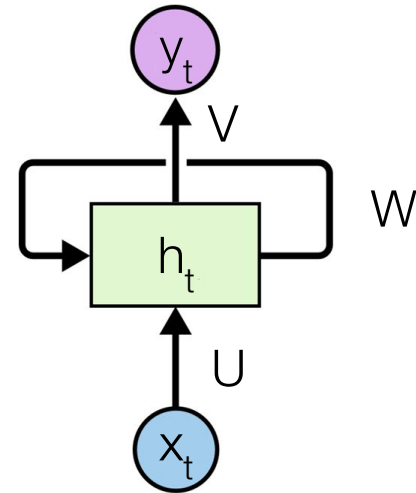
Réseaux de neurones récurrents

- La version la plus simple:

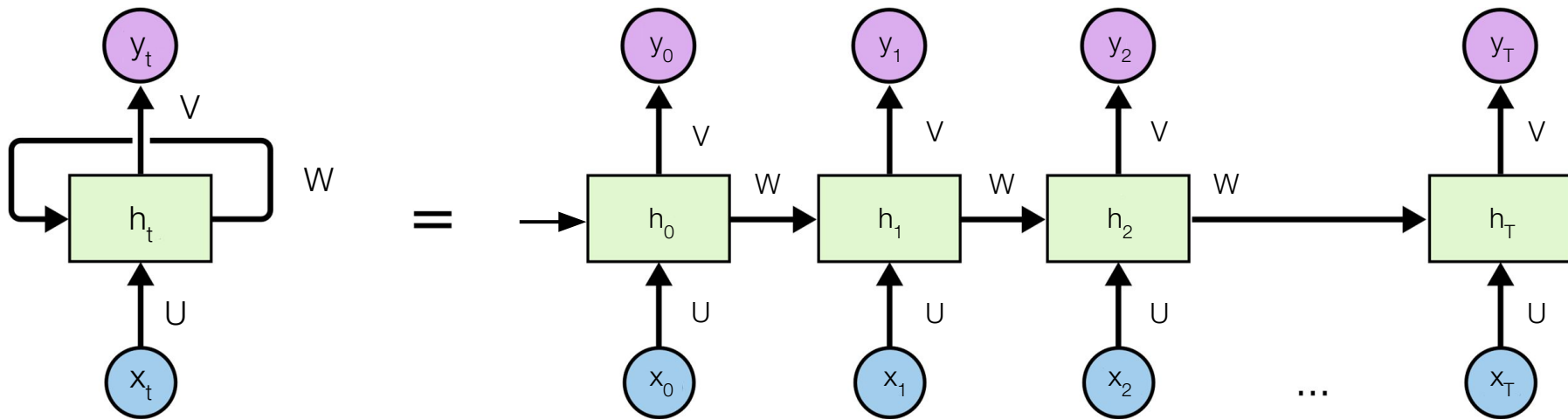
$$h_t = \tanh(Ux_t + Wh_{t-1})$$

$$y_t = f(Vh_t)$$

- W , U et V sont les paramètres du réseau.
 - Ils sont **partagés** à travers le temps.

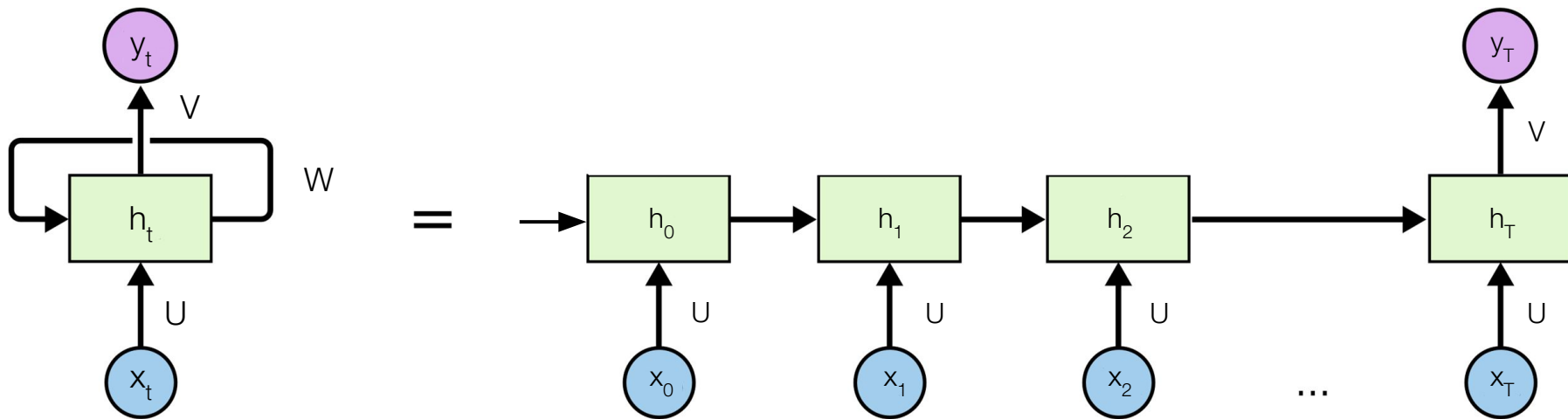


Déroulement dans le temps



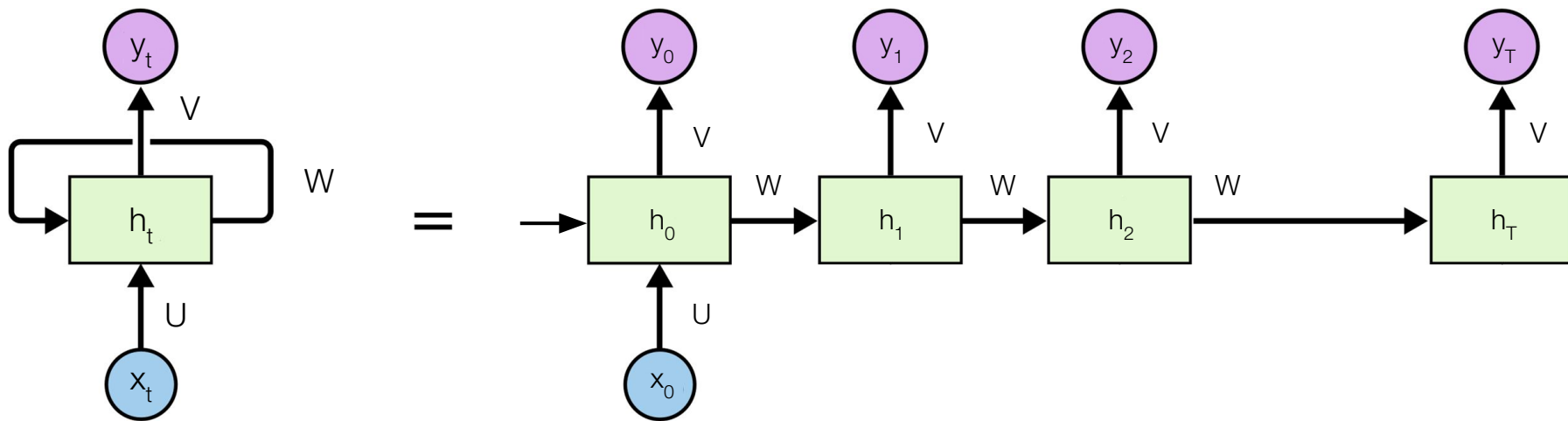
Les paramètres sont **partagés** à travers le temps!

Déroulement dans le temps



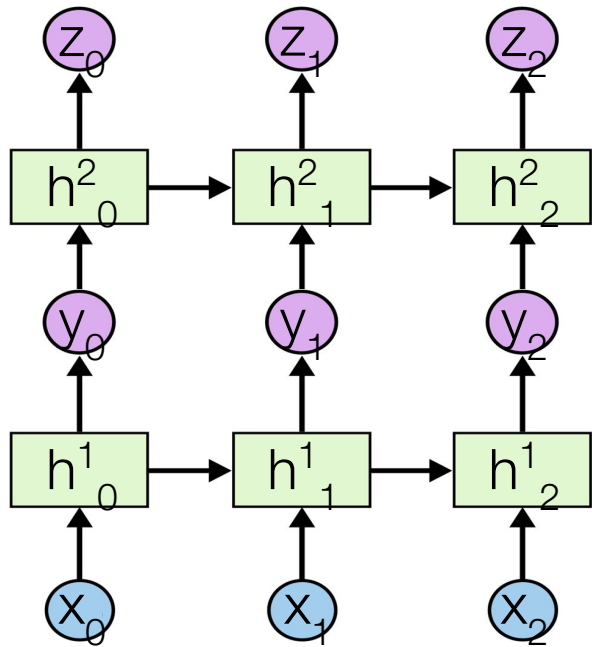
Les paramètres sont **partagés** à travers le temps!

Déroulement dans le temps

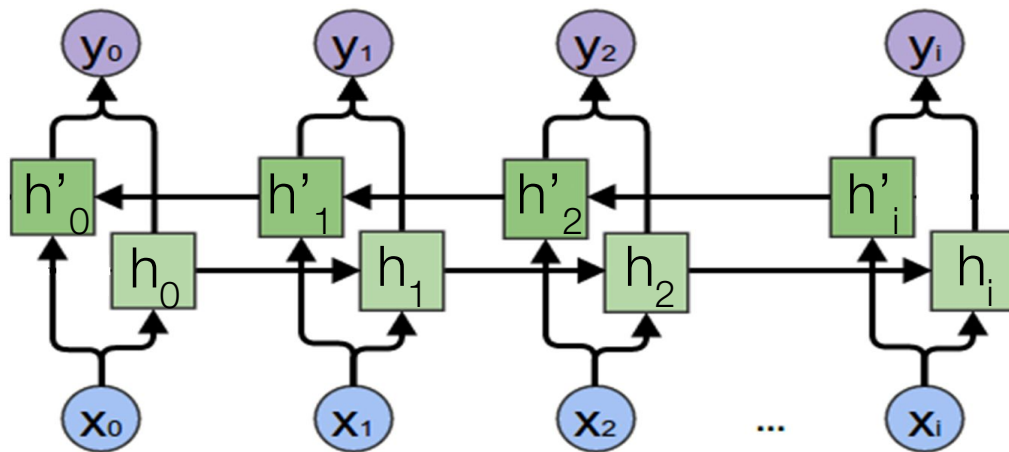


Les paramètres sont **partagés** à travers le temps!

On peut être créatif !

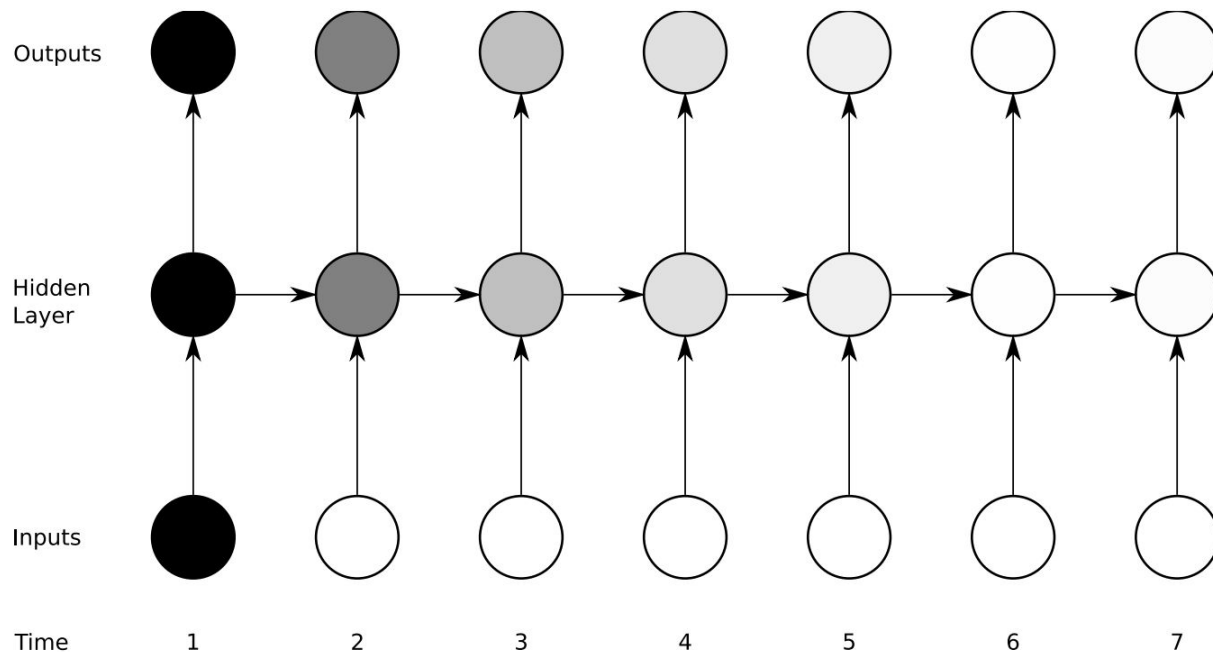


Pile de RNNs



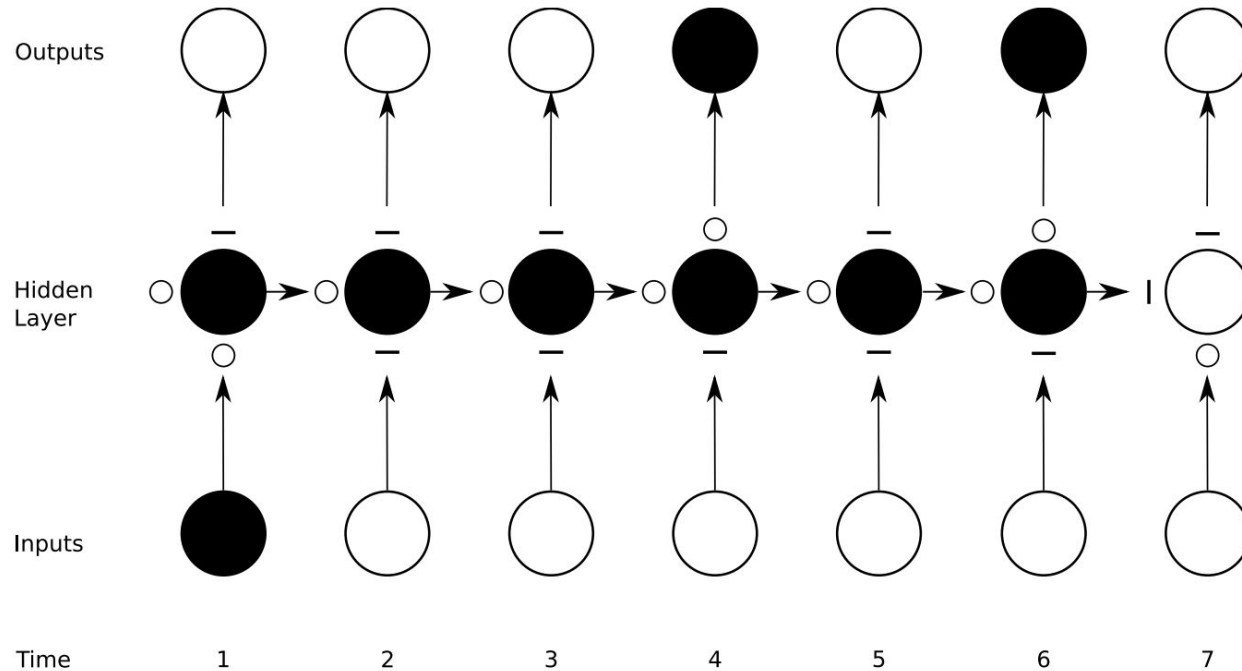
RNN Bidirectionnel

Problème avec le RNN basic



La nuance de gris montre l'influence de l'entrée du RNN au temps 1. Elle décroît au cours du temps, comme le RNN oublie peu à peu sa première entrée.

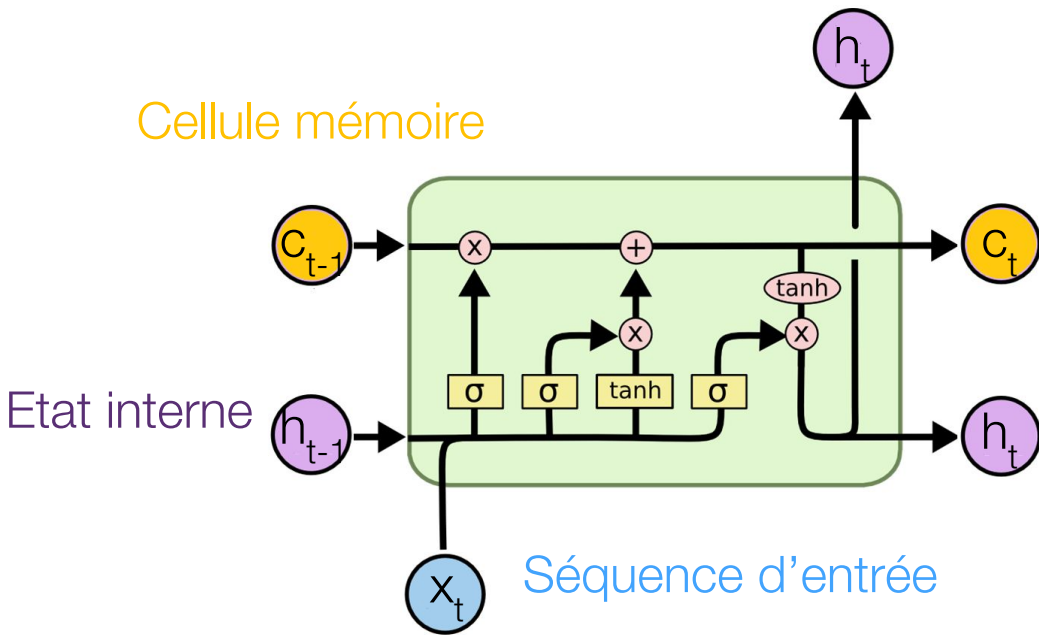
Problème avec le RNN basic



En ajoutant 3 gates (o ouvert; - fermé), qui contrôlent l'entrée, la sortie et l'effacement de l'état, on peut retenir et propager l'information dans le temps.

Long Short-Term Memory (LSTM)

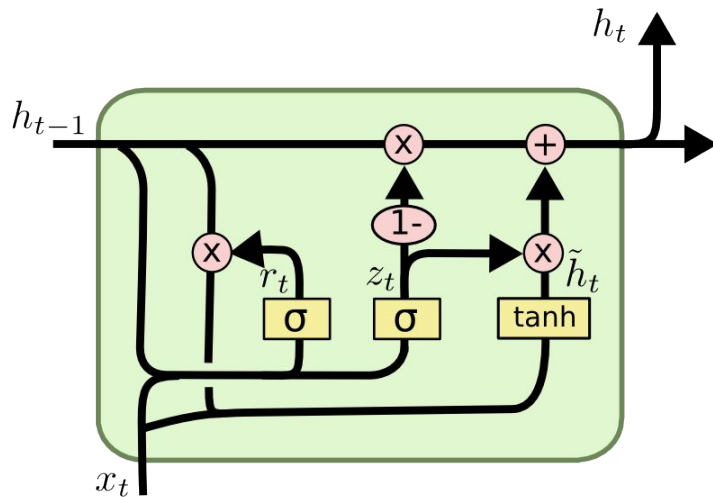
Réduction du problème de dissipation avec **un mécanisme de gates** et une **cellule mémoire**.



$$i_t = \sigma(U_i x_t + W_i h_{t-1} + b_i)$$
$$f_t = \sigma(U_f x_t + W_f h_{t-1} + b_f)$$
$$o_t = \sigma(U_o x_t + W_o h_{t-1} + b_o)$$
$$g_t = \tanh(U_g x_t + W_g h_{t-1} + b_g)$$
$$c_t = i_t \odot g_t + f_t \odot c_{t-1}$$
$$h_t = o_t \odot \tanh(c_t)$$

Gated Recurrent Unit (GRU)

- Une variante populaire de la LSTM.
 - Pas de cellule mémoire explicite.
 - Input et forget gates combinées.
- En pratique, performances égales à la LSTM.
 - Plus rapide à calculer.



$$z_t = \sigma(U_z x_t + W_z h_{t-1} + b_z)$$

$$r_t = \sigma(U_r x_t + W_r h_{t-1} + b_r)$$

$$g_t = \tanh(U_g x_t + W_g (r_t \odot h_{t-1}) + b_g)$$

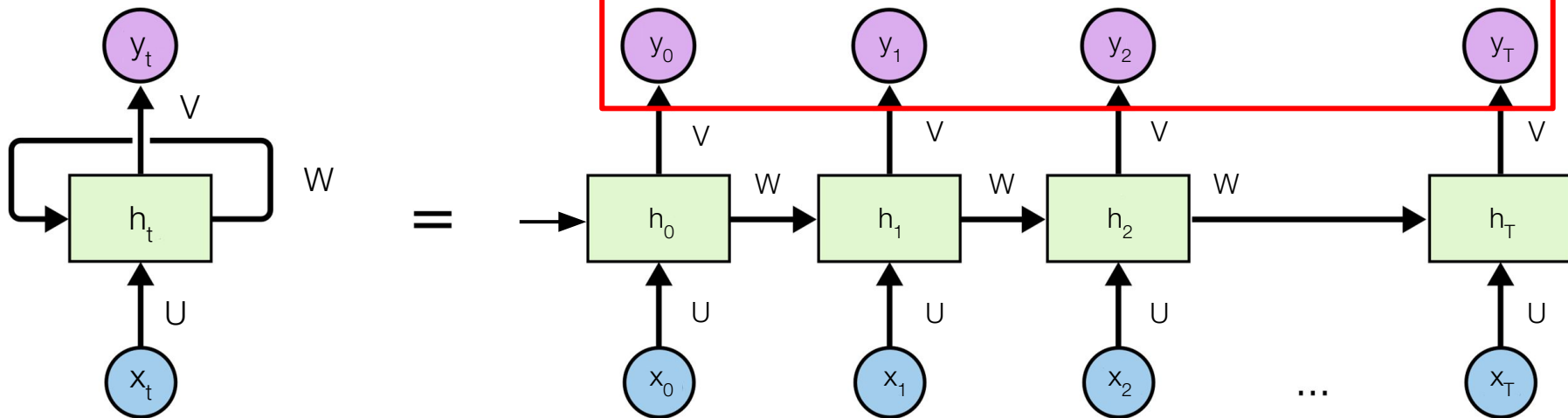
$$h_t = z_t \odot g_t + (1 - z_t) \odot h_{t-1}$$

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Séquence de sortie

- Prédire la probabilité d'un **événement** futur
- On doit s'entendre sur une définition!



La Classification internationale des maladies (CIM) est une classification médicale codifiée classifiant les maladies et une très vaste variété de signes, symptômes, lésions traumatiques, empoisonnements, circonstances sociales et causes externes de blessures ou de maladies. Elle est publiée par l'Organisation mondiale de la santé (OMS) et est mondialement utilisée pour l'enregistrement des causes de morbidité et de mortalité touchant le domaine de la médecine.

1975 - CIM-9 - (OMS)

1990 - CIM-10 - (OMS)

2019 - CIM-11 - (OMS)



“Bientôt!”

Exemples de codes CIM-9:

- 786 Symptoms involving respiratory system and other chest symptoms
- 786.0 Dyspnea and respiratory abnormalities
- 786.1 Stridor
- 786.2 Cough
- 786.3 Hemoptysis
- 786.4 Abnormal sputum
- 786.5 **Chest pain**
- 786.6 Swelling, mass or lump in chest
- 786.7 Abnormal chest sounds
- 786.8 Hiccough
- 786.9 Other

Exemples de code CIM-9 (786.5, *Chest pain*)

Cardialgia (see also Pain, precordial) 786.51
Diaphragmalgia 786.52
chest 786.59
anginoid (see also Pain, precordial) 786.51
chest (central) 786.50
atypical 786.59
midsternal 786.51
musculoskeletal 786.59
noncardiac 786.59
substernal 786.51
wall (anterior) 786.52
costochondral 786.52
diaphragm 786.52
heart (see also Pain, precordial) 786.51
intercostal 786.59
over heart (see also Pain, precordial) 786.51
pericardial (see also Pain, precordial) 786.51

pleura, pleural, pleuritic 786.52
precordial (region) 786.51
respiration 786.52
retrosternal 786.51
rib 786.50
substernal 786.51
respiration 786.52
Pleuralgia 786.52
Pleurodynia 786.52
Precordial pain 786.51
chest 786.59
Prinzmetal-Massumi syndrome (anterior chest wall) 786.52
painful 786.52

Beaucoup de regroupement!

CIM-10 est très détaillé

V97.33XD: **Sucked into jet engine**, subsequent encounter

V00.15: **Heelies Accident**

Applicable To Rolling shoe, Wheeled shoe, Wheelies accident.

Supertypes:

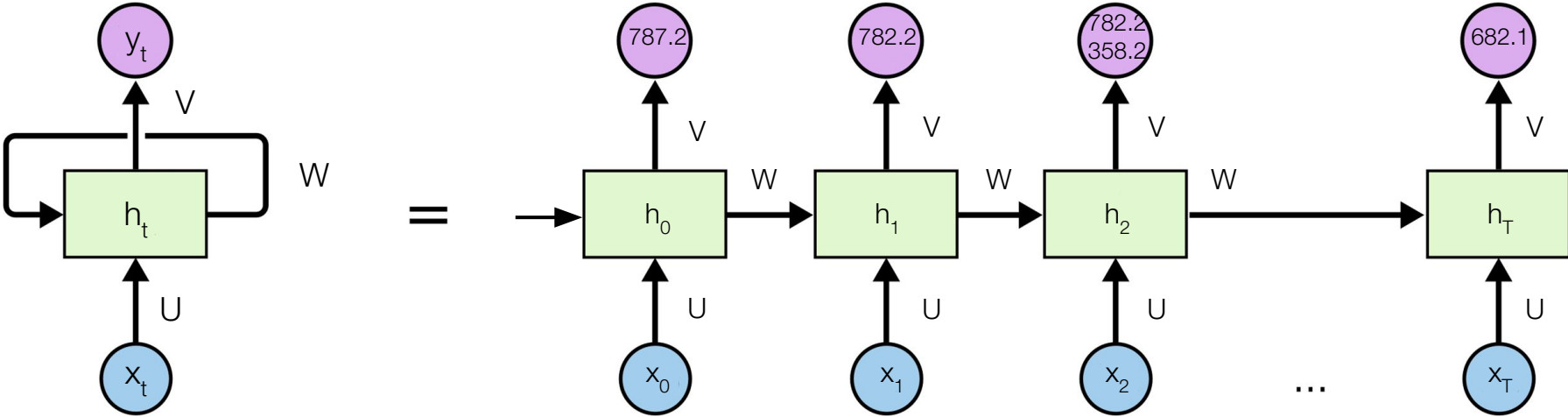
V00-Y99 External causes of morbidity

V95-V97 Air and space transport accidents

V00 Pedestrian conveyance accident

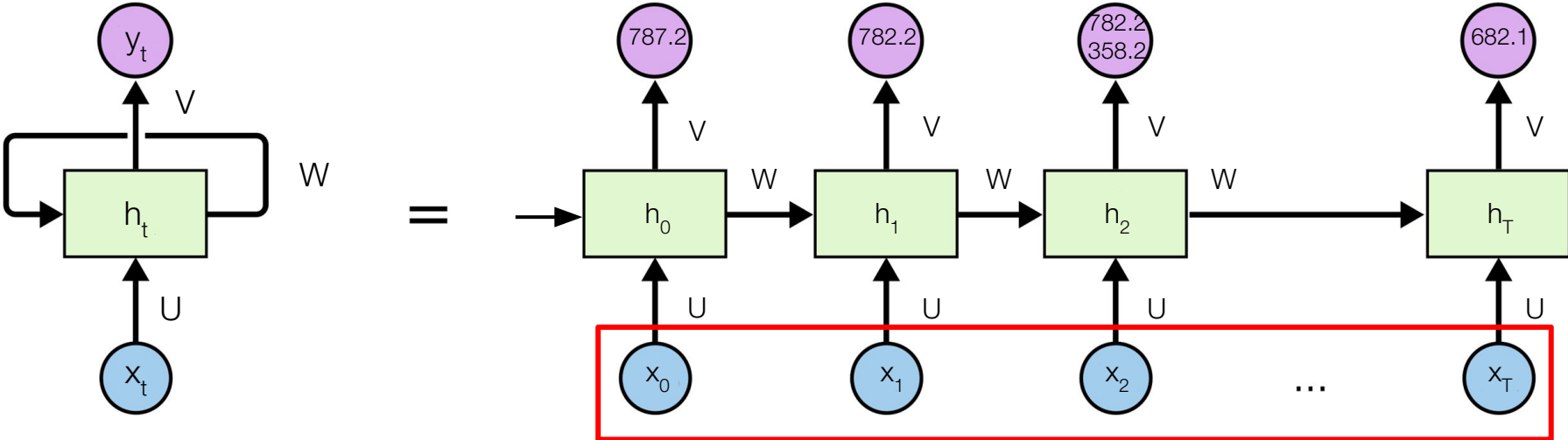
V00.1 Rolling-type pedestrian conveyance accident

Séquences de sortie



Série de codes médicaux à travers le temps

Et les entrées?



Et les entrées?

- Information démographique
- Signes vitaux
 - Fréquence cardiaque, etc.
- Notes cliniques
- Médications
- etc.

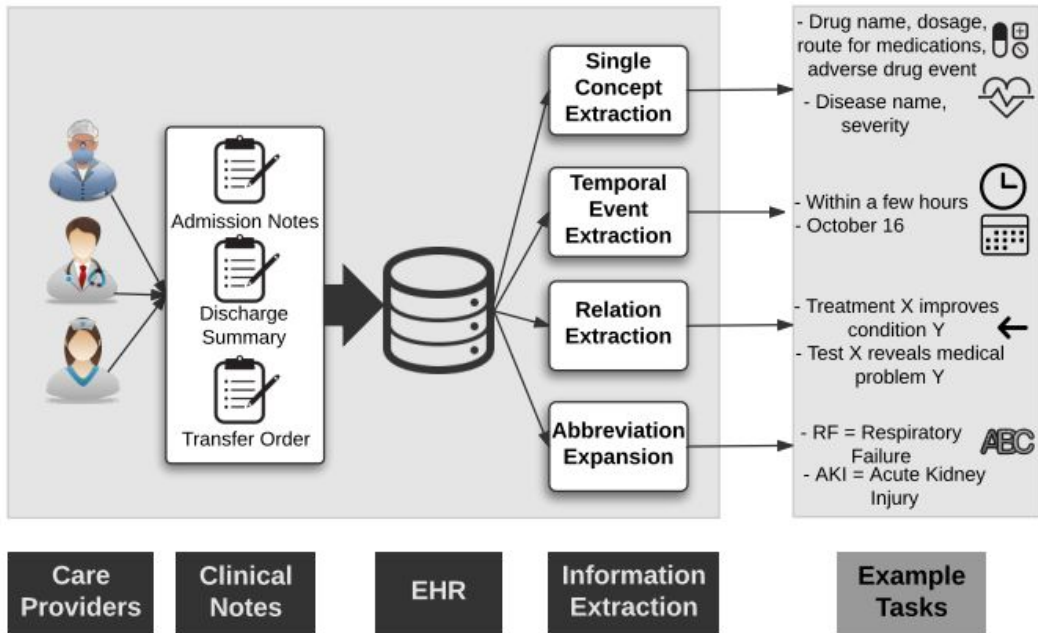
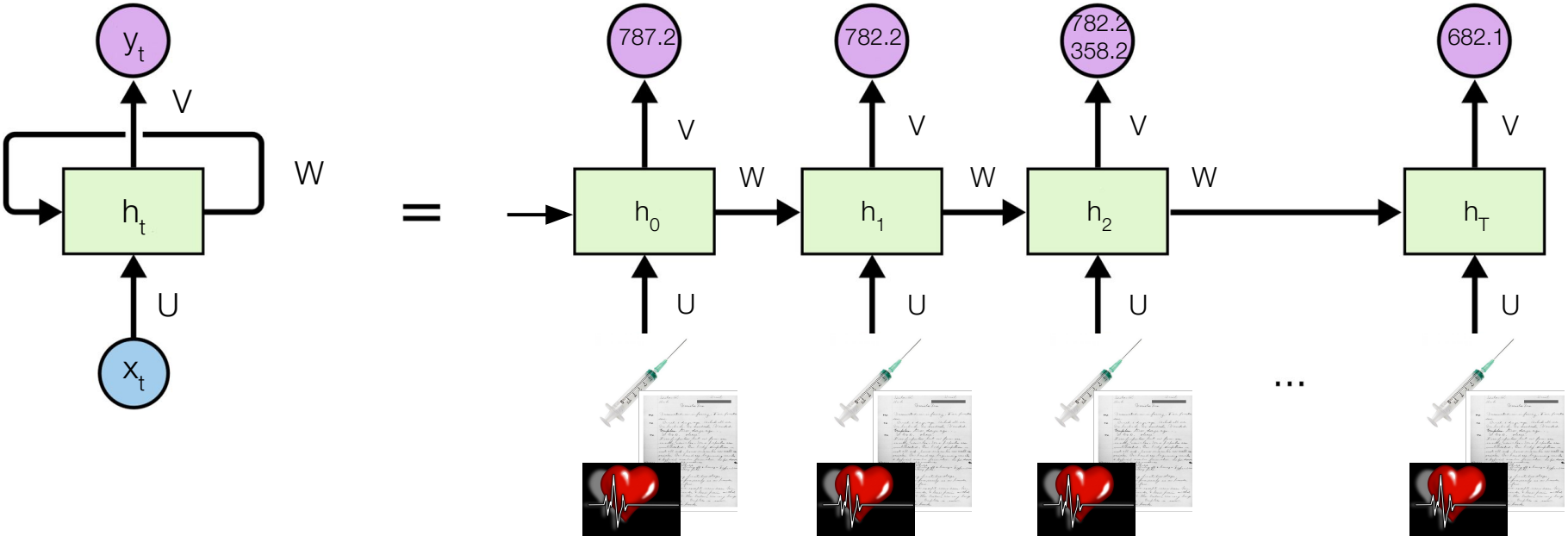


Figure de Deep EHR: A Survey of Recent Advances in Deep Learning Techniques for Electronic Health Record (EHR) Analysis

Et les entrées?



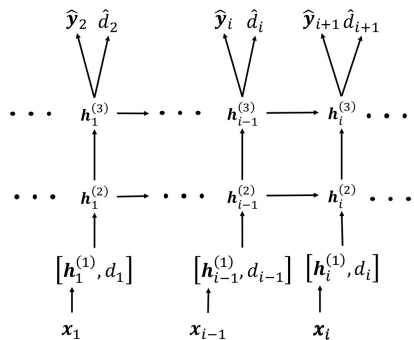
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Prédiction de la prochaine visite (Doctor AI)

$y = \text{codes médicaux } R^{1778}$

$d = \text{durée écoulée depuis la dernière visite}$



Codes médicaux R^{40000}

- Codes médicales: CIM-9, diagnostiques, procédures, médicaments
- Groupe les codes CIM-9

Table 1: Basic statistics of the the clinical records dataset.

# of patients	263,706	Total # of codes	38,594
Avg. # of visits	54.61	Total # of 3-digit Dx codes	1,183
Avg. # of codes per visit	3.22	# of top level Rx codes	595
Max # of codes per visit	62	Avg. duration between visits	76.12 days

Patients provenant de Sutter Health Palo Alto Medical Foundation

Algorithms	Dx,Rx,Time Recall @k			
	k = 10	k = 20	k = 30	R ²
Last visit	26.25			—
Most freq.	48.11	60.23	66.00	—
Logistic	36.04	46.32	52.53	0.0726
MLP	38.82	49.09	55.74	0.1221
RNN-1	53.86	65.10	71.24	0.2519
RNN-2	53.61	64.93	71.14	0.2528
RNN-1-IR	54.37	65.68	71.85	0.2492
RNN-2-IR	54.96	66.31	72.48	0.2534

Doctor AI: Predicting Clinical Events via Recurrent Neural Networks

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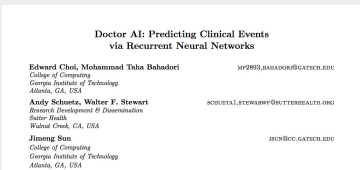
Abstract

Leveraging large historical data in electronic health record (EHR), we developed Doctor AI, a generic predictive model that covers observed medical conditions and medication uses. Doctor AI is a temporal model using recurrent neural networks (RNN) and was developed and applied to longitudinal time stamped EHR data from 200K patients and 1.2M diagnoses over 7 years. Encounter records (e.g. diagnosis codes, medication codes or procedure codes) were input to RNN to predict (a) the diagnosis and medication categories for a subsequent visit. Doctor AI assesses the history of patients to make individual predictions (one label for each diagnosis or medication category). Based on aggregate fitted top- k evaluation, Doctor AI can perform differential diagnosis with up to 79% recall@30, significantly higher than several baselines. Moreover, we demonstrate great interoperability of Doctor AI for selecting the resulting code from one medication to another

Aller au delà des scores

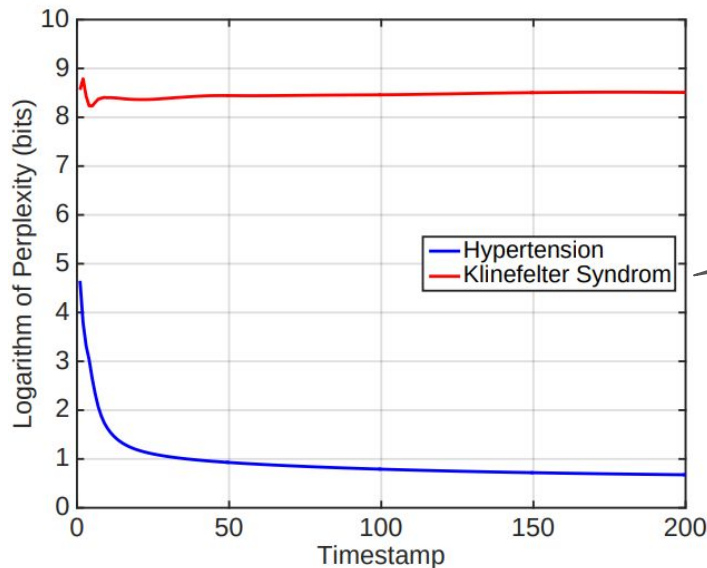
- Difficile à interpréter (black box)
- Mais! On peut étudier le comportement du modèle

Algorithms	Dx,Rx,Time Recall @k			
	k = 10	k = 20	k = 30	R ²
Last visit	26.25			—
Most freq.	48.11	60.23	66.00	—
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Imbalance des classes (Doctor AI)

Marche mieux sur les classes fréquentes



Hommes avec chromosomes XXY

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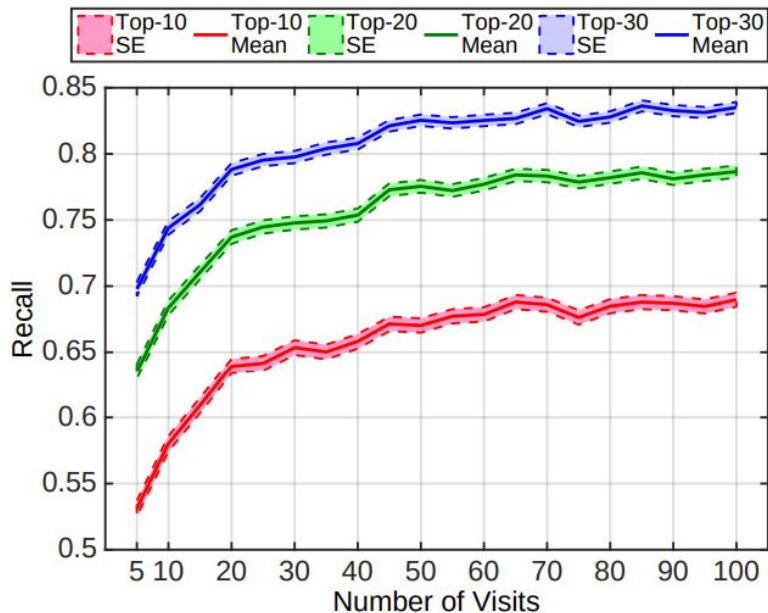
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Abstract

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Durée des visites (Doctor AI)

Devient meilleur avec le temps (plus prévisibles)



Doctor AI: Predicting Clinical Events via Recurrent Neural Networks

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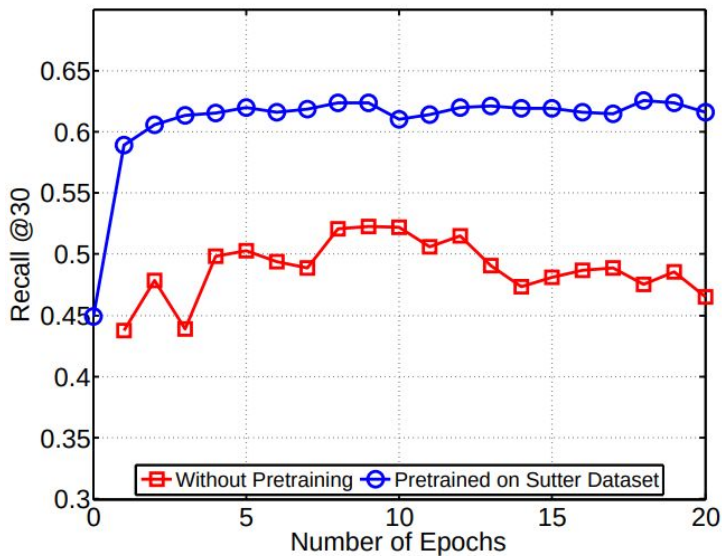
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Transfert de domaine (Doctor AI)

MIMIC II possède 2,695 patients avec 2+ visites

Démographiques différentes



Doctor AI: Predicting Clinical Events via Recurrent Neural Networks

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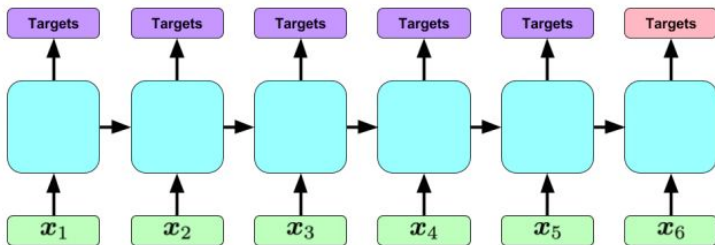
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Abstract

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Diagnostique d'une visite



Données: 10 401 épisodes, durée variables.

Provient de Children's Hospital LA

Entrées: Pression sanguine, pH, température corporelle, etc..., échantillonné à chaque heure.

Sorties: 128 codes, *similaire* à CIM-9

LEARNING TO DIAGNOSE WITH LSTM RECURRENT NEURAL NETWORKS

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ABSTRACT

Clinical medical data, especially in the intensive care unit (ICU), consist of multi-variant time series of observations. For each patient visit (or episode), sensor data and lab test results are recorded in the patient's Electronic Health Record (EHR). While potentially containing a wealth of insights, the data is difficult to mine effectively, owing to irregular length, irregular sampling and missing data. Recurrent Neural Networks (RNNs), particularly those using long Short-Term Memory (LSTM) hidden units, are powerful and increasingly popular models for learning from sequential data. They effectively model varying-length sequences and capture long-range dependencies. We present the first study to empirically evaluate the ability of LSTMs to recognize patterns in multi-variant time series of clinical measurements, specifically, we consider multiclass classification of diagnoses, treating a model to classify 128 diagnoses given 12 frequently but irregularly-sampled clinical measurements. First, we explore the effectiveness of a simple LSTM network for modeling clinical data. Then we demonstrate a straightforward and effective training strategy in which we explicitly target at each sequence step. Trained only on raw time series, our models outperform several leading baselines, including a multivary perceptron trained on hand-engineered features.

Faible gain

Classification performance for 128 ICU phenotypes

Model	Micro AUC	Macro AUC	Micro F1	Macro F1	Prec. at 10
Base Rate	0.7128	0.5	0.1346	0.0343	0.0788
Log. Reg., First 6 + Last 6	0.8122	0.7404	0.2324	0.1081	0.1016
Log. Reg., Expert features	0.8285	0.7644	0.2502	0.1373	0.1087
MLP, First 6 + Last 6	0.8375	0.7770	0.2698	0.1286	0.1096
MLP, Expert features	0.8551	0.8030	0.2930	0.1475	0.1170

LSTM Models with two 64-cell hidden layers

LSTM	0.8241	0.7573	0.2450	0.1170	0.1047
LSTM, AuxOut (Diagnoses)	0.8351	0.7746	0.2627	0.1309	0.1110
LSTM-AO (Categories)	0.8382	0.7748	0.2651	0.1351	0.1099
LSTM-TR	0.8429	0.7870	0.2702	0.1348	0.1115
LSTM-TR-AO (Diagnoses)	0.8391	0.7866	0.2599	0.1317	0.1085
LSTM-TR-AO (Categories)	0.8439	0.7860	0.2774	0.1330	0.1138

LSTM Models with Dropout (probability 0.5) and two 128-cell hidden layers

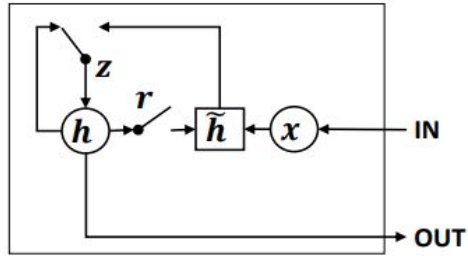
LSTM-DO	0.8377	0.7741	0.2748	0.1371	0.1110
LSTM-DO-AO (Diagnoses)	0.8365	0.7785	0.2581	0.1366	0.1104
LSTM-DO-AO (Categories)	0.8399	0.7783	0.2804	0.1361	0.1123
LSTM-DO-TR	0.8560	0.8075	0.2938	0.1485	0.1172
LSTM-DO-TR-AO (Diagnoses)	0.8470	0.7929	0.2735	0.1488	0.1149
LSTM-DO-TR-AO (Categories)	0.8543	0.8015	0.2887	0.1446	0.1161
LSTM-DO-TR (Linear Gain)	0.8480	0.7986	0.2896	0.1530	0.1160

Ensembles of Best MLP and Best LSTM

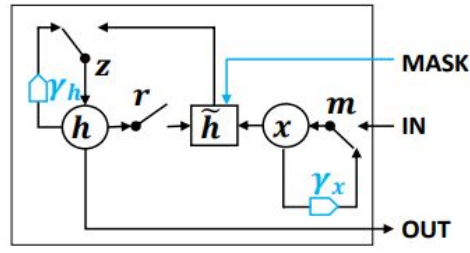
Mean of LSTM-DO-TR & MLP	0.8611	0.8143	0.2981	0.1553	0.1201
Max of LSTM-DO-TR & MLP	0.8643	0.8194	0.3035	0.1571	0.1218

Données manquantes

Ajout de *gates*!



(a) GRU



(b) GRU-D

MIMIC-III	
# of samples (N)	19714
# of variables (D)	99
Mean of # of time steps	35.89
Maximum of # of time steps	150
Mean of variable missing rate	0.9621

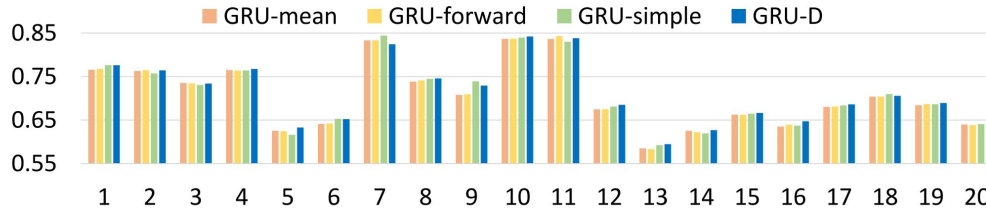


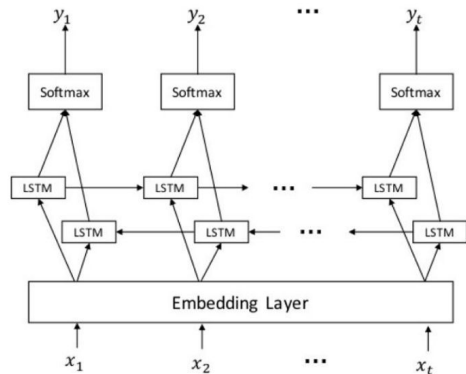
Figure 9: Performance for predicting 20 ICD-9 diagnosis categories on MIMIC-III dataset. x-axis, ICD-9 diagnosis category id; y-axis, AUC score.

Faible gain

Notes cliniques

Mr. Smith is a 63-year-old gentleman with coronary artery disease, hypertension, hypercholesterolemia, COPD and tobacco abuse. He reports doing well. He did have some more knee pain for a few weeks, but this has resolved. He is having more trouble with his sinuses. I had started him on Flonase back in December. He says this has not really helped. Over the past couple weeks he has had significant congestion and thick discharge. No fevers or headaches but does have diffuse upper right-sided teeth pain. **He denies any chest pains, palpitations, PND, orthopnea, edema or syncope.** His breathing is doing fine. No cough. He continues to smoke about half-a-pack per day. He plans on **trying the patches again.**

Extraction d'informations à partir de notes cliniques



Entrées: Note clinique

Sorties: Chaque mot appartient à un groupe.
Médication (Drug name, Dosage, Duration...)
ou *Maladie (ADE, Indication...)*

Données: 780 notes (moyenne de 786 notes).

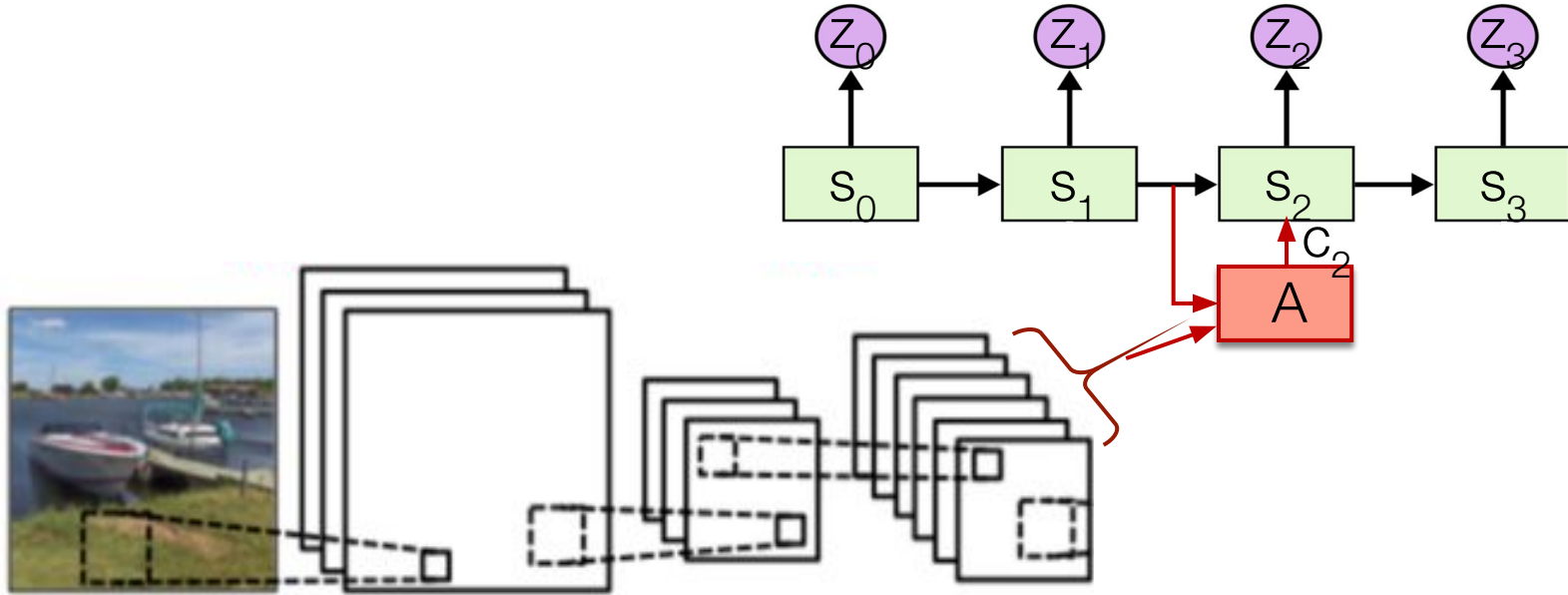
Models	Recall	Precision	F-score
CRF-nocontext	0.6562	0.7330	0.6925
CRF-context	0.6806	0.7711	0.7230
LSTM-sentence	0.8024	0.7803	0.7912
GRU-sentence	0.8013	0.7802	0.7906
LSTM-document	0.8050	0.7796	0.7921
GRU-document	0.8126	0.7938	0.8031

Abstract

Sequence labeling for extraction of medical events and their attributes from unstructured text in Electronic Health Records (EHR) notes is a key step towards semantic understanding of EHR. It has important applications in health informatics including pharmacovigilance and drug surveillance. The state-of-the-art supervised machine learning models in this domain are based on Conditional Random Fields (CRFs) with features calculated from fixed context windows. In this paper, we explore recurrent neural network frameworks and show that they significantly outperform

many disciplines such as genomics, intrusion detection, natural language processing, speech recognition etc. However, sequence labeling in EHR is a challenging task. Unlike text in the open domain, EHR notes are frequently noisy, containing incomplete sentences, phrases and irregular use of language. In addition, EHR notes incorporate abundant observations, rich medical jargons, and their variations, which make recognizing semantically similar patterns in EHR notes difficult. Additionally, different events exhibit different patterns and possess different prevalences. For example, while a medication comprises of at most a few words of a noun, an ADE (e.g., "has not EHR back to his normal self") may span to comprise of a significant part of a sentence.

Génération de légendes



Show, Attend and Tell: Neural Image Caption Generation with Visual Attention

Kabir Ayar
Diyen Lu
Rishabh Iyer
Kyunghyun Cho
Aravind Srinivas
Richard S. Sutton
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Abstract

Inspired by recent work in machine translation and object detection, we introduce an attention-based model that automatically learns to describe the content of images. We describe how we can train this model in a discriminative manner using standard backpropagation techniques and successfully by maximizing a variational lower bound. We also show through visualization how the model is able to automatically learn to focus on salient objects while generating the corresponding words in the output sequence. We validate the use of attention with state-of-the-art performance on four benchmark datasets: Flickr8K, Flickr30K and MS COCO.

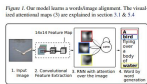
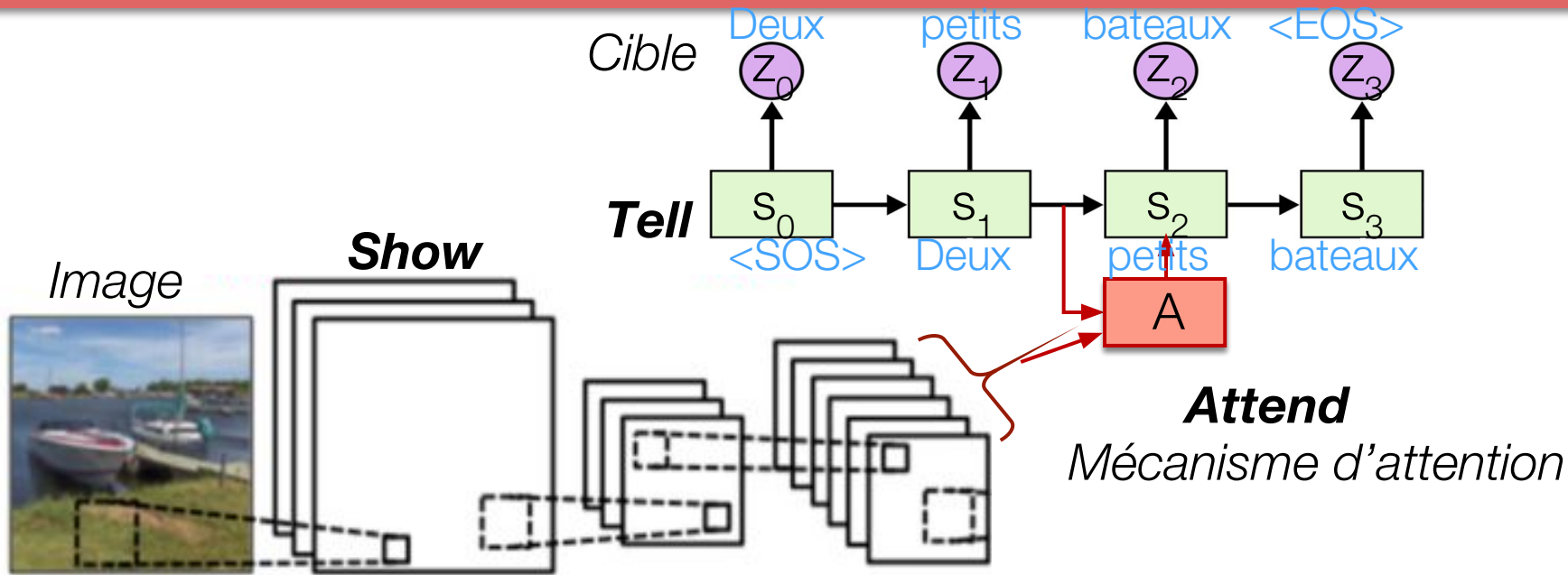


Figure 1: Our model learns a workspace alignment. The visual and attention maps C_t are explained in section 3.1.4.

has significantly improved the quality of caption generation using a combination of convolutional neural networks (CNNs) to learn visual representations of images and

Show, Attend and Tell: Neural Image Caption Generation with Visual Attention, 2016
Diapo de l'École d'automne 2018, César Laurent

Show, Attend and Tell



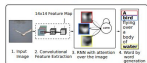
Show, Attend and Tell: Neural Image Caption Generation with Visual Attention

Bahdanau, D.,
 Cho, K., &
 Bengio, Y.
 arXiv:1412.0059 [cs.LG], 2014.

Abstract

Inspired by recent work in machine translation and object detection, we introduce an attention-based model that automatically learns to describe the content of images. We describe how we can train this model in a discriminative manner using standard backpropagation techniques and successfully by maximizing a variational lower bound. We also show through qualitative how the model is able to automatically learn to focus on salient objects while generating the corresponding words in the output sequence. We validate the use of attention with state-of-the-art performance on four benchmark datasets: Flickr8K, Flickr30K and MS COCO.

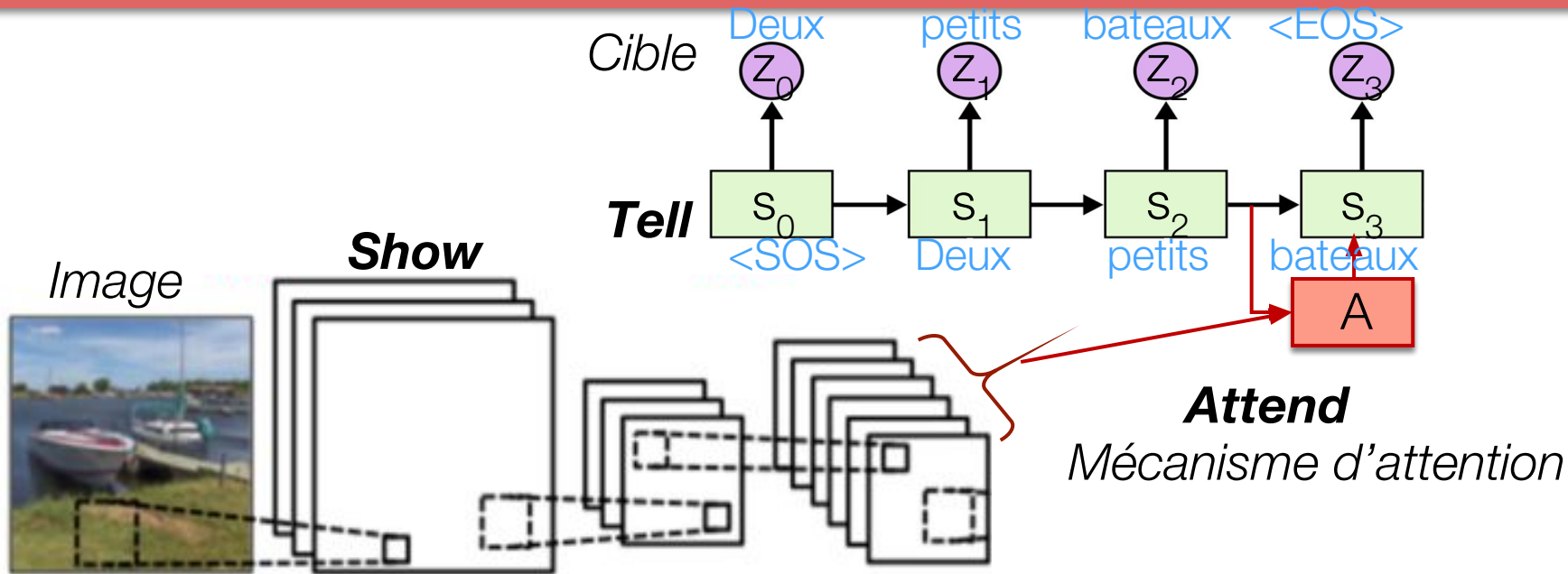
Figure 1: Our model learns a word-image alignment. The visual input attention maps Q are explained in section 3.1.4.



has significantly improved the quality of caption generation using a combination of convolutional neural networks combined to their neural representation of images and

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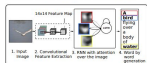
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Figure 1: Our model learns a word-image alignment. The visual input attention maps Z_i are explained in section 3.1.4.



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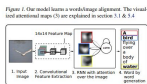


Figure 1. Our model learns a workflow alignment. The visual input attention maps \mathcal{A} are explained in section 3.1 A. 1.4

Show, Attend and Tell: Neural Image Caption Generation with Visual Attention

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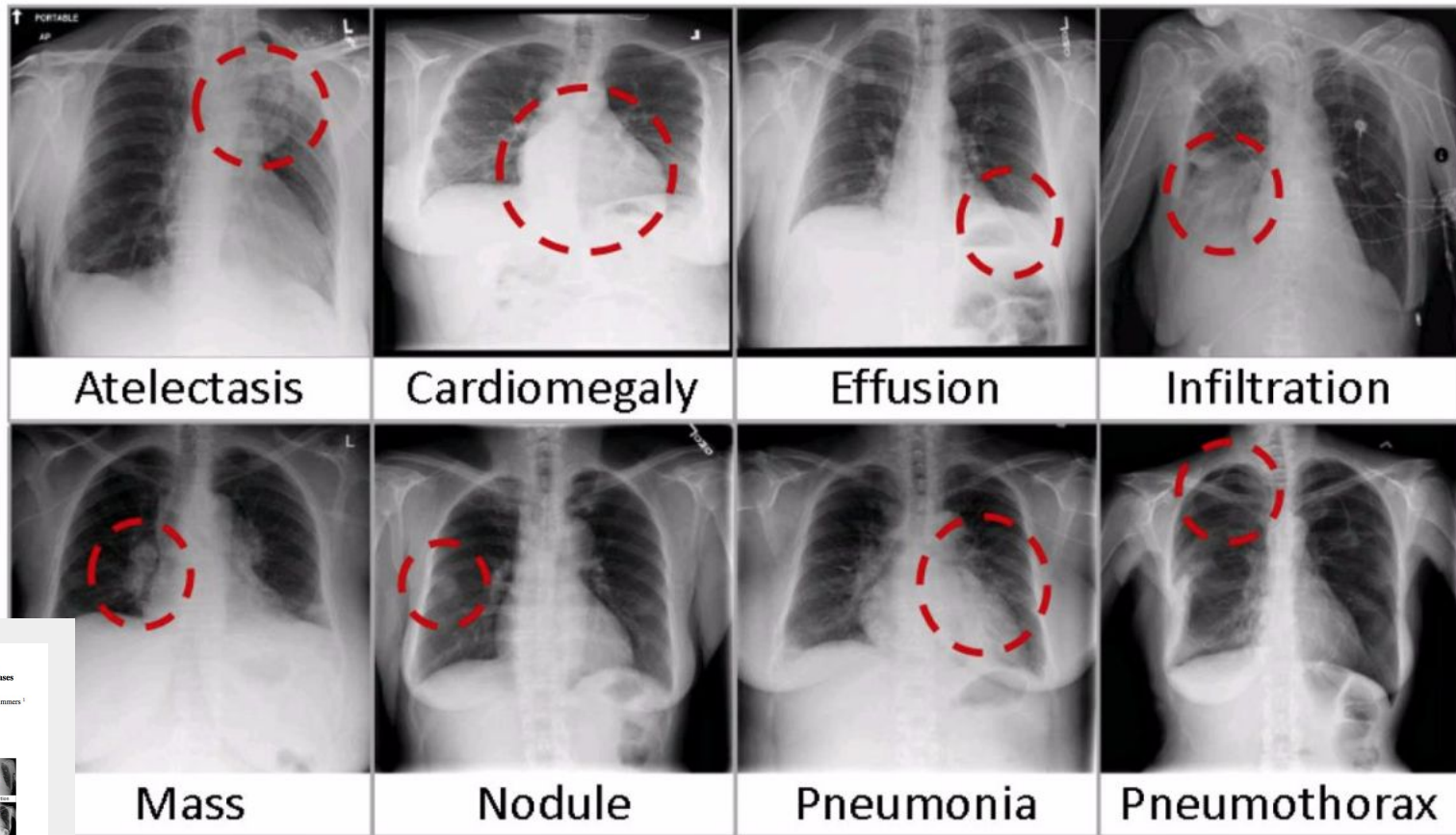
Abstract

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ChestX-ray 8

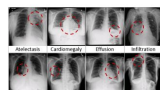


ChestX-ray8: Hospital-scale Chest X-ray Database and Benchmarks on Weakly-Supervised Classification and Localization of Common Thorax Diseases

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²National Center for Biotechnology Information, National Library of Medicine,
 National Institutes of Health, Bethesda, MD 20892
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Abstract

The chest X-ray is one of the most commonly accessible radiological examinations for screening and diagnosis of many lung diseases. It involves a number of X-ray imaging studies accompanied by radiological reports are accumulated and stored in many medical institutions. The raw Archiving and Communication Systems (ACS) on the other side, it is still an open question how the type of hospital-scale thorax database containing invaluable imaging information (i.e., locally labeled) can be accessed within the data hungry deep learning paradigm in building the next large-scale high precision computer-aided diagnosis (CAD) systems.



In this paper, we present a new chest X-ray database, namely "ChestX-ray8", which comprises 108,168 frontal-view X-ray images of 52,772 unique patients with the reported eight disease image labels (where each image can have multiple labels) from the associated radiological reports.

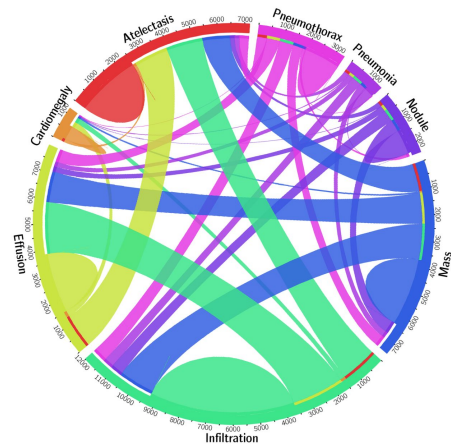
Wang, ChestX-ray8: Hospital-scale Chest X-ray Database and Benchmarks on Weakly-Supervised Classification and Localization of Common Thorax Diseases, 2017

ChestX-ray 8

Setting	Atelectasis	Cardiomegaly	Effusion	Infiltration	Mass	Nodule	Pneumonia	Pneumothorax
AlexNet	0.6458	0.6925	0.6642	0.6041	0.5644	0.6487	0.5493	0.7425
GoogLeNet	0.6307	0.7056	0.6876	0.6088	0.5363	0.5579	0.5990	0.7824
VGGNet-16	0.6281	0.7084	0.6502	0.5896	0.5103	0.6556	0.5100	0.7516
ResNet-50	0.7069	0.8141	0.7362	0.6128	0.5609	0.7164	0.6333	0.7891

AUCs for chaque classes d'un modèle à plusieurs sorties

- 32,717 patients
- 108,948 X-Rays
- Classes extraite de *notes cliniques*



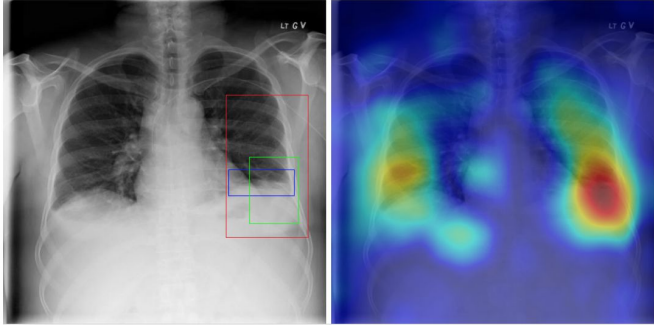
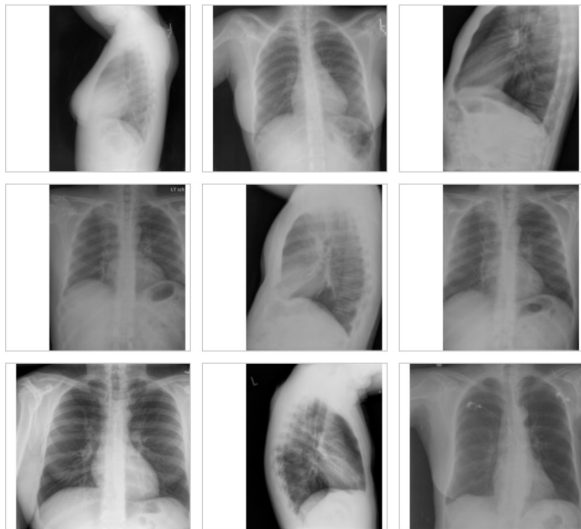
Radiology report	Keyword	Localization Result
<p>findings include: 1. left basilar atelectasis/consolidation. 2. prominent hilum (mediastinal adenopathy). 3. left pic catheter (tip in atriocaval junction). 4. stable, normal appearing cardiomeastinal silhouette.</p> <p>impression: small right pleural effusion otherwise stable abnormal study including left basilar infiltrate/atelectasis, prominent hilum, and position of left pic catheter (tip atriocaval junction).</p>	<p>Effusion; Infiltration; Atelectasis</p>	

Table 8. A sample of chest x-ray radiology report, mined disease keywords and localization result from the “Atelectasis” Class. Correct bounding box (in green), false positives (in red) and the ground truth (in blue) are plotted over the original image.

Rapports de l'hôpital universitaire de l'Indiana

Images de radiographie pulmonaire du réseau hospitalier de l'Université de l'Indiana



[Indiana University Chest X-ray Collection](#)

Kohli MD, Rosenman M - (2013)

Affiliation: Indiana University

ABSTRACT

Comparison: None.

Indication: Positive TB test

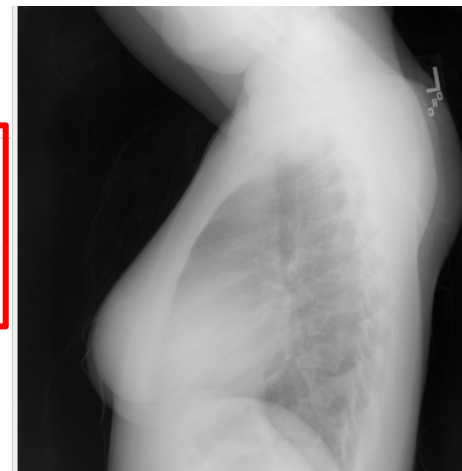
Findings: The cardiac silhouette and mediastinum size are within normal limits. There is no pulmonary edema. There is no focal consolidation. There are no XXXX of a pleural effusion. There is no evidence of pneumothorax.

Impression: Normal chest x-XXXX.

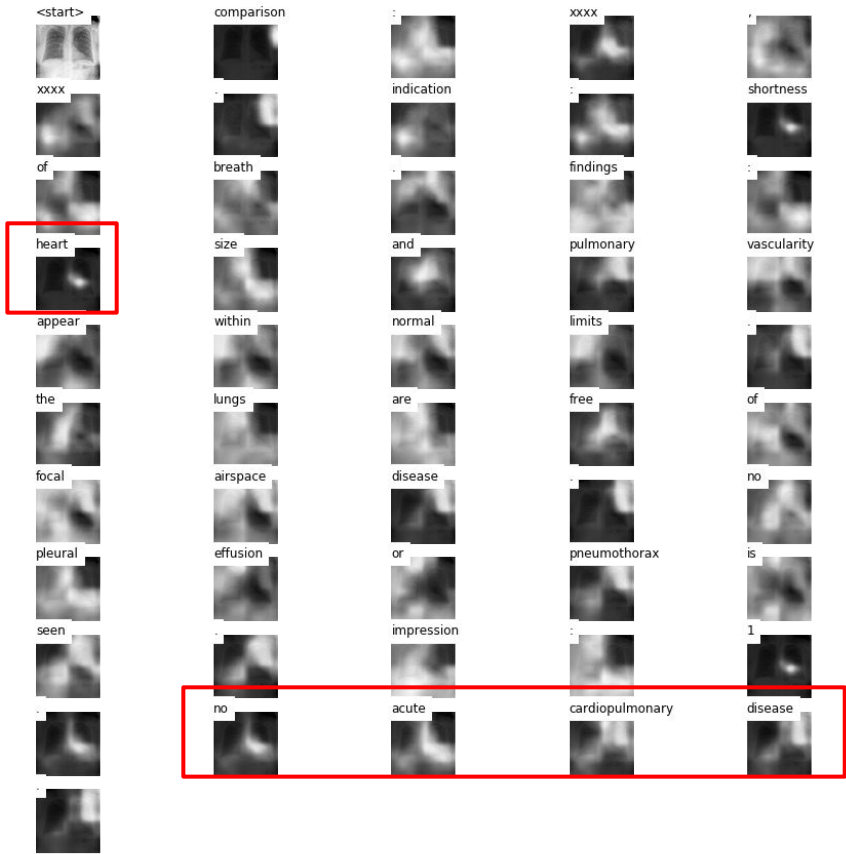
NOTE: The data are drawn from multiple hospital systems.

[Show MeSH](#)

Related in: [MedlinePlus Request Collection](#)



Génération de légendes sur des notes cliniques



Super générique!

Image Sample cases	I	J	K	L
P	Emphysema	Infiltration	Mass Consolidation	No finding Nodule
Original report	<p>minimal-moderate left neck and upper chest subcutaneous emphysema unchanged or minimally decreasing. moderate-marked right chest , minimal-moderate right neck and upper abdomen subcutaneous emphysema.</p>	<p>findings : interval development of left upper lobe patchy nodular infiltrate inferiorly . unchanged radiopaque catheter compatible with vp shunt . stable catheter overlying the stomach . costophrenic angles are clear . cardiac and mediastinal borders are within normal limits of size . impression : interval development of left upper lobe patchy nodular infiltrate</p>	<p>findings : a single ap view of the chest demonstrates unchanged or minimally increasing , dependent positioning , right lung mass/consolidation. the cardiac and mediastinal contours are stable . impression : 1. unchanged or minimally increasing , dependent positioning , right lung mass/consolidation . 2. no evidence of developing infiltrate the visualized left lung</p>	<p>findings : lungs are well aerated with no evidence of infiltrate . cardiac and mediastinal borders are within normal limits of size impression : no evidence of infiltrate</p>
Generated Report	<p>reason for study : s/p vats clinical information : aplastic anemia chest I view : chest x-ray performed on the same day . the heart and mediastinum are normal . the subcutaneous emphysema is seen in the right neck and neck on the right . there is unchanged subcutaneous emphysema seen on the right .</p>	<p>reason for exam (entered by ordering clinician into cris): r/o acute , r/opulmonary disease interval changes no interval change and seen are available of the heart , there are a nodular interstitial infiltrate or scarring as well as mild degenerative changes of the spine .</p>	<p>findings include 1. left lung consolidation . 2. left lung consolidation .</p>	<p>Findings:heartand mediastinum unchanged . lungs unchanged , no evidence of acute infiltrates , nodule projecting on posterior ribposteriorly . osseous structures intact . impression : stable chest I</p>

Questions?