

(51) International Patent Classification:  
*G06K 9/00* (2006.01)(21) International Application Number:  
PCT/US2014/028375(22) International Filing Date:  
14 March 2014 (14.03.2014)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
61/794,238 15 March 2013 (15.03.2013) US(71) Applicant: SONY CORPORATION [JP/JP]; 1-7-1 Kon-  
an, Minato-ku, Tokyo, Tokyo 108-0075 (JP).

(72) Inventors; and

(71) Applicants (for US only): XU, Xun [CN/US]; 800 E.  
Charleston Road, #7, Palo Alto, California 94303 (US).  
NAKAMURA, Akira [JP/US]; 1315 Petal Way, San Jose,  
California 95129 (US). WANG, Su [CN/US]; 3040 Rosato  
Court, San Jose, California 95135 (US).(74) Agent: OWENS, Jonathan O.; 162 North Wolfe Road,  
Sunnyvale, CA 94086 (US).(81) Designated States (unless otherwise indicated, for every  
kind of national protection available): AE, AG, AL, AM,  
AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY,  
BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM,  
DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT,  
HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR,  
KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME,  
MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ,  
OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA,  
SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM,  
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM,  
ZW.(84) Designated States (unless otherwise indicated, for every  
kind of regional protection available): ARIPO (BW, GH,  
GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ,  
UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ,  
TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV,  
MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM,  
TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW,  
KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

[Continued on next page]

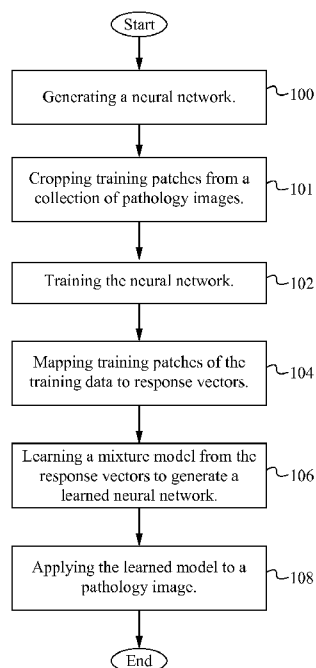
(54) Title: CHARACTERIZING PATHOLOGY IMAGES WITH STATISTICAL ANALYSIS OF LOCAL NEURAL NETWORK  
RESPONSES

Fig. 1

(57) Abstract: For digital pathology imaging, in-  
telligent processing, such as automatic recognition  
or content-based retrieval, is one significant bene-  
fit that drives the wide application of this techno-  
logy. Before any intelligent processing on patho-  
logy images, every image is converted into a fea-  
ture vector which quantitatively capture its visual  
characteristics. An algorithm characterizing patho-  
logy images with statistical analysis of local re-  
sponses of neural networks is described herein.  
The algorithm framework enables extracting soph-  
isticated textural features that are well adapted to  
the image data of interest.



- 
- *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))*

# CHARACTERIZING PATHOLOGY IMAGES WITH STATISTICAL ANALYSIS OF LOCAL NEURAL NETWORK RESPONSES

## CROSS-REFERENCE TO RELATED APPLICATION

5           This application claims the benefit of U.S. Provisional Patent Application Ser. No. 61/794,238, filed on March 15, 2013, and titled "CHARACTERIZING PATHOLOGY IMAGES WITH STATISTICAL ANALYSIS OF LOCAL NEURAL NETWORK RESPONSES" which is hereby incorporated by reference in its entirety for all purposes.

## 10       FIELD OF THE INVENTION

          The present invention relates to the field of digital pathology imaging. More specifically, the present invention relates to extracting features for quantitatively characterizing digital pathology images.

## 15       BACKGROUND OF THE INVENTION

          Digital Pathology is an image-based information environment enabled by computer technology that allows for the management of information generated from a digital slide. Digital pathology is enabled in part by virtual microscopy, which is the practice of converting glass slides into digital slides that can be viewed, managed and analyzed.

20

## SUMMARY OF THE INVENTION

          For digital pathology imaging, intelligent processing, such as automatic recognition or content-based retrieval, is one significant benefit that drives the wide application of this technology. Before any intelligent processing on pathology images, every image is converted  
25       into a feature vector which quantitatively capture its visual characteristics. An algorithm characterizing pathology images with statistical analysis of local responses of neural networks is described herein. The algorithm framework enables extracting sophisticated textural features that are well adapted to the image data of interest.

          In one aspect, a method of converting a pathology image into a feature vector  
30       programmed in a memory of a device comprises generating a neural network, teaching the neural network using a database of training patches cropped from a collection of pathology images, mapping training patches of the training data to response vectors, learning a mixture model from the response vectors and applying the learned model to a pathology image to convert the pathology image into a feature vector. An input to the neural network comprises

a patch of the image. A plurality of local patches of the image are input to the neural network. The neural network is used to extract a low dimensional representation of a set of data. The neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions. The teaching is unsupervised. The unsupervised teaching comprises using image samples that do not have manual labels assigned by a human. Image patches with a matching size to input of the neural network are cropped from training images. Teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network. The neural network comprises a two-layer network with linear or non-linear activation functions. Learning the mixture model comprises K-means or EM algorithm. The method further comprises applying the learned model to a pathology image. Applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location. Quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

In another aspect, a method of analyzing an image programmed in a memory of a device comprises generating a neural network, teaching the neural network using unlabeled samples in a database of training patches cropped from a collection of pathology images, mapping training patches of the training data to response vectors, learning a mixture model from the response vectors and applying the learned model to a pathology image to convert the pathology image into a feature vector. An input to the neural network comprises a patch of the image. A plurality of local patches of the image are input to the neural network. The neural network is used to extract a low dimensional representation of a set of data. The neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions. Image patches with a matching size to input of the neural network are cropped from the training images. Teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network. The neural network comprises a two-layer network with linear or non-linear activation functions. Learning the mixture model comprises K-means or EM algorithm. Applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the

trained neural network to the local image patch at each pixel location. Quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

In another aspect, an apparatus comprises a non-transitory memory for storing an application, the application for: generating a neural network comprising a symmetric architecture, wherein input and output of the neural network have a same number of dimensions, teaching the neural network using image samples that do not have any manual labels assigned by a human in a database of training patches cropped from a collection of pathology images, mapping training patches of the training data to response vectors, learning a mixture model from the response vectors and applying the learned model to a pathology image to convert the pathology image into a feature vector and a processing component coupled to the memory, the processing component configured for processing the application.

The neural network is used to extract a low dimensional representation of a set of data. Image patches with a matching size to input of the neural network are cropped from the training images. Teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network. The neural network comprises a two-layer network with linear or non-linear activation functions. Learning the mixture model comprises K-means or EM algorithm. Applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location. Quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

#### BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 illustrates a flowchart of a method of characterizing pathology images with statistical analysis of local neural network responses according to some embodiments.

FIG. 2 illustrates a block diagram of an exemplary computing device configured to implement the pathology image characterization method according to some embodiments.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

For digital pathology imaging, intelligent processing, such as automatic recognition or content-based retrieval, is one significant benefit that drives the wide application of this technology. Before any intelligent processing on pathology images, every image is converted into a feature vector which quantitatively capture its visual characteristics. An algorithm characterizing pathology images with statistical analysis of local responses of neural networks is described herein. The algorithm framework enables extracting sophisticated textural features that are well adapted to the image data of interest.

Pathology images contain repetitively appearing, but spatially variant, textural patterns. Textural information is important for describing visual contents in pathology images. In the algorithm framework described herein, textural information in pathology images is extracted via statistical analysis of local responses of neural networks. This framework enables extracting sophisticated textural features that are well adapted to the image data of interest.

## Image analysis with neural networks

## Neural network for images

To analyze pathology images, a neural network is constructed whose input is a patch in the image being analyzed. The neural network is able to be an auto-coder or any other alternative network such as Principal Component Analysis (PCA) or Independent Component Analysis (ICA). By scanning through the whole image, the same network is fed with local patches in the image and produces dense local response vectors. The procedure is able to be considered as generalized filtering. In contrast to a conventional linear filter, the neural network acts as a group of highly non-linear filters that transforms every local image region into a response vector.

## Auto-encoder and its training

An auto-encoder is a specific neural network used to learn a low dimensional representation of a set of data. It has a symmetric architecture such that the input and output have the same number of dimensions. The parameters of the auto-encoder are learned from a set of training data so that its output is able to approximate (e.g. reconstruct) the input as accurately as possible. The learning is unsupervised as no manual labels for the samples are required.

To train the auto-encoder for analyzing pathology images, image patches that have a matching size to the network's input are cropped from training images. The auto-encoder network is then learned via a back-propagation algorithm or another algorithm.

After the auto-encoder is learned, its second half (the reconstructive part) is dropped, and the first half (the analytic part) is used for image analysis.

#### Alternative choices of networks

The framework described herein is flexible such that different networks besides the auto-encoder are able to be chosen. For example, by employing a two layer network with linear activation functions, Principal Component Analysis (PCA) or Independent Component Analysis (ICA) is able to be used as specific cases under this framework.

#### Statistical analysis of local neural networks responses

##### Computing and quantizing local responses

After learning the network, e.g. auto-encoder or any other network mentioned above, all training patches are able to be mapped to response vectors. From these vectors, a mixture model is able to be learned via the K-means or Expectation Maximization (EM) algorithm.

As described herein, the learned network is able to be applied to new pathology images to be analyzed. The response vectors are computed at every pixel location by densely scanning the input image, then quantized against the learned model.

##### Image feature from statistics of local responses

Through the quantization procedure, the pathology image is mapped to a quantization map array where every element stores the cluster index assigned to each pixel location. From this map, feature vectors are able to be computed through statistical analysis - the simplest is histogram, or more sophisticated ones such as a co-occurrence matrix from which feature vectors such as Markov Stationary Feature are able to be derived. These feature vectors are concatenated to constitute the final quantitative description of the image to be analyzed.

Figure 1 illustrates a flowchart of a method of characterizing images according to some embodiments. In the step 100, a neural network is generated. The neural network is able to be an auto-encoder or any other network mentioned above. The neural network comprises a symmetric architecture such that the input and output have a same number of dimensions. In the step 101, training image patches are collected by cropping pathology images into a certain size (e.g., 64-by-64) at random locations. In the step 102, the neural

network is learned using a training data set. The neural network is used to extract a low dimensional representation of a set of data. The learning is unsupervised (e.g., requiring no labels). An auto-encoder is able to be learned through a back-propagation algorithm, while a PCA or ICA network is able to be learned by their classic learning algorithm, respectively.

5 After learning, the reconstructive part of the network is dropped, and the analysis part will be used as the feature extractor that maps an image patch to a response vector. In the step 104, training patches of the training data are mapped to response vectors. In the step 106, a mixture model is learned from the response vectors to generate a learned neural network.

Learning the mixture model is able to be implemented in any manner such as K-means or EM  
10 algorithm. In the step 108, the learned model is applied to a pathology image. Applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and quantizing the pathology image response vectors against the learned model. Quantizing includes mapping the pathology image to a quantization map array where every element

15 stores a cluster index assigned to each pixel location, from the quantization map, computing feature vectors through statistical analysis and concatenating the feature vectors to constitute a final quantitative description of the pathology image. In some embodiments, fewer or additional steps are implemented. In some embodiments, the order of the steps is modified. For example, in some embodiments, the neural network is already generated and trained, and  
20 the mixture model is already learned, and the process begins at the step 108. In another example, the process only includes generating and training, and the process ends at the step 108.

Figure 2 illustrates a block diagram of an exemplary computing device configured to implement the pathology image characterization method according to some embodiments.

25 The computing device 200 is able to be used to acquire, store, compute, process, communicate and/or display information such as text, images and videos. In general, a hardware structure suitable for implementing the computing device 200 includes a network interface 202, a memory 204, a processor 206, I/O device(s) 208, a bus 210 and a storage device 212. The choice of processor is not critical as long as a suitable processor with  
30 sufficient speed is chosen. The memory 204 is able to be any conventional computer memory known in the art. The storage device 212 is able to include a hard drive, CDROM, CDRW, DVD, DVDRW, Blu-ray®, flash memory card or any other storage device. The computing device 200 is able to include one or more network interfaces 202. An example of a network interface includes a network card connected to an Ethernet or other type of LAN. The I/O

device(s) 208 are able to include one or more of the following: keyboard, mouse, monitor, screen, printer, modem, touchscreen, button interface and other devices. Pathology image characterization application(s) 230 used to perform the pathology image characterization method are likely to be stored in the storage device 212 and memory 204 and processed as applications are typically processed. More or less components shown in Figure 2 are able to be included in the computing device 200. In some embodiments, pathology image characterization hardware 220 is included. Although the computing device 200 in Figure 2 includes applications 230 and hardware 220 for the pathology image characterization method, the pathology image characterization method is able to be implemented on a computing device in hardware, firmware, software or any combination thereof. For example, in some embodiments, the pathology image characterization applications 230 are programmed in a memory and executed using a processor. In another example, in some embodiments, the pathology image characterization hardware 220 is programmed hardware logic including gates specifically designed to implement the pathology image characterization method.

In some embodiments, the pathology image characterization application(s) 230 include several applications and/or modules. In some embodiments, modules include one or more sub-modules as well. In some embodiments, fewer or additional modules are able to be included.

Examples of suitable computing devices include a personal computer, a laptop computer, a computer workstation, a server, a mainframe computer, a handheld computer, a personal digital assistant, a cellular/mobile telephone, a smart appliance, a gaming console, a digital camera, a digital camcorder, a camera phone, a smart phone, a portable music player, a tablet computer, a mobile device, a video player, a video disc writer/player (e.g., DVD writer/player, Blu-ray® writer/player), a television, a home entertainment system or any other suitable computing device.

To utilize the pathology image characterization method, a device or several devices are used to generate a neural network, train the neural network and then use the neural network to characterize images. Each step is able to be performed automatically, manually or a combination thereof. Using the results of the pathology image characterization method, items are able to be identified such as items for diagnosis. For example, identifying a tumor.

In operation, the highly non-linear transform replaces simple linear filters to obtain more sophisticated features, and the transform learned from the training data replaces pre-defined filters to better adapt to the specific task in interest.

SOME EMBODIMENTS OF CHARACTERIZING PATHOLOGY IMAGES WITH  
STATISTICAL ANALYSIS OF LOCAL NEURAL NETWORK RESPONSES

1. A method of converting a pathology image into a feature vector programmed in a memory of a device comprising:
  - 5 a. generating a neural network;
  - b. teaching the neural network using a database of training patches cropped from a collection of pathology images;
  - c. mapping training patches of the training data to response vectors;
  - d. learning a mixture model from the response vectors; and
  - 10 e. applying the learned model to a pathology image to convert the pathology image into a feature vector.
2. The method of clause 1 wherein an input to the neural network comprises a patch of the image.
- 15 3. The method of clause 1 wherein a plurality of local patches of the image are input to the neural network.
4. The method of clause 1 wherein the neural network is used to extract a low dimensional representation of a set of data.
- 20 5. The method of clause 1 wherein the neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions.
- 25 6. The method of clause 1 wherein the teaching is unsupervised.
7. The method of clause 6 wherein the unsupervised teaching comprises using image samples that do not have manual labels assigned by a human.
- 30 8. The method of clause 1 wherein image patches with a matching size to input of the neural network are cropped from training images.
9. The method of clause 1 wherein teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network.

10. The method of clause 1 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.

5 11. The method of clause 1 wherein learning the mixture model comprises K-means or EM algorithm.

12. The method of clause 1 further comprising applying the learned model to a pathology image.

10

13. The method of clause 12 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.

15

14. The method of clause 13 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

20

15. A method of analyzing an image programmed in a memory of a device comprising:

- a. generating a neural network;
- b. teaching the neural network using unlabeled samples in a database of training patches cropped from a collection of pathology images;
- c. mapping training patches of the training data to response vectors;
- d. learning a mixture model from the response vectors; and
- e. applying the learned model to a pathology image to convert the pathology image into a feature vector.

25

30

16. The method of clause 15 wherein an input to the neural network comprises a patch of the image.

17. The method of clause 15 wherein a plurality of local patches of the image are input to the neural network.
- 5 18. The method of clause 15 wherein the neural network is used to extract a low dimensional representation of a set of data.
19. The method of clause 15 wherein the neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions.
- 10 20. The method of clause 15 wherein image patches with a matching size to input of the neural network are cropped from the training images.
21. The method of clause 15 wherein teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network.
- 15 22. The method of clause 15 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.
23. The method of clause 15 wherein learning the mixture model comprises K-means or EM algorithm.
- 20 24. The method of clause 15 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.
- 25 25. The method of clause 24 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.
- 30 26. An apparatus comprising:
- a. a non-transitory memory for storing an application, the application for:

- 5
- 10
- 15
- 20
- 25
- 30
- i. generating a neural network comprising a symmetric architecture, wherein input and output of the neural network have a same number of dimensions;
  - ii. teaching the neural network using image samples that do not have any manual labels assigned by a human in a database of training patches cropped from a collection of pathology images;
  - iii. mapping training patches of the training data to response vectors;
  - iv. learning a mixture model from the response vectors; and
  - v. applying the learned model to a pathology image to convert the pathology image into a feature vector; and
- b. a processing component coupled to the memory, the processing component configured for processing the application.
27. The apparatus of clause 26 wherein the neural network is used to extract a low dimensional representation of a set of data.
28. The apparatus of clause 26 wherein image patches with a matching size to input of the neural network are cropped from the training images.
29. The apparatus of clause 26 wherein teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network.
30. The apparatus of clause 26 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.
31. The apparatus of clause 26 wherein learning the mixture model comprises K-means or EM algorithm.
32. The apparatus of clause 31 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.

33. The apparatus of clause 32 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

The present invention has been described in terms of specific embodiments incorporating details to facilitate the understanding of principles of construction and operation of the invention. Such reference herein to specific embodiments and details thereof is not intended to limit the scope of the claims appended hereto. It will be readily apparent to one skilled in the art that other various modifications may be made in the embodiment chosen for illustration without departing from the spirit and scope of the invention as defined by the claims.

**CLAIMS**

What is claimed is:

1. A method of converting a pathology image into a feature vector programmed in a memory of a device comprising:
  - a. generating a neural network;
  - b. teaching the neural network using a database of training patches cropped from a collection of pathology images;
  - c. mapping training patches of the training data to response vectors;
  - d. learning a mixture model from the response vectors; and
  - e. applying the learned model to a pathology image to convert the pathology image into a feature vector.
2. The method of claim 1 wherein an input to the neural network comprises a patch of the image.
3. The method of claim 1 wherein a plurality of local patches of the image are input to the neural network.
4. The method of claim 1 wherein the neural network is used to extract a low dimensional representation of a set of data.
5. The method of claim 1 wherein the neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions.
6. The method of claim 1 wherein the teaching is unsupervised.
7. The method of claim 6 wherein the unsupervised teaching comprises using image samples that do not have manual labels assigned by a human.
8. The method of claim 1 wherein image patches with a matching size to input of the neural network are cropped from training images.

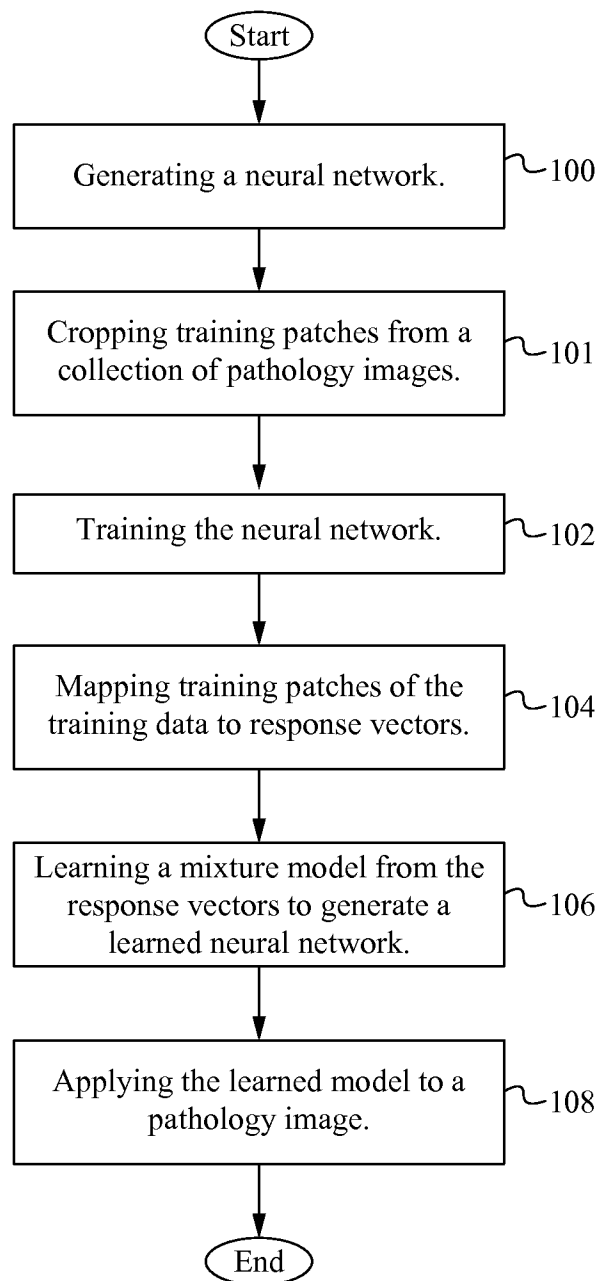
9. The method of claim 1 wherein teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network.
- 5 10. The method of claim 1 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.
11. The method of claim 1 wherein learning the mixture model comprises K-means or EM algorithm.
- 10 12. The method of claim 1 further comprising applying the learned model to a pathology image.
- 15 13. The method of claim 12 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.
- 20 14. The method of claim 13 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.
- 25 15. A method of analyzing an image programmed in a memory of a device comprising:  
a. generating a neural network;  
b. teaching the neural network using unlabeled samples in a database of training patches cropped from a collection of pathology images;  
c. mapping training patches of the training data to response vectors;  
d. learning a mixture model from the response vectors; and  
30 e. applying the learned model to a pathology image to convert the pathology image into a feature vector.
16. The method of claim 15 wherein an input to the neural network comprises a patch of the image.

17. The method of claim 15 wherein a plurality of local patches of the image are input to the neural network.
- 5 18. The method of claim 15 wherein the neural network is used to extract a low dimensional representation of a set of data.
19. The method of claim 15 wherein the neural network comprises a symmetric architecture, wherein input and output have a same number of dimensions.
- 10 20. The method of claim 15 wherein image patches with a matching size to input of the neural network are cropped from the training images.
21. The method of claim 15 wherein teaching the neural network utilizes a back-  
15 propagation algorithm or a proper learning algorithm for the specific type of network.
22. The method of claim 15 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.
- 20 23. The method of claim 15 wherein learning the mixture model comprises K-means or EM algorithm.
24. The method of claim 15 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the  
25 pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.
25. The method of claim 24 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to  
30 each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

26. An apparatus comprising:
- a. a non-transitory memory for storing an application, the application for:
    - i. generating a neural network comprising a symmetric architecture, wherein input and output of the neural network have a same number of dimensions;
    - ii. teaching the neural network using image samples that do not have any manual labels assigned by a human in a database of training patches cropped from a collection of pathology images;
    - iii. mapping training patches of the training data to response vectors;
    - iv. learning a mixture model from the response vectors; and
    - v. applying the learned model to a pathology image to convert the pathology image into a feature vector; and
  - b. a processing component coupled to the memory, the processing component configured for processing the application.
27. The apparatus of claim 26 wherein the neural network is used to extract a low dimensional representation of a set of data.
28. The apparatus of claim 26 wherein image patches with a matching size to input of the neural network are cropped from the training images.
29. The apparatus of claim 26 wherein teaching the neural network utilizes a back-propagation algorithm or a proper learning algorithm for the specific type of network.
30. The apparatus of claim 26 wherein the neural network comprises a two-layer network with linear or non-linear activation functions.
31. The apparatus of claim 26 wherein learning the mixture model comprises K-means or EM algorithm.
32. The apparatus of claim 31 wherein applying the learned model to the pathology image includes: computing pathology image response vectors at every pixel location of the pathology image by densely scanning the pathology image and applying the trained neural network to the local image patch at each pixel location.

33. The apparatus of claim 32 wherein quantizing comprises: mapping the pathology image to a quantization map array where every element stores a cluster index assigned to each pixel location; from the quantization map, computing feature vectors through statistical analysis; and concatenating the feature vectors to constitute a final quantitative description of the pathology image.

5

**1/2****Fig. 1**

2/2

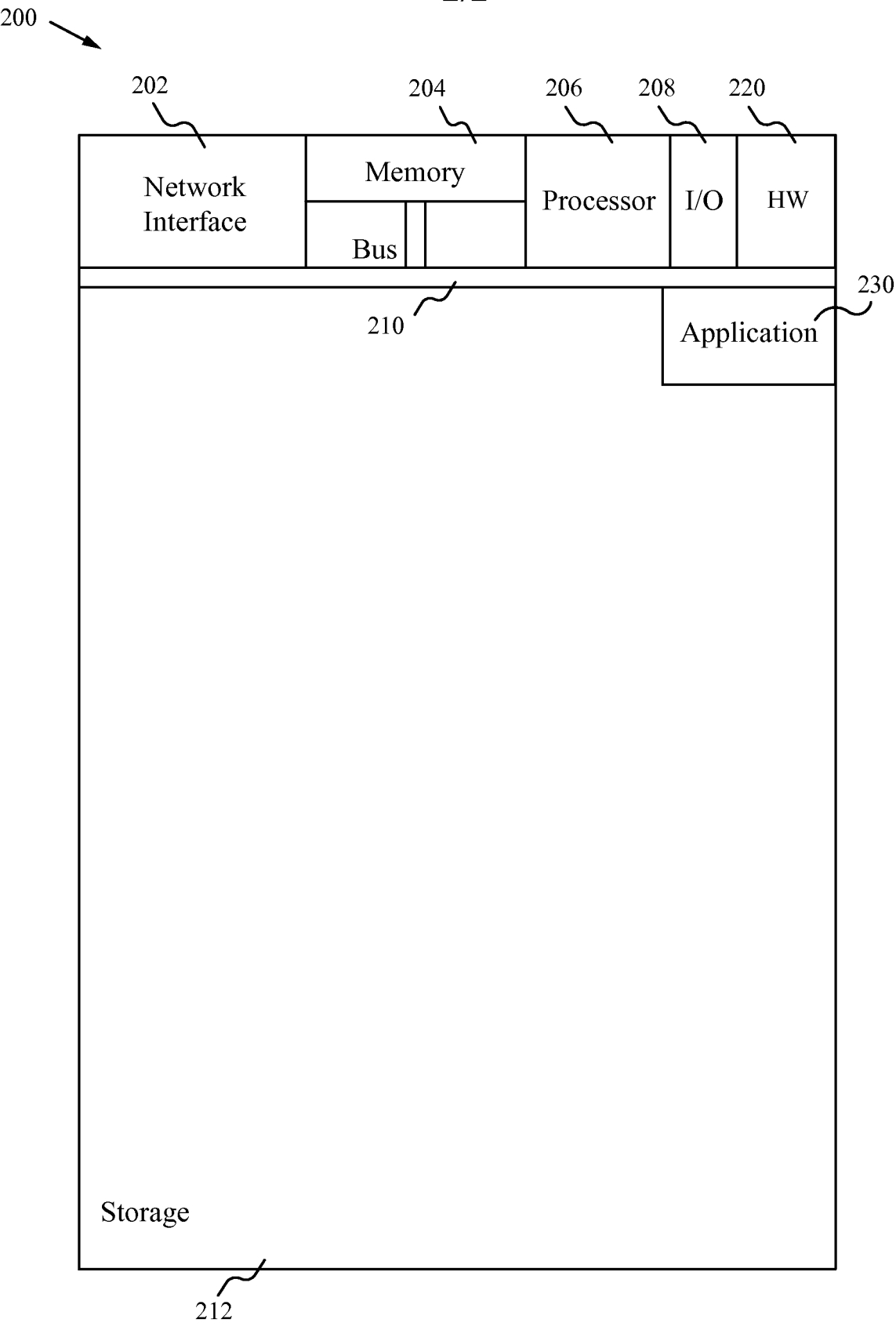


Fig. 2

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2014/028375

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - G06K 9/00 (2014.01)

USPC - 382/128

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - A61B 5/05; G06F 15/18; G06K 9/00 (2014.01)

USPC - 382/128; 382/190; 702/19; 706/16; 706/27

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched  
CPC - G06K 9/00147 (2014.02)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PatBase, Orbit, Google Patents, Google Scholar

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                                                                               | Relevant to claim No.     |
|-----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------|
| Y         | WO 2011/162213 A1 (LI et al.) 29 December 2011 (29.12.2011) see machine translation                                                                                                                                                                                                                                                                                                                                                                                                              | 1 - 33                    |
| Y         | US 2012/0189176 A1 (GIGER et al.) 26 July 2012 (26.07.2012) entire document                                                                                                                                                                                                                                                                                                                                                                                                                      | 1 - 33                    |
| Y         | US 2001/0032198 A1 (PAO et al.) 18 October 2001 (18.10.2001) entire document                                                                                                                                                                                                                                                                                                                                                                                                                     | 5, 9-10, 19, 21-22, 26-33 |
| Y         | US 2012/0099771 A1 (LAO) 26 April 2012 (26.04.2012) entire document                                                                                                                                                                                                                                                                                                                                                                                                                              | 8, 20, 28                 |
| Y         | US 6,438,268 B1 (COCKSHOTT et al.) 20 August 2002 (20.08.2002) entire document                                                                                                                                                                                                                                                                                                                                                                                                                   | 14, 25, 33                |
| Y         | ADALI et al. Applications of Neural Networks to Biomedical Image Processing. Handbook of NEURAL NETWORK SIGNAL PROCESSING, pages 1-28. CRC Press LLC, 2002. Retrieved on [2014-07-16].<br><URL: <a href="http://3.tiera.ru/ShiZ/math/Neural%20Networks/Hu%20Hwang/Handbook%20of%20Neural%20Network%20Signal%20Processing/2359_PDF_12.pdf">http://3.tiera.ru/ShiZ/math/Neural%20Networks/Hu%20Hwang/Handbook%20of%20Neural%20Network%20Signal%20Processing/2359_PDF_12.pdf</a> >. entire document | 11, 23, 31, 32            |

☐ Further documents are listed in the continuation of Box C.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

17 July 2014

Date of mailing of the international search report

08 AUG 2014

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents  
P.O. Box 1450, Alexandria, Virginia 22313-1450

Facsimile No. 571-273-3201

Authorized officer:

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300  
PCT OSP: 571-272-7774