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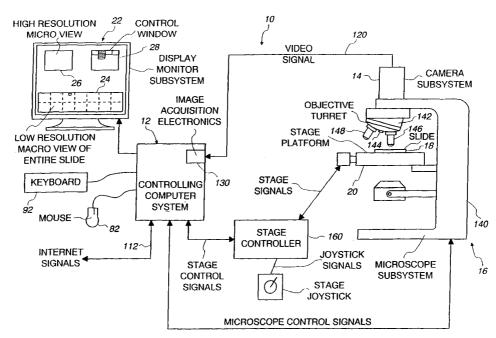
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(54) Title: METHOD AND APPARATUS FOR INTERNET, INTRANET, AND LOCAL VIEWING OF VIRTUAL MICROSCOPE SLIDES



(57) Abstract: A method of and apparatus for viewing microscopic images include transmitting tiled microscopic images from a server to a client (112). The client assembles the tiled images into a seamless virtual slide or specimen image and provides tools for manipulating image magnification and viewpoint (24). The method and apparatus also provides a virtual multi-headed microscope function which allows scattered viewers to simultaneously view and interact with a coherent magnified microscopic image (146).



WO 01/54052 A1



For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

-1-

METHOD AND APPARATUS FOR INTERNET, INTRANET, AND LOCAL VIEWING OF VIRTUAL MICROSCOPE SLIDES

CROSS REFERENCE TO RELATED APPLICATIONS

Priority is claimed from U.S. provisional application number 60/177,550, filed January 21, 2000, the content of which is hereby incorporated by reference.

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BACKGROUND OF THE INVENTION

The invention relates to a method of and an apparatus for storing and viewing virtual microscope slides. The method and apparatus are usable over the Internet, an intranet, or on a local computer, and provide an integrated and interlocked combination of a digital image server and multiple virtual microscope client viewers.

Examination of tissue sections, aspirated tissue, and the like, has typically been a localized activity. That is, the tissue is sectioned in a lab. It may be stained and microscopically examined by a light microscope after which a technician and/or a pathologist reaches a conclusion as to the characteristics of the tissue; for instance whether the tissue is benign or malignant and what stage of malignancy the tissue might

be in. A number of patents awarded to the instant inventors are directed to that sort of system.

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In some cases, however, it may be desirable where results are indefinite or where particular sophistication is needed for the human analysis of the images to be able to supply the slides to an offsite expert who might be across the country or on the other side of the world. In the past, the approach which has been taken to solve this problem has involved the transfer of the slides themselves by air express or post, often involving significant time delays which it would be desirable to avoid if a patient is suspected of being severely ill.

In the alternative, telepathology systems have been made available involving the use of television transmissions requiring a 6 MHz bandwidth, either through a satellite link or possibly through a coaxial cable, both of which must, in effect, be dedicated lines and previously set up. Such a system, however, requires a great deal of customization and expense although such systems do include the use of computer-controlled microscopes. Such microscopes receive commands from a remote location to move to a particular position on a slide so that the television camera may send a television signal out representative of the field of view.

This type of system is relatively expensive and clumsy to use do to the necessity for a very expensive robotically-controlled microscope which receives specialized signals over a dedicated link.

What is needed then is a system and apparatus which can allow a remote consult to take place related to tissue specimens, and the like, which may be done quickly, conveniently, and easily.

-3-

SUMMARY OF THE INVENTION

The invention relates to a method for viewing virtual microscope slides. Virtual microscope slides comprise sets of tiled images. The tiles of the tiled images represent a field of view which may be captured from a microscope having a high-precision controlled stage typically with a stage resolution in the neighborhood of a 1/10th micron step. The images are captured on a CCD array which generates images in color or black and white and stores them in a frame buffer or on disk in tiled format. Such images are usually very large due to the number of pixels required to reproduce a substantial size tissue specimen at a high magnification, such as 40 power. In addition, in order to provide ease of use, particularly on a remote basis, other sets of tiled images have a lower magnification, for instance at 1.25 power. All of the images are tiled and stored in digital format on a server which may communicate using the hypertext transport protocol used for web-based communications over a packet switching network such as the Internet or an intranet. Because the images have already been captured and coordinated in tiled form, it is unnecessary to provide a robotically-controlled microscope or even the original specimens themselves.

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One or more clients may communicate with the server containing the image to download a portion or all of the tiled image. The client provides requests to the server indicating the portion which is desired to be viewed and the server supplies the appropriate tiles for that portion of the image. The tiles are received by the client and are assembled into a seamless view which may be scrolled through and scanned in the same manner as a

-4-

pathologist may move about a microscope slide to find regions of interest. In addition, the low-magnification image may be displayed in a first window at the client and a higher-magnification image may simultaneously be displayed which retains coherence with the lower-magnification image in order to provide ease of scanning for areas of interest by the pathology, or the like.

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Furthermore, the client/server relationship may be carried out over multiple clients with one of the clients having control over the image positioning as fed by the server for all other clients via communication between the first client and the server, and then subsequent updating coherent communication between the server and the downstream clients. This does not necessarily require that repeated loading take place of the client images, but only that signals be sent between the server and the secondary clients reflecting the field which the first client is viewing. In this way, the overall system can operate similarly to a multiheaded optical microscope of the type used to train physicians in pathology. Furthermore, the system can be used as a multiheaded microscope during a consult so that al persons simultaneously involved in the consult are looking at the same portion of the image and no confusion can arise.

A further advantage of the present invention is to provide packet switched chat communications along with the multiheaded virtual microscope feature to allow text to be transferred among the various clients while the images are being viewed.

Finally, additional lines of communication may be provided among the users of the multiple remote client locations so that they can discuss telephonically or even using a voice-over-Internet protocol-based system to

-5-

confer in real time on the images that are being seen at each of the client stations.

Furthermore, the client in control of the image may relinquish control to a second client; the first client operating on a peer basis with the other clients in a secondary relationship thereafter.

In order to provide further analysis features, a linear measuring or tape measuring feature may be provided in order to determine the distance in microns, or the like, between a pair of points identified by pointing and clicking on portions of the image in order to determine the actual size of particular features shown in the specimen image. The size, of course, is computed on the basis of the magnification of the image being shown.

Other objects and advantages of the present invention will become obvious to one of ordinary skill in the art upon a perusal of the following specification and claims in light of the accompanying drawings.

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BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a block diagram of a system according to the invention for creating and transmitting locally, over an intranet or via the Internet data structures of an image of specimen on a microscope slide;

FIG. 1A is representation of a microscope slide which has been arbitrarily assigned to be scanned into eighty tiled images;

FIG 1B is a representation of the detected signals of the individual pixel sensors in a CCD optical array after detecting a selected image area to tile and the

-6-

referenced data files containing the information describing the detected signals;

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FIG. 2 is a screen view of a system embodying the present invention showing a low magnification image of a specimen on a microscope slide in one window, a high magnification image of a portion of the low magnification image selected by a region marker and a control window;

FIG. 3 is a view of a display screen of the apparatus embodying the present invention showing the control window a low magnification window having a plurality of high magnification micro image regions delineated therein and a high magnification window including one or more of the micro image regions;

FIG. 4 is a view of a macro image of an actual breast cancer specimen displayed at 1.25X as seen on a computer monitor;

FIG. 5 is a view of the grid portion of FIG. 4 outlining a region of interest selected by a pathologist displayed at 40X magnification;

FIG. 6 is a block diagram of the steps in the mapping of the scanned image from the optical sensor array to computer bit map in memory to the display on a user's monitor;

FIG. 7A is a file listing such as would be seen under Windows 95 file manager showing the data files included in a data structure for a breast cancer specimen;

FIG. 7B is a file listing of a Java applet for controlling a data structure;

FIG. 8 is file listing such as would be seen under Windows 95 file manager showing the data files included in an alternate data structure for a breast cancer specimen;

-7-

FIGS. 9A and 9B are a block diagram of the apparatus embodying the present invention;

FIG. 10 is a block diagram of a portion of the apparatus shown in FIG. 9 showing details of a mechanical arrangement of a microscope;

FIG. 11 is a flow diagram related to operation of the apparatus;

FIG. 12 is a flow diagram of details of one of the steps in FIG. 11;

FIG. 13 is a display screen showing control parameters to be manipulated thereon;

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FIG. 14 is a flow chart for a region outlying routine;

FIG. 15 is a flow chart for a scanning and analyzing routine;

FIG. 16 is a schematic showing of the limits of travel of the microscope stage with respect to the image tiles;

FIG. 16A is a perspective view of the microscope stage and stepper motors and encoders providing a closed loop drive for the motors;

FIG. 17 is a block diagram of a networked system allowing multiple workstations to obtain access to the microscope and to manipulate the microscope locally at each workstation;

FIG. 17A is a view of the system described in connection with FIG. 10;

FIG. 18 is a block diagram of a remote networked system for distributing and accessing diagnostic images and data, i.e. virtual microscope slides, through a hypertext transport protocol based server directly or over a packet network;

-8-

FIG. 19 shows a system having interlinking and an integrated combination of image viewer and server concept using an Internet or intranet connection embodying the present invention;

FIG. 20 shows a server comprising a portion of the system shown in FIG. 19 and functioning as a listening socket to respond to GET requests and create event threads in a simultaneous multi-threaded operating environment;

FIG. 21 shows logic to determine valid GET requests;

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FIG. 22A shows an interaction between a thin client browser program and the Internet or intranet server computer with a server program as shown in FIG. 20:

FIG. 22B shows an HTML-embedded Java applet viewer window for a client subsystem of the system shown in FIG. 19;

FIG. 23 shows an interaction between a Java applet program and Internet or intranet servers executing a server program and embodying the present invention;

FIG. 24 shows a thin client browser main window upon initial activation of the thin client browser shown in FIG. 22A:

FIG. 25 shows a main window with a Slide Tray tab activated, showing available images from a remote server;

FIG. 26 shows a selection in the tray holding slide name Prost-zl and showing a thumbnail image of a virtual slide together with associated identification information;

FIG. 27 shows a main window of the thin client browser showing a tab after selection of a virtual slide for detailed viewing in response to the Slide Tray tab;

-9-

FIG. 28 shows a Slide View window chosen by selecting a point on the browser main window thumbnail image, a Slide View image shows an overlay set of a tiled region from which one or more higher-magnification Field View images may be chosen;

FIG. 29 shows a Field View window chosen by selecting an image tile region of the Slide View window shown in FIG. 28 using a pointer;

FIG. 30 is a flow chart of a typical sequence of interactions to view an image;

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FIG. 31 shows a Server tab, showing options for multiple client interaction;

FIG. 32 shows a right mouse click activated pop-up menu when a pointer is positioned on an x, y location in the image area;

FIG. 33 shows a pointer position after choosing a "Set the Pointer" option in the menu of FIG. 32;

FIG. 34 shows a flow chart for major steps in process of filling in display windows with tiles; and

FIG. 35 shows an HTML-embedded Java applet viewer window.

FIGS. 36A through 36D are flow charts showing the operation of a server and a plurality of clients connected to the server for performing a virtual multiheaded microscope task.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Referring now to the drawings and especially to 30 FIG. 1, a system 10 according to the invention is shown therein for creating, and transmitting over an intranet or via the Internet a virtual microscope slide, i.e. interrelated data structures, which may or may not

-10-

include display procedures, depicting at multiple resolutions, images of a specimen on a microscope slide. The system includes a microscope with a digital platform for supporting the microscope slide. Digital platform or stage 11 has been specially calibrated to include a large number of increments for locating portions of specimen images with high precision. After calibration and initial registration of stage 11 in the microscope setup, a microscope slide 13 or other substrate with a specimen 13a to be scanned is placed on stage 11.

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For exemplary purposes, the creation of virtual microscope slide specimen according to the invention will be described with respect to a breast cancer specimen. The first step in creating a data structure according to the invention is to establish a macro image of the entire specimen (or that portion of the specimen desired to be stored as the macro image). The purpose for creating the macro or large area thumbnail image is to enable the viewer to see the entire specimen at once and to use the entire image to choose those significant portions thereon for viewing at greater magnification. In this example, the user has selected 1.25% as the magnification to display the entire breast cancer slide. Once specimen .13a has been placed on stage 11, rotating optical assembly 15 are rotated to select lens 17 which corresponds to the 1.25% magnification.

In accordance with the teachings of the prior patent application, the computer controlled microscope is moved to scan the entire image of specimen 13a. The focusing system is programmed to step through increments which detect/select only the high resolution center area of the field of view in order to avoid storing the blurred areas at the periphery of the field of view. In

this example, the macro image will be stored in a 10 by 8 array, for a total of 80 contiguous image tiles, as shown in FIG. 1A.

A typical microscope slide is about 77mm by 25mm, where the usable area, without including the label, is about 57mm by 25m. Each of the 80 image segments is about 4.8mm by 3.5mm in dimension. This means each of the 80 image segments will be scanned separately and stored as a separate image tile.

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The precision of the microscope systems is set up so that each step of the motor has a precision of .1 micron (micrometer). In this example, the microscope is set up to move 48,143 steps in the X direction and 35,800 steps in the Y direction at 1.25X magnification for each of the 80 image areas. At higher magnifications, the image areas to be scanned are considerably smaller, so the number of steps is corresponding smaller. For each of the 80 image areas, the microscope lens will detect only the high resolution center area of the field of view.

The optical image from the desired image area is then detected by an optical array sensor 19, which preferably is a CCD sensor array. In this embodiment each of the 80 scanned areas is sensed by the entire array 19, which includes 752 pixels by 480 pixels. The optical array sensor 19 sends electrical signals indicative of the detected image to a microscope-controlled computer 32. The computer 32 stores the scanned images, including the top left X-Y stage coordinates for each of the 80 individual areas of the microscope slide. Each of the 80 scanned image areas' pixel locations are stored in a bit-mapped file (i.e., a file which contains a map of the location of each bit in

-12-

the area) which corresponds to the layout of the individual images thereon. Thus, all of the pixels from the image tile derived from region A on FIG. 1A, which is the seventh from the left and in the top row, are individually assigned unique locations in the computer memory's bit-mapped file (FIG. 6), and are also stored in the data structure image tile file as shown in FIG. 1B.

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Each of the stored data image tiles is a standard image file with extension .bmp, and is of the order of one megabyte, i.e. each of the 752 x 480 pixels is stored as 3 bytes of red, green and blue image data $(752 \times 480 \times 32 = 1,082,880 \text{ bytes})$. Since the location of each image tile is known according to the bitmap, the complete microscope image can be recreated by painting (displaying) each image tile in accordance with its grid location.

To display the resulting image, the computer 32 calculates the appropriate portion to be displayed from each image tile depending upon the relative size of the display screen. Since the stored image data is usually greater than the size of the typical monitor, the viewer must scroll through the image on the window to view it entirely. However, an optional compression algorithm can be used to compress the entire image into the viewing The X-Y coordinate information is used by the viewing and manipulation program to reconstruct the image tiles into a complete image of the specimen. The resulting image is larger, and with better resolution than would be achieved if optics technology were able to construct a single lens capable of viewing the entire specimen in one field of view. In this example, each of the 80 image tiles has digital resolution of 752×480 pixels, with corresponding optical resolution of

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approximate .2 microns at 40X to approximately 6.4 microns at 1.25X.

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After the macro or thumbnail images are digitally scanned and stored with their X-Y coordinate information, the user then examines the macro image or original specimen for significant details. Typically, the user will highlight with a marking pen the areas to be viewed at higher magnification. The user then changes the magnification of optics system 15 to the desired higher magnification, moves the scanning system to bring the selected region into view. The computer 32 then repeats the scanning and image tile creation process for the selected region, but at higher magnification and with a new grid system to locate the scanned selected regions.

In the preferred embodiment example, the user has selected region B shown on FIG. 1A to perform a second view at a higher magnification. For example the user selects a 40X magnification. The computer 32 calculates the number of tiles needed to fill the selected area at 40X magnification and sets up a second grid.

It should be noted that region B crosses over several of the larger tiles in FIG. 1A. Because of the extremely precise 0.1 micron resolution of the instrument, locating such selected regions with high resolution is readily accomplished. As noted above, the computer 32 calculates the size of the image portion, in this case as an example, X = 1500 and Y = 1200 stepping increments. Each image portion at the 40X resolution is detected by the optical sensor array, 752 by 480 pixels. Each resulting data file is stored in a separate, high magnification mapped area of memory so that the computer can easily recall the location of region B, or any of its 200 individual image tiles, when requested by a user.

-14-

Once the user has completed selecting and having the computer controlled microscope system scan and store the digital images in image tiles, the computer 32 stores the mapped .bmp files along with their coordinate information and creates the slide image data structure 31 shown in FIG. 1. Slide image data structure 31 includes all of the bit-mapped image tile files at both magnifications (note that similarly, additional images could be stored at further magnifications, if desired), as well as X-Y coordinate information for the location of the various image tiles.

FIG. 7A is a file listing such as would be seen under a Windows 95 file manager showing the data files included in a data structure for a breast cancer specimen. Included in the file listing are FinalScan.ini and SlideScan.ini as well as sixty bit-mapped data files. Slidescan.ini is a listing of all the original bit-mapped (.bmp) files. The bit-mapped files represent the individual image tiles in the scan at, say, 1.25X magnifications. Slidescan.ini is set forth below in Table 1 and describes the X-Y coordinates for each image tile file. When the data structure is viewed by a control program, the program uses the X-Y coordinates to display all the image tiles contiguously.

TABLE 1 -- Slidescan.ini

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	[Header]	[Ss2]
	x=278000	x=133571
30	y=142500	y=142500
	lXStepSize=48143	[Ss3]
	lYStepSize=35800	x=37285
	iScannedCount=37	y=106700
	[Ss1]	[Ss4]
35	x=181714	x=85428
	y=142500	y=106700

-15-

	[Ss5] x=133571
5	y=106700 [Ss6] x=181714
	y=106700 [Ss7] x=229857 y=106700
10	[Ss8] x=229857 y=70900
15	[Ss9] x=181714 y=70900 [Ss10] x=133571
20	y=70900 [Ss11] x=85428 y=70900 [Ss12]
25	x=37285 y=70900 [Ss13] x=-10858 y=70900
30	[Ss14] x=-10858 y=35100 [Ss15] x=37285
35	y=35100 [Ss16] x=85428 y=35100 [Ss17]
40	x=133571 y=35100 [Ss18] x=181714 y=35100
45	[Ss19] x=229857 y=35100 [Ss20] x=278000
5 0	y=-700 [Ss21]

x = 229857

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y = -700[Ss22] x=181714y = -700[Ss23] x=133571y = -700[Ss24] x = 85428y = -700[Ss25] x = 37285y = -700[Ss26] x = -10858y = -700[Ss27] x = -10858y = -36500[Ss28] x = 37285y = -36500[Ss29] x = 85428y = -36500

-16-

[Ss30] x=133571y = -36500[Ss31] x=1817145 y = -36500[Ss32] x = 229857y = -36500[Ss33] 10 x = 278000y = -36500[Ss34] x=278000y = -7230015 [Ss35] x = 229857y = -72300[Ss36] 20 x=181714y = -72300[Ss37] x=133571y = -7230025

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Table 2 is a listing of the file FinalScan.ini, which is a listing the X-Y coordinates of the high magnification image tiles scanned and stored.

TABLE 2 - FinalScan.ini

[Header] dMagnification=40 tPatientID=mda027 lAnalysisImageCount=105 lCalibrationImageCount=0 35 tAccession= tOperatorID=jwb [Da0] tTimeOfScan=8/4/97 1:19:56 x = 214532y = 65584lXStageRef=278000 [Da1] lYStageRef=142500 x = 21299640 iImageWidth=752 y = 65584iImageHeight=480 [Da2] lXStepSize=1590 x = 211460y = 65584lYStepSize=1190 45 lXOffset=-1900 [Da3] lYOffset=-400 x = 209924

-17-

5	y=65584 [Da4] x=208388 y=65584 [Da5] x=206852 y=65584 [Da6]	x=208388 y=63216 [Da21] x=206852 y=63216 [Da22] x=205316 y=63216	
10	x=205316 y=65584 [Da7] x=203780 y=65584	[Da23] x=203780 y=63216 [Da24] x=214532	
15	[Da8] x=214532 y=64400 [Da9] x=212996	y=62032 [Da25] x=212996 y=62032 [Da26]	
20	y=64400 [Da10] x=211460 y=64400 [Da11]	x=211460 y=62032 [Da27] x=209924 y=62032	
25	x=209924 y=64400 [Da12] x=208388 y=64400	[Da28] x=208388 y=62032 [Da29] x=206852	
30	[Da13] x=206852 y=64400 [Da14] x=205316 y=64400	y=62032 [Da30] x=205316 y=62032 [Da31]	
35	y=04400 [Da15] x=203780 y=64400 [Da16] x=214532	x=203780 y=62032 [Da32] x=214532 y=60848 [Da33]	
40	y=63216 [Da17] x=212996 y=63216 [Da18]	x=212996 y=60848 [Da34] x=211460 y=60848	
45	x=211460 y=63216 [Da19] x=209924	[Da35] x=209924 y=60848 [Da36]	
50	y=63216 [Da20]	x=208388 y=60848	

-18-

5	[Da37] x=206852 y=60848 [Da38] x=205316 y=60848 [Da39] x=203780	y=58480 [Da54] x=205316 y=58480 [Da55] x=203780 y=58480
10	x=203780 y=60848 [Da40] x=214532 y=59664 [Da41]	[Da56] x=180740 y=82160 [Da57] x=179204 y=82160
15	x=212996 y=59664 [Da42] x=211460 y=59664	[Da58] x=177668 y=82160 [Da59] x=176132
20	[Da43] x=209924 y=59664 [Da44]	y=82160 [Da60] x=174596 y=82160
25	x=208388 y=59664 [Da45] x=206852 y=59664 [Da46]	[Da61] x=173060 y=82160 [Da62] x=171524 y=82160
30	x=205316 y=59664 [Da47] x=203780 y=59664	[Da63] x=180740 y=80976 [Da64] x=179204
35	[Da48] x=214532 y=58480 [Da49] x=212996	y=80976 [Da65] x=177668 y=80976 [Da66]
40	y=58480 [Da50] x=211460 y=58480 [Da51]	x=176132 y=80976 [Da67] x=174596 y=80976
45	x=209924 y=58480 [Da52] x=208388 y=58480	[Da68] x=173060 y=80976 [Da69] x=171524
50	[Da53] x=206852	y=80976 [Da70]

-19-

	x=180740 y=79792 [Da71] x=179204	[Da87] x=176132 y=77424 [Da88]
5	y=79792 [Da72] x=177668	x=174596 y=77424 [Da89]
10	y=79792 [Da73] x=176132	x=173060 y=77424 [Da90]
	y=79792 [Da74] x=174596	x=171524 y=77424 [Da91]
15	y=79792 [Da75] x=173060 y=79792	x=180740 y=76240 [Da92] x=179204
20	[Da76] x=171524 y=79792	y=76240 y=76240 Da93] x=177668
	[Da77] x=180740 y=78608 [Da78]	y=76240 [Da94] x=176132 y=76240
25	x=179204 y=78608 [Da79] x=177668	y-70240 [Da95] x=174596 y=76240 [Da96]
30	y=78608 [Da80] x=176132 y=78608	x=173060 y=76240 [Da97] x=171524
35	[Da81] x=174596 y=78608 [Da82] x=173060 y=78608	y=76240 [Da98] x=180740 y=75056 [Da99] x=179204
40	[Da83] x=171524 y=78608 [Da84]	y=75056 [Da100] x=177668 y=75056
45	x=180740 y=77424 [Da85] x=179204 y=77424 [Da86]	[Da101] x=176132 y=75056 [Da102] x=174596 y=75056
50	x=177668 y=77424	[Da103] x=173060

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y=75056 [Da104] x=171524 y=75056

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Computer 32 can also use the scanned image files to create a self-executing data structure. By compressing the .bmp images to .jpg and adding a dynamic, self-executing program which enables the user to view, reconstruct and manipulate the image tiles, the user can use the data structure as a virtual microscope slide of the original specimen. Preferably, the dynamic, self-executing program is a Java applet, such as shown on FIG. 7B.

15 Computer 32 can provide the slide image data structure 31 directly or via an intranet browser 33 to local viewer 34, or via an Internet server 38. Slide image data structure 37 is shown as being directly accessible from Internet server 38. Alternatively, a user can download the slide image data structure on his own computer 39, use an internet browser 43 and view the reconstructed images. Another alternative is for computer 32 to store the slide image data structure on a CD-ROM, Jazz drive or other storage medium.

To view slide image data structure 31 or 37, the user, who for example, has acquired the data structure via a CD-ROM, first installs the CD-ROM in the CD-ROM drive of his computer. Then the user opens up a browser or other applications program which can read the Java applet installed on the CD-ROM with the image tiles. Note that in some instances no separate browser program may be required. In some case, the CD-ROM may include the complete applications program for viewing, reconstructing and manipulating the image tiles. In the instant example, the user will then select the icon or

file listing for the slide image data structure and the control program will display the data files.

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FIG. 2 is a screen view of a system embodying the present invention showing a low magnification image 24 of a specimen on a microscope slide in one window, a high magnification image 26 of a portion of the low magnification image selected by a region marker 30 and a control window 28. FIG. 3 is a view of a display screen of the apparatus embodying the present invention showing the control window 28, a low magnification window 24 having a plurality of high magnification micro image regions 310 delineated therein and a high magnification window 26 including one or more of the micro image regions 310, 314, 316. FIG. 4 is a view of a macro image of an actual breast cancer specimen displayed at 1.25% as seen on a computer monitor. FIG. 5 is a view of the grid portion of FIG. 4 outlining a region of interest selected by a pathologist displayed at 40X magnification.

Recall that region A in FIG. 1A was about 4.8mm by 3.5mm. This area creates 752 by 480 pixels of sensed data, or 360,930 pixels of information. Each pixel sends information about its location and the image it sensed to the computer. The computer stores this information in a series of data files (typically .bmp format, but .tif or .gif could also be used). Thus, it can be seen that several more pixels of sensed data are available for viewing on a computer monitor operating at 640 by 480. To view the entire image, the user must scroll through the image tiles. However, scrolling need not be done on a tile, by tile basis. Rather, the user scrolls by pointing to a pixel on the monitor.

Figure 6 is a block diagram showing how the control program locates and scrolls through the stored

image tiles. Using the example from Figure 1a, a complete data structure has been created. When the user loads the data structure (of the microscope slide) into his personal computer or views it from an Internet browser, the control program recreates a bit map of the stored data. The bit map of the entire slide is shown in Figure 6. Image tile A is also high-lighted. This bit map enables a user to point to or otherwise reference a location on the slide.

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The X-Y coordinate information specified in the data structure enables X-Y translation of the specific image tiles and specific pixels within the image tile. When the control program first loads the image, because this image file is so large, only a small number of the available tiles are displayed in the active window on the user's monitor. The user uses his mouse or pointing device to scroll through the active window to view the entire macro image. The X-Y coordinate information selected by the mouse translates into specific image tiles or portions therein. The computer takes the mouse pointer information and retrieves the image data from the series of stored tile images and displays them on the monitor for viewing the by user.

Because of the large amount of CCD pixel information stored, actual CCD pixel information can be recreated in the viewing window. The entire system operates in a loop, where the user inputs a mouse location, the computer translates the mouse location from the screen coordinates (screen pixels) to the X-Y coordinates on the bit map.

Similarly, the user may select the high magnification data images. These are outlined by a dark grid, indicating the areas stored. The user operates the

-23**-**

mouse in the same manner as described above. The control program locates the stored X-Y coordinates and retrieves the selected parts of the image, CCD stored pixel by CCD stored pixel.

As mentioned above, to save storage space, 5 computer 32 can perform a data compression on each of the image tile files. A preferred data compression is JPEG, which is readily transferred and recognized by most Internet browser programs. Also, JPEG allows flexibility in the amount of data to be compressed, from 20 to 80 10 percent. FIG. 8 is file listing such as would be seen under Windows 95 file manager showing the data files included in an alternate data structure, one in which the data files have been compressed or converted to JPEG (.jpg) format for a breast cancer specimen. 15 index.html (shown in Table 3) is the listing which contains the X-Y coordinate information for these data files. This is the information that is read by the dynamic, self-executing program for viewing, reconstructing and manipulating the image tiles into the 20

TABLE 3 -- index.html

25

<HTML>

macro and micro views.

-24-

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PCT/US01/01782

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-26**-**

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-27-

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-29-

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Referring now to the drawings, and especially to FIGS. 9A, 9B and 10, apparatus for synthesizing low magnification and high magnification microscopic images is shown therein and generally identified by reference numeral 10. The system includes a computer 12 which is a dual Pentium Pro personal computer in combination with a Hitachi HV-C20 video camera 14 associated with a Zeiss Axioplan 2 microscope 16. The computer system 12 is able to receive signals from the camera 14 which captures light from the microscope 16 having a microscope slide 18 10 positioned on an LUDL encoded motorized stage 20. encoded motorized stage 20 includes a MAC 2000 stage controller for controlling the stage in response to the computer 12. A microscope slide 18 includes a biological specimen 21 which is to be viewed by the microscope and 15 whose image is to be digitized both at low magnification and at high magnification as selected by a user. The low magnification digitized image is then displayed on a 21 inch Iiyama video display monitor 22 having resolution of 1600 by 1200 to provide display screens of the type shown 20 in FIGS. 1 through 3 including a low magnification image 24, for instance, at 1.25 power, a high magnification image 26, for instance at 40X power and a control window or image 28. The low magnification image may have 25 identified therein a region 30 which is reproduced at high magnification in high magnification screen or window 26 so that a pathologist or other operator of the system can review architectural regions of interest in low magnification image 24 and simultaneously view them in high magnification in the high magnification screen or 30 window 26 to determine whether the cells forming a portion of the architectural feature need be examined further for cancer or the like or not.

-31-

The computer 10 is constructed around a PCI system bus 40 and has a first Pentium Pro microprocessor 42 and a second pentium pro microprocessor 44 connected thereto. The system bus 40 has connected to it a PCI bus 50 and an ISA bus 52. The PCI bus 50 has a SCSI controller 60 connected thereto to send and receive information from a hard disk 62. The hard disk 62 also is coupled in daisy chain SCSI fashion to a high capacity removal disk and to a CD Rom drive 66. The hard disks 62 contains the programs for operating the system for controlling the 10 microscope 16 and for processing the images as well as for doing a quantitative analysis of the selected portions of the histological specimens being viewed on the slide 18. The system bus 40 also has connected to it 15 a random access memory 70 within which portions of the program being executed are stored as well as a read only memory 72 for holding a bootstrap loader as well as portions of the basic input/output operating system. floppy disk controller 74 is coupled to the system bus 40 and has connected to it a floppy disk drive 76 for 20 reading and writing information to a floppy disk as appropriate. A mouse controller 80 is coupled to the system bus and has a mouse 82 which operates as a pointing device for controlling manipulations on the 25 screen 22 and within the windows 24, 26 and 28. A keyboard controller 90 is connected to the system bus and has a keyboard 92 connected thereto. The keyboard 92 may be used to send and receive alpha numeric signals to other portions of the computer. An audio controller 100 30 has a plurality of speakers 102 and a microphone 104 connected thereto for audio input and output and is coupled to the system bus 40. A network interface, such as a network interface card 104, is connected to the

-32-

system bus and can provide signals via a channel 106 to other portions of a network or internet to which the system may be connected. Likewise, signals can be sent out of the system through a modem 110 connected to the ISA bus 52 and may be sent via a channel 112, for instance, to the internet. A printer 116 is connected via a parallel I/O controller 118 to the system bus in order to provide printouts as appropriate of screens and other information as it is generated. A serial I/O controller 122 is connected to the system bus and has 10 connected to it a camera controller 124 which is coupled to CCD sensors 126 in the cameras. The CCD sensors 126 supply pixel or image signals representative of what is found on the slide 18 to an Epix pixci image acquisition 15 controller 130 coupled to the PCI bus 50.

The microscope 16 includes a base 140 having a stage 20 positioned thereon as well as an objective turret 142 having a plurality of objectives 144, 146 and 148 thereon. The objective 144, for instance, may be of 1.25x objective. The objective 146 may be a 20X objective. The objective 148 may be a 40X objective. Signals from the camera sensors and controller are supplied over a bus 128 to the image acquisition system where they are digitized and supplied to the PCI bus for storage in RAM or for backing storage on the hard disk 62.

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When a specimen is on the slide 18 the stage 20 may be manipulated under the control of the computer through a stage controller 160 coupled to the serial I/O controller 122. Likewise, a microscope controller 162 controls aspects of the microscope such as the illumination, the color temperature or spectral output of a lamp 168 and the like. For instance, in normal

operation, when a specimen is placed on the slide, specimen slide 18 is placed on the stage 20 in a step 200, as shown in FIG. 14, the processors 42 or 44 send a command through the system bus to cause the serial I/O controller 122 to signal the microscope controller to change magnification to 1.25X in a step 202. This is done by rotating the objective turret of the Axioplan 2 microscope to select the objective 144. Likewise, the controller sets the color temperature of the lamp 168, sets a pair of neutral density filter wheels 170 and 172 and sets a field diaphragm 174 for the correct illumination. A condenser diaphragm 176 is also controlled and a color filter wheel 180 may also be controlled to apply the appropriate filter color to the CCD censors 126 in the camera. The entire slide is then scanned in a step 204. The images are tiled and melded together into the overall image 24 supplied on the screen 22 to provide the operator in the step 206 with a visually inspectable macro image of relevant regions of the slide of interest.

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In order to provide the magnified image, the mouse may be moved to identify a marker segment or region which, for instance, may be a rectangular region which will cause the microscope to change magnification as at step 208 to 4x, 20x, 40x, etc., by rotating the turnet to bring the appropriate objective lens system into viewing position.

Next the user, in a step 209a, uses the mouse to select the region on the macro image in order to select the micro image to be viewed on the screen 22. In a step 209b a test is made to determine whether the user has commanded continued inspection. If the user has, a test is made in a step 209c to determine if the magnification

-34-

is to be changed by changing the selected objective. In the event the magnification is to be changed control is transferred to the step 208. If the magnification is to remain unchanged control is transferred to the step 209a. In the event inspection is not to continue the region selected is outlined for higher magnification scan in a step 209d. In a step 209e, a command may be received to scan or acquire the higher magnification image for display in screen 26. The image may then be archived for later analysis, displayed or analyzed immediately.

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In order to perform the magnification called for in step 208, the overall illumination and control of the microscope will be controlled so that in a step 210 the objective turret 142 will be rotated to place the higher power objective above the slide 18. In a step 212 voltage to the lamp will be changed to adjust the lamp 168 to provide the proper illumination and color temperature as predetermined for the selected objective. In a step 214, the condenser diaphragm 176 will have its opening selected as appropriate to provide the proper illumination for that objective. In a step 216, the filter turret 180 will select the proper light wavelength filter to be supplied to the camera sensors. For instance, a red, blue or green filter, as appropriate, particularly if the specimen has been stained. In a step 218 the field diaphragm 174 will have its opening changed. In a step 220 the neutral density filter wheel 170 will select a neutral density filter and in a step 222 the neutral density filter wheel 172 will also select a neutral density filter. In a step 224 the X, Y and Z offsets will be used for reconstruction of the recorded image at the magnification and in a step 226 the current

position will be read from encoders in the stage which are accurate to .10 micron.

In order to identify the selected region the mouse is moved to that area of the region in a pointing operation in a step 240 as shown in FIG. 14. The mouse may be moved to draw a box around the region selected. In a step 242 the X and Y screen points are computed for the edges of the regions selected and the computed image or pixel points are translated to stage coordinate points in order to control the stage of the microscope. In a step 244 a list of all of the X fields for positioning the stage for the objective is stored in random access memory and may be backed up on the hard disk. The information from the X offsets for the objective and the stage offsets is used as well as the size of the field to position the slide properly under the objective to capture the micro image.

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When the slide has been positioned properly, as shown in FIG. 15 in a step 250 the stage is positioned for each of the X and Y coordinate values in stage coordinate values and the digitized image is captured by the cameras and stored in RAM and backed up on the hard disk. The image may be then analyzed quantitatively in various manners such as those set forth in the previously-identified United States application. Optionally the image may be stored for archival purposes in a step 254.

In order to override the specific control functions that take place as shown in FIG. 12, a screen is provided as shown in FIG. 13 wherein the X-Y step size can be edited, the X, Y and Z offset can be edited, the lamp voltage can be selected, the neutral density filter can be selected as well as the opening of the field

diaphragm and several other microscopic characteristics. FIG. 13 is a view of the settings of the microscope objective properties of the Axioplan 2, computer-controlled microscope.

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The X and Y positioning is specifically carried out as shown in FIG. 16 where the slide 18 is shown with a slide boundary 270, 272, 274 and 276. Stage boundary for limits of the stage travel for purposes of the stage the stage can be moved all the way from an upper left hand corner of travel 276 to a lower right hand corner of travel 280. At the upper left hand bounded corner of travel 278 limits which a signal that the end of travel has been reached and the stage is then translated a short distance 282 in the extra action and a short distance 284 in the Y direction to define the first tile 288 in terms of a reference point 290 at its upper left hand corner. Since the size of the macro image tile 288 is known, the next macro image tile 292 may be placed contiguous with it by moving the stage appropriately and by measuring the location of the stage from the stage in counters without the necessity of performing any image manipulation. image tiles 288 and 292 may be abutted without any substantial overlap or they may be overlapped slightly, such as a one pixel with overlap, which is negligible insofar as blurring of any adjacent edges of abutted image tiles. The upper left hand corner 300 of the tile 292 defines the rest of 292 and other tiles can be so defined. Micro image tiles can likewise be defined so that they are contiguous but not substantially overlapping, as would interfere with the composite image. This avoids the problems encountered with having to perform extended computations on digital images in a frame storer or multiple frame storage in order to match

-37**-**

or bring the images into contiguity without blurriness at the edges of contiguous image tiles. It may be appreciated that the low power image 24 has a plurality of micro images defined therein which are tiled and which are shown in higher magnification as individual tiles 312, 314, 316 and the like. In addition, the region 310 when magnified as shown in the window 26 may exceed the bounds of the window and thus the window may include scroll bars or other means for allowing the image 310 which is larger than the window 26 to be examined from within the window 26.

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The stage 200 is best seen in FIG. 16A and includes the X and Y stepper motors 279 and 281 with their respective encoders, which provide a closed loop system to give the .1 micron accuracy versus the usual 5 or 6 micron accuracy of most microscope stages without a closed loop system. This closed loop system and this very high accuracy allow the abutting of the tile images for both high magnification and low magnification images without the substantial overlap and the time-consuming and expensive software currently used to eliminate the overlap and blurriness at the overlapping edges of adjacent image tiles. With the precisely positioned stage and by using the tiling system described in connection with FIG. 16, where the slide is precisely positioned relative to a center point CP for the slide, and the known position of point 278 is always taken from the same point, the tiles may be positioned precisely in a horizontal row and precisely in vertical rows to reconstruct the macro image and the micro image. This reconstruction is done without the use, as in the prior art, of extensive software manipulation to eliminate

-38-

overlapping image tiles, horizontally or vertically or the haphazard orientation of image tiles.

The present invention also includes the facility for allowing remote observation to occur by being able to couple the system either over a network communication facility to an intranet, for instance via the network interface, or via a modem or other suitable connection, to an internet so that once the image has been scanned and stored in memory on hard disks or other storage, remote users may be able to access the low magnification image as well as the high magnification image and move around within both images to make determinations as to the histological characteristics of the samples.

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An additional feature of the system includes a 15 plurality of networked workstations coupled to a first computer console 12 having a display screen 22 connected to the microscope 14. Satellite work stations 350 and 352 are substantially identical to the work station 12 including respective computers 354 and 356 coupled to displays 358 and 360. The devices can be manipulated through input devices 360 and 362 which may include a keyboard, mouse and the like. Also a third device can be connected including a work station 370, having a display 372, a computer 374 and an input device 376. Each of the devices is connected over respective network lines 380, 382, 384 to the computer 12 which transmission may be via either net or the like. Each of the different operators at the physically separate viewing stations can locate regions from the view of entire tissue cross sections via a macro view and label the regions for subsequent scanning and/or quantitative analysis. A single operator at the instrument station 12 can locate regions to view the entire tissue cross section. Those regions can be

-39-

labeled for subsequent scanning and/or quantitative analysis with subsequent review and physically remote viewing stations, for instance, in an operating room or in individual pathologists' signout areas in order to review analysis results while still maintaining and reviewing the entire macro view of the tissue and/or the individual stored images from which the quantitative results were obtained. The viewing stations 350, 352 and 370 can comprise desk top computers, laptops, etc. There is no need for a microscope at the network stations 350, 352 and 370.

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In a still further alternative embodiment, remote workstations 400, 402, 404, 406 and 408 may be connected through a server 410 which may be supplied via a packet switched network. The server 410 and may be a hypertext transport protocol based server of the type used for the World Wide Web or may be a telnet type server as used previously in internet remote operation applications. The server 410 communicates via a communications channel 414 with a local computer 416 having a display 418 associated therewith, the local computer 416 being connected to the microscope 420. Each of the remote work stations 400, 402, 404, 406 and 408 may perform the same operations as the stations 350, 352 and 370 although they do it from nearby buildings or even from around the world, thus providing additional flexibility for others to make use of the specimen obtained and being viewed under the microscope 420. In addition, stored images may be disseminated through the server 410 to the remote servers 400 through 408 for further analysis and review.

The server was designed to interact with either a thin client browser or with a Java applet viewer,

-4.0-

operating through an HTML browser such as Netscape or the Microsoft Internet Explorer.

The server runs on a standard PC under a Windows operating system. It uses HTTP Internet communication protocols. The computer has stored on its storage media already collected data files having the data structure disclosed above. This data structure consists of "tiled" sets of digital images, with x, y information organized to aid the viewer program to "reconstruct" and spatially align physically-contiguous images, at multiple resolutions. The server responds to HTTP "Get" requests from multiple thin client browsers or other browsers with embedded Java applet viewers. As such, it uses a "listening socket" and a number of short-lived "threads" which handle "Get" requests independently and simultaneously, as shown in FIG. 28.

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After initial logic, as shown in FIG. 29, to determine whether the HTTP request is valid and, if so, whether it is a Java request for a thin client request, the server generates a response thread, depending upon the request as detailed in Table 1, to send back the requested information to the client. Large numbers of these requests can be handled at one time.

The server 12 was designed to interact with a client having either a thin client browser or with a Java applet viewer, operating through an HTML browser such as Netscape Navigator or Microsoft Internet Explorer.

The server 12 runs on a standard PC under a Windows operating system. It uses the HTTP communication protocol. The computer 12 has stored on its storage media already collected data files of with the data structure disclosed in U.S. application no. 09/032,514, filed February 27, 1998, which is incorporated herein by

-41-

reference. This data structure consists of "tiled" sets of digital images, with x, y information organized to aid the viewer program to "reconstruct" and spatially align physically-contiguous images, at multiple resolutions.

The server responds to HTTP "GET" requests from multiple thin client browsers or other browsers with embedded Java applet viewers. As such, it uses a "listening socket" and a number of short-lived "threads" which handle "GET" requests independently and simultaneously, as shown in 10 FIG. 19.

> After initial logic, as shown in FIG. 20, to determine whether the HTTP request is valid and, if so, whether it is a Java request or a thin client request, the server generates a response thread, depending upon the request as detailed in Table 4, to send back the requested information to the client. Large numbers of these requests can be handled at one time.

Table 4. Client - Server "GET" Interactions

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Client Requests	Server Responses		
Login Request > User Name Nickname E-mail address	< Acknowledges Assigns and sends ID# to Client		
Slide Tray Request >	 Sends Slide Tray Information List of image names and URL path locations on the server, extracted folder names and header text 		

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-42-

Client Requests		Server Responses		
Update Request User Name Nickname E-mail address Tray index Slide Name Slide View Window Information Zoom Level	>	<	Sends same information to requesting Clien for all of Clients currently logged in, i.e., Us Name, Nickname, etc.	
x, y position Field View Window Information Zoom Level x, y position Action Status				
Pointer Location x, y Chat Buffer Index				
Chat Line Request	>	<	Sends Chat Line message string	
Select Slide Request Modified URL Path of Selected Slide	>	<	Sends x, y coordinate list for all tiles associated with clients selected URL and the Preview Slide image.	
lmage Request	>	<	Send specified image, e.g., an image tile or thumbnail image	
Logoff Request	>	<	Acknowledge Release User ID#	
Java Applet Request	>	<	Send Java Applet	
Java Login and Virtual Slide Request Slide Name Verify Server Identity	>	<	Send thumbnail and Preview Images and x, list of title images	
Java Image Tile Request	>	<	Send requested image tile	

In addition to the tiled image data, and the x, y coordinate lists for each tile of the image data, as set forth in Table 5 below there are several small reconstructed images that are stored in the individual folder, or on the server. These facilitate bringing image content to the client viewing screen rapidly, and can be used as an aid in determining what viewing options to choose in the various viewing programs.

-43-

Τ	a	b	1	е	5	

	DA0	JPG	57,996	Da0.jpg
	Da1	JPG	75,646	Dal.jpg
5	Da10	JPG	75,874	Da10.jpg
	Da100	JPG	61,564	Dal00.jpg
	Da101	JPG	65,982	Dal01.jpg
	Da102	JPG	76,912	Dal02.jpg
	Da103	JPG	75,729	Dal03.jpg
10	Da104	JPG	70,727	Da104.jpg
	Da105	JPG	68,184	Da105.jpg
	Da106	JPG	73,355	Da106.jpg
	Da107	JPG	21,296	Dal07.jpg
	Da108	JPG	29,384	Dal08.jpg
15	Da109	JPG	28,163	Da109.jpg
	Dall	JPG	79,808	Dall.jpg
	Da110	JPG ·	76,373	Dall0.jpg
	Da111	JPG	35,540	Dalll.jpg
	Da112	JPG	21,293	Dall2.jpg
20	Da113	JPG	34,366	Dall3.jpg
	Da114	JPG	76,120	Dall4.jpg
	Da115	JPG	70,933	Dall5.jpg
	Da116	JPG	47,658	Dall6.jpg
	Da117	JPG	77,465	Dall7.jpg
25	Da118	JPG	79,024	Dall8.jpg
	Da119	JPG	78,256	Dall9.jpg
	Da12	JPG	72,381	Dal2.jpg
	Da120	JPG	76,733	Dal20.jpg
	Da121	JPG ′	79,086	Da121.jpg
30	Da122	JPG	79,003	Dal22.jpg
	Da123	JPG	71,881	Da123.jpg
	Da124	JPG	75,408	Da124.jpg
	Da125	JPG	74,486	Dal25.jpg
	Da126	JPG	80,568	Dal26.jpg
35	Da127	JPG	79,061	Dal27.jpg
	Da128	JPG	79,495	Dal28.jpg
	Da129	. JPG	70,019	Da129.jpg
	Da13	JPG	73,489	Da13.jpg
	Da14	JPG	76,530	Da14.jpg
40	Da15	JPG	76,353	Da15.jpg
	Da16	JPG	29,611	Dal6.jpg
	Da17	JPG	72,668	Dal7.jpg
	Da18	JPG	66,130	Da18.jpg
	Da19	JPG	83,813	Da19.jpg
45	Da2	JPG	76,115	Da2.jpg

-44-

	Da20	JPG	69,762	Da20.jpg
-	Da21	JPG	79,036	Da21.jpg
	Da22	JPG	80,779	Da22.jpg
	Da23	JPG	38,576	Da23.jpg
5	Da24	JPG	65,975	Da24.jpg
	Da25	JPG	73,812	Da25.jpg
	Da26	JPG	80,660	Da26.jpg
	Da27	JPG	72,939	Da27.jpg
	Da28	JPG	88,332	Da28.jpg
10	Da29	JPG	66,672	Da29.jpg
	Da3	JPG	78,399	Da3.jpg
	Da30	JPG	29,994	Da30.jpg
	Da31	JPG	57,465	Da31.jpg
	Da32	JPG	74,006	Da32.jpg
15	Da33	JPG	78,765	Da33.jpg
	Da34	JPG	54,120	Da34.jpg
	Da35	JPG	82,550	Da35.jpg
	Da36	JPG	63,735	Da36.jpg
	Da37	JPG	41,253	Da37.jpg
20 .	Da38	JPG	69,759	Da38.jpg
	Da39	JPG	49,376	-Da39.jpg
	Da4	JPG	77,922	Da4.jpg
	Da40	JPG	52,514	Da40.jpg
	Da41	JPG	68,291	Da41.jpg
25	Da42	JPG	69,726	Da42.jpg
	Da43	JPG	79,840	Da43.jpg
	Da 44	JPG	80,526	Da44.jpg
	Da 45	JPG	84,245	Da45.jpg
	Da46	JPG	50,315	Da46.jpg
30	Da47	JPG	73,069	Da47.jpg
	Da48	JPG	73,188	Da48.jpg
	Da49	JPG	69,155	Da49.jpg
	Da5	JPG	69,257	Da5.jpg
	Da50	JPG	69,087	Da50.jpg
35	Da51	JPG	74,156	Da51.jpg
	Da52	JPG	82,847	Da52.jpg
	Da53	JPG	74,838	Da53.jpg
	Da54	JPG	69,003	Da54.jpg
	Da55	JPĠ	73,524	Da55.jpg
40	Da56	JPG	65,242	Da56.jpg
	Da57	JPG	67,796	Da57.jpg
	Da58	JPG	70,367	Da58.jpg
	Da59	JPG	39,998	Da59.jpg
	Dаб	JPG	68,210	Da6.jpg
45	Da60	JPG	14,487	Da60.jpg
	Da61	JPG	76,801	Da61.jpg

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	Da 62	JPG	74,394	Da62.jpg
	Da 63	JPG	69,446	Da63.jpg
	Da63	JPG .	63,296	Da64.jpg
	Da 65	JPG	17,568	Da65.jpg
5	Da 66	JPG	71,935	Da66.jpg
J	Da 67	JPG	71,736	Da67.jpg
	Da 68	JPG	67,406	Da68.jpg
	Da 69	JPG	74,488	Da69.jpg
	Da7	JPG	69,660	Da7.jpg
10	Da70	JPG	45,382	Da70.jpg
	Da71	JPG	69,849	Da71.jpg
	Da72	JPG	12,009	Da72.jpg
	Da73	JPG	62,862	Da73.jpg
	Da74	JPG	68,522	Da74.jpg
15	Da75	JPG	67,734	Da75.jpg
	Da76	JPĢ	60,510	Da76.jpg
	Da77	JPG	28,689	Da77.jpg
	Da78	JPG	.68,839	Da78.jpg
	Da79	JPG	67,137	Da79.jpg
20	Da8	JPG	71,914	Da8.jpg
	Da80	JPG	65,232	Da80.jpg
	Da81	JPG	78,365	Da81.jpg
	Da82	JPG	63,535	Da82.jpg
	Da83	JPG	74,889	Da83.jpg
25	Da84	JPG	71,895	Da84.jpg
	Da85	JPG	65,744	Da85.jpg
	Da86	JPG	76,849	Da86.jpg
	Da87	JPG	74,373	Da87.jpg
	Da88	JPG	73,449	Da88.jpg
30	Da89	JPG	69,255	Da89.jpg
	Da9	JPG	74,054	Da9.jpg
	Da90	JPG	65,637	Da90.jpg
	Da91	JPG	62,566	Da91.jpg
	Da 92	JPG	75,703	Da92.jpg
35	Da93	JPG	70,315	Da93.jpg
	Da94	JPG	63,884	Da94.jpg
	Da95	JPG	62,949	Da95.jpg
	Da96	JPG	69,046	Da96.jpg
4.0	Da 97	JPG	77,595	Da97.jpg
40	Da 98	JPG	71,528	Da98.jpg
	Da99	JPG	58,862	Da99.jpg

Each image has a PreviewSlide.jpg image contained in its data structure. This is a "thumbnail" image

-46-

reconstructed from all of the tiles from the low magnification, 1.25x slide view image tiles. The reconstructed composite image has been digitally reduced to an image size of 454 x 240. During server startup, for each data structure found as described below, this Preview Slide image is further converted to an additional thumbnail image of 232 x 120. The use of the Preview Slide and thumbnail images will be described below. Also, if specific HTML Java applet views have been chosen, four reconstructed .jpg images from each view, corresponding to four different magnifications have also been stored on the server, as described in detail below under the Java applet creator description and image viewer descriptions.

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FIGS. 21A, 21B and 22 illustrate two different virtual microscope slide viewing implementations. suit two different needs. The thin client browser has three screens and many more functions. As described in more detail below, there is a main screen that displays the thumbnail Preview Slide image, and uses a tabbed interface to implement different functionalities to the browser. Some of these important functionalities are: (1) a SlideTray tab, which allows for the selection of any of the stored images hosted on the server computer; (2) a server tab, which allows coordination of views and chats with multiple other clients all logged-in at the same time; and (3) an Applet Creation tab to select specific region views for HTML applets viewed by the Java Applet viewer. The other two windows, Slide View and Field View, allow viewing of low-magnification tiled images and high-magnification tiled images with scrolling and coordination between the two views.

-47-

The thin client browser is more suited to secondary opinion expert pathology consultations, and sophisticated professional pathology users in departmental pathology practice, for review of cases and as archival backup virtual slide records. In operation, the browser program is loaded separately, once on a client computer. After that it can be used to access any number of servers, as described below, by simply typing in the Internet address of the server. It is faster than the JAVA applets because it comprises code which is already compiled, and is not based upon interpreted applet execution. It is unnecessary to load the thin client browser for every virtual microscope slide viewed. During creation of the image, only smaller regions of specific diagnostic material need be scanned at high magnification, thus saving time during the scanning process.

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The HTML applet viewer is simpler than the thin client browser, and may be used in medical student, dental student, veterinary and undergraduate biology teaching situations. Advantage is taken of the fact that most students are familiar with an HTML browser.

Instructors can easily add course "content" text to provide different descriptions of the virtual microscope slide images. Since the virtual microscope slides will often be used for longer periods, and since there is no premium on speed of scanning, entire specimens can be scanned offline at high magnification which takes a longer time. In this viewer simply acts as a "portal," or a small window, in a fixed position on a specific HTML page.

As described below, each applet instance relates to a specific image on a specific server computer. There

-48-

are two parts to the view, the upper part of the portal is a display of the Preview Slide image. The bottom part of the portal initially shows a selected view from that image at one of four magnifications. A plurality of radio button choices loaded on a bar between the views allows for additional magnification choices in the bottom view. The bottom view is also scrollable, and can be changed by pointing the mouse to a region on the Preview Slide image.

It will be appreciated that this viewer is simpler to learn initially and to operate than the thin client browser. It has the disadvantage of being slower and of only addressing one image at a time. It has an advantage of being simple, having various types of explanatory text right next to the image, and of being cross platform with regard to operating system, computer type and HTML browser type. These are all helpful in the educational market.

The Slide Tray concept is used in the server and the browser programs and is central to providing an organizational construct to collections of images. It is set forth in Table 6 below.

Table 6.

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	FINALS~1	INI	3,902	FinalScan.ini
	PREVIE~1	JPG	6,210	PreviewSlide.jpg
	SLIDES~1	INI	654	SlideScan.ini
	SS1	JPG	10,285	SS1.jpg
30	ss10	JPG	63,150	ss10.jpg
	SS11	JPG	70,838	SS11.jpg
	SS12	JPG	15,535	SS12.jpg
	SS13	JPG	12,071	SS13.jpg
	SS14	JPG	73,847	SS14.jpg
35	SS15	JPG	70,783	SS15.jpg
	SS16	JPG	25,178	SS16.jpg

-49-2,983 SS17.jpg SS17 JPG SS18 9,035 SS18.jpg JPG SS19 JPG 15,629 SS19.jpg SS2 JPG 25,194 SS2.jpg 5 4,200 SS20.jpg SS20 JPG SS3 JPG 9,936 SS3.jpg SS4 JPG 10,118 SS4.jpg SS5 4,559 SS5.jpg JPG SS6 JPG . 35,961 SS6.jpg 10 SS7 JPG 86,933 SS7.jpg SS8 JPG 16,212 SS8.jpg SS9 JPG 33,872 Ss9.jpg [Header] 15 tPatientID=Prostate tAccession= tOperatorID= tTimeOfScan=9/17/98 4:56:31 PM 1XStageRef=278000 20 1YStageRef=142500 iImageWidth=752 iImageHeight=480 1XStepSize=1588 1YStepSize=1184 25 1XOffset=0 1YOffset=0. dMagnification=40 tImageType=.jpg iFinalImageQuality=60 30 1AnalysisImageCount=130 1CalibrationImageCount=0 iiTotalBytes=9221691 tFolder=Test WSTP [Da0] 35 x=164208y = 45264[Dal] x=162672y = 4526440 [Da2] x=161136y = 45264[Da3] x=159600 45 y = 45264[Da4]

x=158064

-50-

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[Da5]
        x=156528
        y = 45264
 5
        [Da6]
        x=154992
        y = 45264
        [Da7]
        x=164208
10
        y=44080
        [Da8]
        x=162672
        y = 44080
        [Da9]
15
        x=161136
        y = 44080
        [Dal0]
        x=159600
        y=44080
20
        [Dall]
        x=158064
        y = 44080
        [Dal2]
        x=156528
25
        y = 44080
        [Dal3]
        x=154992
        y = 44080
        [Da14]
30
        x=164208
        y=42896
        [Da15]
        x=162672
        y=42896
35
        [Da16]
        x=161136
        y=42896
        [Da17]
        x=159600
40
        y = 42896
        [Dal8]
        x=158064
        y=42896
        [Da19]
45
       x=156528
       y=42896
```

y=45264

-51-

```
[Da20]
        x=154992
        y=42896
        [Da21]
 5
        x=164208.
        y = 41712
        [Da22]
        x=162672
        y = 41712
10
        [Da23]
        x=161136
        y=41712
        [Da24]
        x=159600
15
        y=41712
        [Da25]
        x=158064
        y=41712
        [Da26]
20
        x=156528
        y=41712
        [Da27]
        x=154992
        y = 41712
25
        [Da28]
        x=164208
        y = 40528
        [Da29]
        x=162672
30
       y = 40528
        [Da30]
       x=161136
       y = 40528
        [Da31]
35
       x=159600
       y=40528
        [Da32]
       x=158064
       y=40528
40
       [Da33]
       x=156528
       y = 40528
       [Da34]
       x=154992
45
       y = 40528
       [Da35]
```

-52-

```
x=164208
       y=39344
       [Da36]
       x=162672
       y=39344
       [Da37]
       x=161136
       y=39344
       [Da38]
       x=159600
10
       y=39344
       [Da39]
       x = 158064
       y=39344
15
       [Da40]
       x=156528
       y = 39344
       [Da41]
       x=154992
20
       y=39344
       [Da42]
       x=164208
       y=38160
       [Da43]
25
       x=162672
       y=38160
       [Da44]
       x=161136
       y=38160
30
       [Da45]
       x=159600
       y=38160
       [Da46]
       x=158064
35
       y=38160
       [Da47]
       x=156528
       y = 38160
       [Da48]
40
       x=154992
       y=38160
       [Da49]
       x=164208
       y=36976
45
       [Da50]
       x=162672
```

-53-

```
y=36976
       [Da51]
       x=161136
       y=36976
 5
       [Da52]
       x=159600
       y=36976
       [Da53]
       x=158064
10
       y=36976
       [Da54]
       x=156528
       y=36976
       [Da55]
15
       x=154992
       y=36976
       [Da56]
       x=130160
       y=48076
20
       [Da57]
       x=128624
       y=48076
       [Da58]
       x=127088
25
       y=48076
       [Da59]
       x=125552
       y = 48076
       [Da60]
       x=124016
30
       y=48076
       [Da61]
       x=130160
       y=46892
35
       [Da62]
       x=128624
       y = 46892
        [Da63]
       x=127088
40
       y=46892
        [Da64]
       x=125552
       y = 46892
       [Da65]
45
       x=124016
       y = 46892
```

-54-

```
[Da66]
        x=130160
        y=45708
        [Da67]
 5
        x=128624
        y = 45708
        [Da68]
        x=127088
        y = 45708
10
        [Da69]
        x=125552
        y = 45708
        [Da70]
        x=124016
15
        y=45708
        [Da71]
        x=130160
        y = 44524
        [Da72]
20
        x=128624
        y=44524
        [Da73]
        x=127088
        y = 44524
25
        [Da74]
        x=125552
        y = 44524
        [Da75]
        x=124016
30
        y = 44524
        [Da76]
        x=130160
        y = 43340
        [Da77]
35
        x=128624
        y = 43340
        [Da78]
        x=127088
        y = 43340
40
        [Da79]
        x=125552
       y = 43340
        [Da80]
        x=124016
45
        y = 43340
      [Da81]
```

-55-

```
x=130160
       y = 42156
       .[Da82]
       x=128624
 5
       y=42156
       [Da83]
       x=127088
       y=42156
       [Da84]
10
       x=125552
       y=42156
       [Da85]
       x=124016
       y=42156
15
       [Da86]
       x=130160
       y = 40972
       [Da87]
       x=128624
20
       y = 40972
       [Da88]
       x=127088
       y = 40972
       [Da89]
25
       x=125552
       y = 40972
       [Da90]
       x=124016
       y = 40972
30
       [Da91]
       x=130160
       y=39788
       [Da92]
       x=128624
35
       y=39788
       [Da93]
       x=127088
       y=39788
       [Da94]
40
       x=125552
       y=39788
       [Da95]
       x=124016
       y=39788
45
       [Da96]
       x=130160
```

-56-

```
y = 38604
       [Da97]
       x=128624
       y=38604
 5
       [Da98]
       x=127088
       y=38604
       [Da99]
       x=125552
10
       y=38604
       [Da100]
       x=124016
       y=38604
       [Dal01]
15
       x=130160
       y=37420
       [Da102]
       x=128624
       y=37420
       [Da103]
20.
       x=127088
       y=37420
       [Dal04]
       x=125552
.25
       y = 37420
       [Dal05]
       x=124016
       y = 37420
        [Da106]
       x=148848
30
       y=24988
       [[Da107]
       x=147312
       y=24988
35
        [Da108]
       x=145776
       y = 24988
        [Dal09]
       x=144240
40
       y=24988
        [Dal10]
       x=148848
       y=23804
        [Dall1]
45
       x=147312
```

y = 23804

-57-

```
[Dal12]
       x=145776
       y=23804
       [Dall3]
 5
       x=144240
       y = 23804
       [Dall4]
       x=148848
       y = 22620
10
       [Dal15]
       x=147312
       y=22620
       [Dal16]
       x=145776
15
       y=22620
       [Dal17]
       x=144240
       y=22620
       [Dal18]
20
       x=148848
       y=21436
       [Dall9]
       x=147312
       y=21436
25
       [Da120]
       x=145776
       y=21436
       [Dal21]
       x=144240
30
       y=21436
       [Da122]
       x = 148848
       y=20252
       [Da123]
35
       x=147312
       y=20252
       [Dal24]
       x=145776
       y=20252
40
       [Da125]
       x=144240
       y=20252
       [Dal26]
       x=148848
45
       y=19068
       [Da127]
```

-58-

x=147312 y=19068 [Da128] x=145776 y=19068 [Da129] x=144240

y = 19068

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It provides a flexible filing structure, whether the images are located in multiple places on a computer running a server program, or are collections held on removable storage media such as CD-ROMs and are just being viewed locally. The image data structure includes two modifiable text string byte arrays which are used to hold the file name and the folder name that identifies an individual image. When the server program is initiated, it searches all of its available storage (indicated in a setup file), finds any images present, reads the folder names and the file names of all of the images and creates URL path extensions for each one.

When the image browser initially starts its Main Window looks like FIG. 24. This is before a Login request has been initiated. The browser first sends a client Login Request using a specific server Internet address, such as shown in the address line of FIG. 20, and as indicated in Table 4. After the Login Request has been acknowledged, the browser then sends a Slide Tray Request. The server response to this is to send the list of image names and header text, their associated file folders, and the URL path extensions depending upon various image data structure storage locations on the server. The browser then constructs and displays in the Slide Tray tab of its main window a file folder tree structure display such as shown in FIG. 25. This is a

-59-

dynamic display, such that a mouse click on the file folder opens up the file and displays its contained images. The browser responses are set forth in Tale 7 below.

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TABLE 7.

```
tResponse := tResponse + IntToStr0j0 + '&';
          tResponse := tResponse + FrmMain.Client[j].tUserName + '&';
          tResponse := tResponse + FrmMain.Client[j].tNickName + '&';
10
          tResponse := tResponse + FrmMain.Client[j].tEmail + '&';
          tResponse := tResponse + FrmMain.Client[j].tTrayIndex + '&';
          tResponse := tResponse + FrmMain.Client[j].tSlide + '&';
          tResponse := tResponse + FrmMain.Client[j].tSlideZoomLevel + '&';
          tResponse := tResponse + FrmMain.Client[j].tSlideXRef + '&';
15
          tResponse := tResponse + FrmMain.Client[j].tSlideYRef + '&';
          tResponse := tResponse + FrmMain.Client[j].tFinalZoomLevel + '&';
          tResponse := tResponse + FrmMain.Client[j].tXRef + '&';
          tResponse := tResponse + FrmMain.Client[j].tYRef + '&';
          tResponse := tResponse + FrmMain.Client[j].tSlideScanMode + '&';
20
          tResponse := tResponse + FrmMain.Client[j].tPointerX + '&';
          tResponse := tResponse + FrmMain.Client[j].tPointerY + '&';
          if FrmMain.bLogoffClients then
            tResponse := tResponse + 'Server logoff issued...&'
25
          else
            tResponse := tResponse + FrmMain.Client[j].tStatus + '&';
          Inc(iCount);
        end;
      end:
```

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A mouse click on a specific image file name activates a client Image Request to the server, and the server sends back the requested thumbnail image which is displayed in the tab image area, as shown in FIG. 25. If one of the virtual microscope images is of further interest for more detailed observation, it can be retrieved by further mouse clicks, either on the thumbnail image or by a double click on the Slide Tray tree structure file name. In this case, the client browser sends a Select Slide Request. As indicated in Table 1, the server then sends the larger Preview Slide image along with the x, y coordinate list of all image tiles associated with that virtual slide. The tab

-60-

changes from the Slide Tray to the image tab and the Preview Slide image is displayed in the image display area, as shown in FIG. 26.

One of the advantages of this virtual slide tray organizational design is that the folder names are carried as part of the image data set structure. This is different from a standard file structure where the file name is created and files are moved into the created folder. In a virtual microscope slide environment, collections of slides may come from different sources, e.g., on CD-ROMs or other storage media. This method carries the file folder information with the slide. server can then automatically organize, on startup, all of the file folders depending upon the media in place at that time. For read/write media, the folder names can be edited to put specific images into different folders. This method also allows for automatic folder generation during the image creation process, which reduces the possibility of mixup for collections of slides that go together.

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As described above, the image data set is created initially by scanning the microscope slide at two different magnifications. The initial scan, which is referred to as the Slide View scan, is performed with a 1.25x objective lens and can potentially use as many as 8 x 10, or 80 tiles, to cover the region of tissue or cells deposited on the slide. The second, higher-magnification scan is referred to as the Field View scan, and can occupy variable regions. These regions are mapped to the Slide View regions, and can be shown as overlaid areas.

As shown in FIG. 22, there are a number of overlays in the image tab of the main image browser window that can be used as aids in navigating the images.

Two of these are shown there. They indicate potential regions that could have been scanned and those that were actually scanned on the specimen. Clicking on one of these regions, using the mouse as a pointer, instructs the browser to bring up the Slide Scan window, as shown in FIG. 27. Depending upon the size of the Slide View window and the location point specified in the Preview Slide image, the browser program can use the x, y image list and associated URL information that was transferred in response to the Select Slide Request to determine which Slide View scan image tiles are necessary. The browser then issues an Image Request for each image tile and paints in the received tiles to fill in the image display area in the window.

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There are optional navigation overlays for this window also. The illustrated overlay shows regions where higher-magnification image tiles exist in the image data structure. By clicking in the region of one of these tiles, the browser is instructed to bring up its third window, the Field View window, shown overlain on top of the other two windows in FIG. 28. It uses the same procedure, e.g., the size of the Field View window to determine which high-magnification image tiles to request. The size of the Field View and Slide View windows can be changed to suit the user, for example, to fill the available viewing screen, and the browser program will request and fill in the necessary tiles to fill the viewing area.

A number of other viewing options are available, including changing the digital image magnification, i.e., lowering from 40x to 5x. In this case, more tiles are requested to fill in the available viewing area. The combination of the ability to change the various windows

position and size, and the digital magnification (zoom) allows for full inspection of the virtual microscope specimen at high and low magnifications throughout the entire specimen. As additional image tiles are requested, they are cached locally so that additional inspection becomes quicker.

FIG. 29 is a flow chart of typical usage to further illustrate the above. This flow chart is shown as a sequence of related steps since some should occur before others and this is a typical sequence. However, it should be appreciated that the browser is multithreaded as well as event driven. Most of the time, for example, the Update Request process is running on its own thread concurrently with client user event-driven processes, a shown in FIG. 29.

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Referring back to FIGS. 18 and 19, Table 4 and the server description, it is clear that multiple clients can be logged-in at one time. All such clients independently view the same or different images. The design of the total combined system or all components is more powerful than that, however, through the use of the Update Request indicated in Table 1. Update Requests are generated by each user logged in the client browser at one-second intervals. Through the use of these Update Requests, the server is essentially functioning as a total system "state machine" for all of the logged-in users. each user is assigned an ID number upon login, the server can pass information regarding all of the other logged-in users, with regard to which slide they are viewing, where on that slide they are looking, the status of any pointer locations, etc. This all happens at one-second intervals for all logged-in clients. The browser then can use this information if desired to view the same images seen by

other clients. This essentially means that the network of client viewers operates as a virtual multi-headed microscope, letting each other simultaneously view the same virtual slide.

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Additional features of the browser, as shown in FIG. 30, enhance this capability. The server tab in the main browser window, shown in FIG. 30, is used to activate a multi-headed virtual microscope function. A browser logged onto a server initially displays only the current user's information in the server tab. As Update Requests are serviced, if additional clients log onto the same server that information is also displayed in the Server tab, using additional login lines.

FIG. 30 shows two users logged into the same server. Also shown are buttons "Display another's view" and "Sync with another's view." After point and click highlighting of one of the logged-in user lines, the current user can then, for example, click on the button "Display another's view" and the browser will use the last update information on that user to send a Select Slide Request, and whatever Image Tile requests are necessary to display the same image view that the user is looking at. In a similar manner, if the user clicked on "Sync with another's view," then the browser would continue to use the update requests to change fields, zoom levels, etc. In the meantime, the various clients involved could communicate through the chat screen about the specimen under consideration.

As shown in FIG. 28, a pointer may be drawn at any x, y location on an image screen view. A right click mouse event on an image where the pointer is desired activates program code which creates a pop-up menu, as shown in FIG. 31. When the "Set the Pointer" menu option

is chosen, the position of the pointer is computed in x, y stage coordinate units and those position values are put in the main window Pointer tab and kept in memory to pass along to the server on the next update. Also, a pointer is placed on the image, as shown in FIG. 32. when another client, logged on at the same time, activates "Display another's view" (as shown in FIG. 30) for the client displaying the pointer, then that second client's browser would use the Update Request transferred x, y pointer position from the first client to put a pointer on the second client's image, after any Image Requests to the server were satisfied. In this way, two clients can pass arrows back and forth.

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This is additionally facilitated by the right click mouse menu that each can use when she has the same image in front of her. Usually, this occurs when both parties are on the telephone, using the Internet and talking to each other while they move pointers back and forth, or synchronize on each other's views as desired.

They can also communicate through the Chat process using the Server tab, as shown in FIG. 28, or through email through the Server tab. It should be appreciated that more than two clients may be logged on and participate in this process. This provides a multineaded virtual microscope environment with pointers for multiple client users simultaneously.

One of the most important technological improvements in the "tiling" methodology is the improved resolution of image capture and display compared to previous methods of capturing images and transferring them over the Internet. The reason for this relates to microscopy optical resolution compared to digital camera sensor resolution, and the limited "field of view"

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imposed by the aperture sizes of the microscopy system. In order to match the optical resolution to the digital sensor resolution at high magnification with readilyavailable sensors, only a small part of the specimen can be captured at one time. Attempting to capture a larger view, e.g., with a lower magnification (and as a result lower optical resolution) objective microscope lens onto digital camera sensor, and then digitally magnifying the resulting captured image, results in "pixelated," "false" magnification. Tiled images can be captured at a matching pixel and optical resolution, and displayed seamlessly by the present invention, to achieve true virtual images. The same method automatically overcomes the limited "field of view" issue to preserve high resolution over large areas in the original highmagnification image plane of the microscope specimen.

The method of retrieving and displaying these tiles as a coherent connected image is depicted in the flow diagram of FIG. 33. This flow diagram is relevant for choosing by a point and click, an image point in the Preview Slide image of the main browser window to open and display the Slide View window (or to choose another region to display in an already open Slide View window), or to open and display at a higher magnification the Field View window from a point in the Slide View window, or to display image areas not already pre-loaded in the Java applet portal window in an HTML browser page. important factor in accomplishing seamless tiled image display according to the methods of this invention is to maintain an image x, y pixel reference to the original mechanical stage x, y coordinate reference. In the preferred embodiment, the x, y stage resolution is .1 micrometers per step. Each image tile is a known number

-66-

of pixels, in this instance 752 x 480 pixels. Through calibration setup procedures during instrument construction, the number of stage coordinate steps per pixel is determined. This varies slightly from system to system and is different for each microscope objective. It is therefore recorded as part of each image data set. Table 8 shows some typical examples of one system.

<u>Table 8</u>. Example Stage x, y Coordinates per Image Tile Pixel

Objectives	.1 Micrometer Stage Steps Per Pixel	Pixel Spatial Resolution In Micrometers
1.25x	69	6.9
10x	9	.9
20x	5	.5
40x	2	.2

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Using the values from Table 8, if a Slide View image data set consisted of a full component of 8 x 10 image tiles, then there would be 7,520 pixels along the x direction and 3,840 pixels in the y direction. This would result in an x, y coordinate system for this slide of 518,880 x coordinate values and 264,960 y coordinate values. This, in effect, creates a virtual coordinate reference system for each tiled image data set. As each tile is collected, the initial upper left starting pixel location in stage coordinate values is stored in a separate subfile list as part of the image data structure file, along with, of course, that .jpg tile image. are associated with each other by the name of the image tile being used as the name in the list associated with the x, y coordinates. In this way, each data structure has contained in it a list of x, y coordinate positions.

The x, y coordinate position list is transferred to a specific client in response to the client issuing a Select Slide Request.

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Referring again to FIG. 33, the initial step is to translate the starting display image size in pixels into the virtual stage coordinates. For example, if the image is the 452 x 240 Preview Slide image then each x pixel increments by 1,148 x virtual stage coordinates and each y pixel increments by 1,104 virtual stage coordinates. A given mouse click resulting in an x, y pixel location can then be easily translated into a known virtual image x, y location. Next, the new display image window, in this case the Slide View image, is opened, and some of the possible 8 x 10 1.25x image tiles may be displayed. This window will either have a present initial size or will have been set by a previous call. In either case the size of the window in pixels can be determined from the associated windows properties parameters, accessible to the program. The size and placement of this window can then be calculated in the virtual coordinate space. program assumes that the pixel point chosen in the previous window is associated with the center of the new window to do this.

Next, the image stage coordinate list is searched. The image stage coordinate list was previously transferred to find all candidate tiles which should be displayed according to size of the window.

As shown in FIG. 33, the tiles can be two types; they may already have been viewed and are there, and are therefore cached and available locally, or they exist on the server. If they are on the server, a Send Image Request is initiated and the server sends back the requested tile. Otherwise, they are read from the cache.

It should be appreciated again in the case of the program's execution, shown in the flow chart of FIG. 33, that the program is event driven and multi-threaded. The final operation is to fill in the display window with the chosen tile. This same, or an analogous method of filling in tiles for display images is used in scrolling, zooming in and out, and in retrieving tiles for the Field View window (coming from the Slide View window), and in retrieving image tiles from the server for the fixed size Java applet viewer.

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Even though in many instances these five images would be sufficient, the additional approach of this invention is to make available to the applet, the entire virtual slide. This is accomplished using the techniques 15 already described for the browser. In this instance, the upper panel Preview Slide Image can be used by a mouse point and click, to locate an x, y position. This is translated into x, y virtual stage coordinates, and the needed tiles are requested through an Image Request to the server. If the magnification choices are used the operation of this application is handled by the same methods of zoom and calling for images as in the browser, all relating to the size of the window and which image tiles are needed from what virtual x, y location to fill in the window. In a similar way, the lower portion of the portal window is also enabled for scrolling. So the virtual slide advantage of scrolling and zooming in and out are available but in a limited size window. They are accessible, however, from an HTML document that has embedded content.

An additional feature of this approach, as shown by comparing FIGS. 21A, 21B and 22, is that the controlling HTML web-page code may be calling the content

-69-

for the page from a computer other than the image computer. The advantage of this is that it decouples the text content from the image collections. In a teaching environment this enables many different users to create their own course content, using standard HTML methods, and simply provides a call to the server at appropriate places in the HTML code.

As indicated in FIGS. 18 and 19, and as discussed previously, the server also interacts with a second type of viewer, an HTML embedded applet, in this case written in the Java programming language, as set forth in Table 9 below.

TABLE 9.

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```
15
                     <APPLET CODEBASE="http://209.100.40.94/" CODE="WebSlide"</pre>
      ALIGN="m
      iddle" HEIGHT="590" NAME="Histology06a" WIDTH="464" ALT="WebSlide">
                      <PARAM NAME="lslidexrefpos" VALUE="82458">
                      <PARAM NAME="webslideurl"
20
      VALUE="http://209.100.40.94/WebSlides/
      Histology06a/">
                      <PARAM NAME="izoomlevel" VALUE="2">
                      <PARAM NAME="lyrefpos" VALUE="23768">
25
                      <PARAM NAME="lxssstepsize" VALUE="48062">
                      <PARAM NAME="lxrefpos" VALUE="92237">
                      <PARAM NAME="instance" VALUE="Histology06a">
                      <PARAM NAME="lyssstepsize" VALUE="35892">
                      <PARAM NAME="1slideyrefpos" VALUE="17177">
                      This browser does not support Java v1.1 applets!
30
                    </APPLET>
```

The interaction of this viewer with the server is also shown in FIG. 22. This viewer is simpler, and used for different purposes than the browser, but uses many of the same techniques of transferring image tiles.

FIG. 34 illustrates the layout and features of the HTMI portal window created by this applet. This viewer consists of two views; a low-magnification view (which is the Preview Slide image discussed above) shown as an upper portion in FIG. 34, and a higher-magnification view shown in the lower

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portion. The two views are separated by a menu bar with four magnification choices. As described below, there is an HTML applet creation process which is another browser tab portion. This enables the creation of both the HTML code to generate a Java applet request and additional pre-configured images for the applet to use when it runs.

In an application of interest for this type of viewer, specific regions are identified in the image which are of . primary interest, and the need is to see this region as quickly as possible and to change between magnifications rapidly. In order to enable this the applet creation process enables the location of a specific view on a given image, i.e., it specifies a center x, y position for the region and specifies a final view window size, of the same size as the lower portion of the portal window, and assembles from the tiled data structure four zoom level views corresponding to the menu bar magnification options. The zoom levels start with the highest Field View magnification level, usually 40x or 20x, and the viewer creates a lower-magnification image of each tile by using every other pixel at each lower zoom magnification. Additional tiles are brought in and assembled from the image data structure as needed to fill in the fixed field size of the lower HTML portal window. These four assembled images are referred to as Preview images, are given specific names in the creation process and are stored in a file accessible to the server program, on the same computer that the related image is located.

The first thing the Java applet does then after it is loaded is to send a Login and Virtual Slide Request as indicated in Table 1. If the slide name and server identity is correct, the server response is to send the Preview Slide image for the upper panel, the four Preview images that will be used for the lower panel, and the x, y list of all image

-71-

tiles in the associated data structure. The HTML applet generation process specified which of the magnification choices would be loaded first. The other are available to the applet through the radio button event generated from the menu bar.

The advantage of this approach, of using the pre-stored Preview Slide and Preview images, is that they are small and can be transmitted relatively rapidly, essentially only five tiles, and are in essence pre-cached, in terms of the relationship to the browser description. One problem with applets is that they are interpreted rather than compiled; hence, they are slower than native machine code such as that used in the browser. Thus, this approach helps to overcome that. In addition, for many purposes, e.g., in an educational setting, these views are all that are needed to achieve the initial purpose. For the presentation of a microscope specimen, especially in anatomic pathology or histology, an overall view of the specimen, such as that shown in the upper portion, and localization of a specific region, with the ability to zoom in and out is sufficient.

The virtual slide link is set forth in Table 10 below.

TABLE 10.

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25 [WebSlide Link] tWebSlideURL=http://209.100.40.94/ iMainTop=0 iMainLeft=0 tScanFilename=Prost-z2 iMainOverlays=1 bGraticles=1 bScanArea=1 bMultiMag=1 bTileLoction=0 35 bSlideView=1 bFieldView=1 iSlideViewTop=0 iSlideViewLeft=600 iSlideViewHeight=478

iSlideViewWidth=1000

-72-

iSlideViewWindowState=1
bDisplayTileLocationOverlay=1
iSlideViewZoomLevel=1
1SlideXRefPos=44397
5 1SlideYRefPos=55668
iFieldViewTop=478
iFieldViewLeft=0
iFieldViewHeight=402
iFieldViewWidth=472
10 iFieldViewWindowState=1
iFieldViewZoomLevel=1
1FieldViewXRefPos=58436
1FieldViewYRefPos=55520
tSlideScanMode=0

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In order to perform the multiheaded microscope function of emulation, a plurality of clients are logged on, which might include a client A and a client B. After having logged on, client B elects to consult with logged on client A and highlights client A's name in logged on list in a step 800, as shown in FIG. 35A. The client B then selects a synchronization and user function by clicking on the sync on user button and a thin client browser enters a synchronization state keyed on signals from client A in a step 802.

During the one-second interval update command for the browser, client B monitors client A's update state variables, as set forth in the listing in Table 6, and uses the variables necessary to display the same location and magnification of the slide data set that client A is currently viewing. A plurality of the state variables include state variable values that indicate whether those variables are disabled, for instance 999999999. Otherwise, the variable state is considered to contain active data and, during the one-second interval update, decisions are made by the state variables by client B, as set forth in step 804. Control is then transferred to a step 806 to determine whether the chat messenger index on the server is greater than the current state variable index. If it is, control is transferred to a step 808 to request each missing chat message from the server

-73-

and displayed in the chat window at the client until the chat message index on the server is equal to the state variable index following which the routine returns in a step 810 to a test in a step 812 to determine whether the state variables have been placed in sync mode. If they have not, control is transferred back to the step 806, as shown in FIG. 35D.

If the system is in sync mode, a test is made in a step 814, as shown in FIG. 35A, to determine whether the virtual slide image selected from the slide tray data collection is the same as the one that is currently displayed. If it is not, the position in the slide tray is updated in a step 816. If it is, control is transferred either from step 814 or 816 to a step 818 where a test is made to determine whether the low-magnification x, y position location state variables are in the disabled state. If they are, control is transferred back to step 814. If they are not, the slide view window is displayed and updated for the low-magnification view to the lower-magnification position previously selected by client A using client A's current magnification state variable in step 820 in order to synchronize the views.

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A test is then made in a step 822 similar to the step 818 to determine whether the high-magnification x, y location state variables are in the disabled state in a step 822. If they are disabled, control is transferred back to step 814. If they are not, control is transferred to a step 824 which displays the field view window on the client and/or updates the high-magnification view to synchronize with client A's x, y high-magnification selected position also using client A's current magnification state variables. The slide scan mode state variable indicates whether what is being displayed is the low-magnification or high-magnification data and each of the data's associated coordinate systems in field of view.

-74-

Control is then transferred to a step 830, as shown in FIG. 35C, where a test is made to determine the mouse pointer or display pointer x, y position state variables in the disabled state or not. If they are not disabled, the pointer is displayed at the location selected by client A and control is transferred to step 814. If the state variables are disabled, control is transferred directly to step 814.

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It should be appreciated that the updating function from the client A variables may take place not just with one client, client B, but over multiple clients in order to provide image coherency from the client, in this example client A, which in effect controls the command token for the virtual multiheaded microscope remote emulation.

While there has been illustrated and described a

particular embodiment of the present invention, it will be
appreciated that numerous changes and modifications will occur
to those skilled in the art, and it is intended in the
appended claims to cover all those changes and modifications
which fall within the true spirit and scope of the present
invention.

-75-

What is claimed is:

1. A method for viewing virtual microscope slides comprised of sets of digitized tiled images over a common communication channel, the method comprising:

providing a transmitting station connected to the common communication channel and accessible by a number of remote receiving stations connected to the common communication channel;

storing a plurality of sets of virtual microscope, digitized slide images at the transmitting station;

transmitting control information to the requesting computer for use in aligning the transmitted sets of digitized tiled images to form a composite, coherent, seamless digitized, virtual microscope, slide image from a set of digitized tiled images;

displaying on a viewer at a remote receiving station a thumbnail view of a specimen or portion thereof on the virtual microscope slide;

displaying on the viewer at the remote receiving station an aligned set of digitized tiled images at a higher resolution than the resolution of the thumbnail view; and

zooming by the viewer back and forth between the thumbnail view and the higher resolution set of digitized tiled images.

2. A method in accordance with claim 1 further comprising:

providing a plurality of digitized tiled images each at a different resolution and each a higher resolution than the thumbnail view; and

zooming back and forth between the plurality of higher resolution images as well as with the thumbnail image.

-76-

3. A method in accordance with claim 2 further comprising operating a magnification selector at the receiving station to change between the plurality of higher resolution images.

4. A method in accordance with claim 3 further comprising:

transmitting from the transmitting station an entire set of digitized slide images of several resolutions from the transmitting station to the receiving station; and

operating the magnification selector at the remote station to select from the stored digitized slide images at the receiving station those images of the selected magnification.

- 5. A method in accordance with claim 1 wherein transmitting a control program comprises downloading a control program as an applet.
- 6. A method in accordance with claim 5 further comprising transmitting a dynamic, self-executing program for viewing, manipulating, and reconstructing image tiles.
- 7. A method of viewing virtual microscope slides in accordance with claim 1 further comprising displaying to the viewer descriptive text about the composite digitized tiled slide image being viewed by the viewer at the remote station.
- 8. A method in accordance with claim 1 further comprising using an HTML browser and a personal computer at the remote viewing station for receiving the control program and set of digitized, slide images.

-77-

9. A method in accordance with claim 1 further comprising changing tiled sets of digital images from a smaller size to a larger size.

10. A method in accordance with claim 7 further comprising:

providing viewing windows of different sizes each for viewing a set of digitized, tiled images; and filling each of the windows of different sizes with

a different number of reconstructed, digitized tiled images.

11. A method in accordance with claim 1 further comprising:

changing the size and position of viewing windows for viewing of sets of digitized tiled images; and

changing the image magnification to allow zooming between high and low magnifications of the sets of digitized tiled images.

12. A method in accordance with claim 1 further comprising:

selecting a region of a displayed image to be viewed at a higher resolution;

determining the size of the window and selecting the image tiles which are needed for filling the window at the requested resolution; and

displaying the selected higher-resolution digitized image tiles and filling the window therewith.

13. A method in accordance with claim 1 further comprising scrolling along the displayed image to remove some image tiles from the window and to add other image tiles to the window for viewing.

14. A method in accordance with claim 1 further comprising transmitting a set of low-magnification, digitized tiled images for reconstruction into the thumbnail view.

15. A method for viewing virtual microscope slide specimen image views at different magnifications using sets of digitized, image tiles comprised of a predetermined number of pixels per tile, comprising:

scanning and digitizing a field of view taken through a microscope;

providing a microscope stage travel having a resolution greater than a resolution of the pixels;

translating the digitized pixel resolution into a stage X, Y coordinate system of a known resolution;

storing a point of reference for each tile as part of a data structure for the slide image view;

assembling a plurality of tiles using the X, Y stage coordinates into a seamless image as a first view at a first magnification on a display device;

selecting a region on the first, tiled image view for viewing at a second higher magnification;

using the selected region as a reference point for image tiles to be used to form a higher magnification second view of the selected region;

opening a display window for the higher magnification second view of a known size and translating the window size into the X, Y stage coordinate system;

using the X, Y stage coordinate system and the reference point to select the tiles to be used for the view; and

using the X, Y stage coordinate system for assembling and displaying on the display device the selected

-79-

tiles to form a seamless image for the second view of the selected region and at the higher magnification.

16. A method in accordance with claim 15 further comprising:

providing a common communication channel; transmitting digitized image tiles from a first station to a remote requesting station at which the views are displayed; and

storing as part of a transmitted data structure at the remote station tiles for use in assembling into the selected view of the selected region and at a higher magnification.

17. A method in accordance with claim 16 further comprising:

searching tiles cached at the data structure to determine whether the desired tiles have already been transmitted and stored; and

requesting the desired cached tiles from the transmitting station that are needed and that were not previously transmitted and stored at the receiving station.

- 18. A method in accordance with claim 16 further comprising transmitting all of the tiles needed for the first and second views at their respective first and second magnifications as part of the data structure transmitted to the receiving station.
- 19. A method in accordance with claim 16 further comprising:

opening a view window of a known size for the second view; and

-80-

using an X, Y coordinate list of tiles when selecting the image tiles needed to fill the window in order to display the selected region at a higher magnification for the second view.

- 20. A method in accordance with claim 19 further comprising using the reference point as an appropriate center of the window and selecting tiles from the X, Y coordinate list of tiles located about the reference point to fill the window.
- 21. A method in accordance with claim 15, wherein the resolution of stage travel relative to pixel resolution comprises:

more than one stage step per pixel for a higher magnification pixel; and

more than one hundred stage steps per pixel for a lower magnification pixel.

- 22. A method in accordance with claim 21, wherein there are 500 or more stage steps per pixel at the lower magnification.
- 23. A method in accordance with claim 15 further comprising scrolling the higher magnification view and using the stage X, Y coordinate system to remove image tiles and to select new image tiles for addition to the currently-displayed image tiles.
- 24. A method in accordance with claim 15 further comprising:

-81-

providing a third view comprised of image tiles taken at a third magnification using a third resolution of stage steps per pixel; and

zooming in and out between the first, second and third views.

25. A method in accordance with claim 15 further comprising:

storing in stage X, Y coordinate system the location of a corner of a tile; and

measuring the stage movements in counters from the respective tile corners in the X and Y directions to form tiles of a uniform size for a view at a given magnification.

- 26. A method in accordance with claim 25 further comprising using a closed loop microscope image stage on the microscope to provide stage steps of .1 micrometer or less.
- 27. A method in accordance with claim 15 further comprising using a reduced percentage of the pixels from the original microscope scan and digitized field of view tile.
- 28. A method in accordance with claim 27 comprising providing a thumbnail view of the specimen using digitally demagnified tiles of the scanned and digitized field of view tile.
- 29. A method of providing tiled, digitized image tiles of specimens over a common communication channel to viewers at remote locations, comprising:

storing at a central location data for sets of digitized image tiles of a plurality of specimens;

-82**-**

requesting over the common communication channel access to the data for the stored, digitized image tiles of at least one specimen of the stored image tiles;

sending back over the common communication channel information to the remote location to aid in the selection of a digitized image tile for viewing by the remote user;

using the sent information for selecting at the remote location and requesting a transmission of specific digitized image tiles from those stored at the central location;

sending from the central station the stored data for the selected digitized image tiles over the common communication channel to the remote location; and

making available at the remote location the digitized image tiles requested for viewing the specimen or a portion thereof.

30. A method in accordance with claim 29, wherein sending the information back over the common communication channel to remote locations further comprises:

presenting to the viewer thumbnail views of specimens as information for use in selecting; and requesting transmission of a specific digitized image for the selected specimen.

31. A method in accordance with claim 29 wherein the sending of the stored data further comprises:

transmitting a data structure having a selfexecuting program and digitized image tiles to the receiving station; and

wherein making available the digitized images further comprises selecting stored digitized image tiles from

-83-

- 32. A method in accordance with claim 29 wherein making available the digitized image tiles for viewing the specimen further comprises transmitting over the common communication channel sets of digitized image tiles for different resolutions and for different regions of the specimen.
- 33. A method in accordance with claim 29, wherein sending back information over the common communication channel to the remote location further comprises presenting to the viewer a thumbnail digitized image of a specimen and an enlarged preview, digitized image of the specimen and an x, y list image tiles.
- 34. A method in accordance with claim 29 further comprising:

using a personal computer to communicate over the common transmission channel; and

using a Windows operating system for displaying on a screen of the personal computer the transmitted, digitized image tiles.

35. A method in accordance with claim 29, wherein the storing of digitized image tiles and the sending of information to the remote location comprises:

providing a server at the central location; and providing at the server data structures having tiled sets of digitized images with x, y information to aid the viewer program to reconstruct, to spatially align, physically contiguous images at multiple resolutions.

36. A method in accordance with claim 29, wherein an HTML browser is installed at the remote user's personal

-84-

37. A method in accordance with claim 29 further comprising providing descriptive text with the digitized tiled image to instruct about the specimen being viewed.

38. A method in accordance with claim 35 further comprising:

storing a plurality of digitized image tiles of different resolutions on the server; and

selecting at the remote location different resolution image tiles to be transmitted from the server to the remote location.

39. A method in accordance with claim 29 further comprising:

providing at the remote location a plurality of folders having a virtual microscope slide comprised of digitized image tiles therein in an organized system; and

selecting at the remote location one of the folders from the organized set of folders for transmission of its associated virtual microscope slide.

40. A method in accordance with claim 39 further comprising:

providing three screens on a viewing device for viewing of virtual microscope slides;

presenting a thumbnail view of the specimen on one screen;

presenting a larger preview view comprised of digitized, image tiles of the specimen on a second screen for selection of a higher resolution, segment of the preview image; and

-85-

presenting the selected higher magnification region comprised of digitized image tiles on a third screen to the viewer.

- 41. A method in accordance with claim 40 further comprising changing the size of the window and changing the magnification to allow a full inspection of the specimen at higher and lower magnifications.
- 42. A method in accordance with claim 29 further comprising:

providing a digitized, tiled image of a portion of a specimen at a first predetermined resolution; and

overlaying a digitized, tiled image of the specimen at a lower resolution than the predetermined resolution.

43. A method in accordance with claim 29, wherein the making available at the remote location of the digitized tiled image comprises:

changing the size of a viewing window; and filling the necessary digitized image tiles to fill the viewing windows of different sizes.

44. A method in accordance with claim 43 further comprising:

requesting a lowered resolution of the digitized image tiles at a first higher resolution presented on the window; and

using more digitized image tiles to fill the window at a second lower resolution than used to fill the window at the higher resolution.

-86-

45. A method in accordance with claim 29, wherein at the remote location the user is provided with the options of:

selecting a folder associated with a given digitized image tiles from an organized set of folders;

selecting to interact with other multiple users on the same digitized tiled image; or

selecting an HTML applet of a specific digitized tiled image of a specific region of a specimen.

46. A method in accordance with claim 29 further comprising:

selecting spaced points on the digitized, tiled image; and

measuring the distance between the selected spaced points and reporting the distance to a viewer.

- 47. A method in accordance with claim 29 further comprising selecting from a plurality of collected data files stored at the first station the requested virtual microscope slides for transmitting over the common communication channel to the viewer.
- 48. A method in accordance with claim 29 further comprising:

providing a server at the first station; and selecting by the server from RAM and CD media the stored digitized, image tiles for transmission.

49. A method in accordance with claim 29 further comprising loading a browser program onto computers at the multiple receivers at the receiving stations for assistance in assembling the digitized tiled images.

-87-

50. A method in accordance with claim 29 further comprising:

providing a plurality of first stations each capable of transmitting virtual microscope slides over the common communication channel; and

addressing one of the plurality of stations and requesting a desired virtual microscope slide therefrom.

51. A method of providing a virtual, multiheaded microscope allowing a plurality of viewers at remotely located different stations to simultaneously view the same virtual microscope slide comprised of tiled digital images comprising:

providing a common communication channel;

transmitting over the common communication channel a virtual microscope slide to a first receiving station for viewing by a first viewer;

transmitting over the common communication channel the same virtual microscope slide to a second viewing station for viewing by a second viewer; and

indicating by the first of the users an area on the virtual microscope slide at the first receiving station for discussion and transmitting from the first station information for locating the same area on the virtual microscope slide being viewed at the second station for discussion of the same indicated area between the first and second viewers; and

communicating over a carrier between the first and second viewers about the indicated area on the virtual microscope slides being displayed simultaneously to both of the first and second viewers.

52. A method in accordance with claim 51 further comprising:

-88-

placing one of the first and second viewers in control and allowing this viewer to change the sets of tiled images to be viewed simultaneously by each of the viewers at their respective receiving stations;

allowing one of the viewers to change the magnification between tiled images of high and lower resolutions; and

transmitting from a central station the newly changed resolution tiled images to the respective first and second receiving stations.

- 53. A method in accordance with claim 51 further comprising passing control of an indicator from the first viewer to the second viewer to allow the second viewer to shift the indicator to a region that the second viewer wants to discuss with the first viewer.
- 54. A method in accordance with claim 53 further comprising indicating with a pointer controlled by a computer controller device.
- 55. A method in accordance with claim 54 further comprising using a mouse as the computer control device for shifting the pointer on the virtual microscope slide.
- 56. A method in accordance with claim 51 wherein, the communicating between the first and second viewer is by speaking over a telephone.
- 57. A method in accordance with claim 51 wherein, the communicating between the first and second viewer is by written messages over an Internet common communication

-89-

58. A method of providing a virtual, multiheaded microscope allowing a plurality of viewers at remotely located different stations to simultaneously view the same virtual microscope slide view comprised of digital image tiles, comprising:

providing a common communication channel; storing at a common repository sets of digitized image tiles at a central station connected to the common communication channel for transmission of digitized image tiles to multiple users connected to the common communication channel;

transmitting over the common communication channel digitized image tiles to a first receiving station to provide a view for viewing by a first viewer;

transmitting over the common communication channel the same digitized image tiles to a second viewing station to provide a view for viewing by a second viewer;

the first viewer causing a change in the side image being viewed by sending a request for a subset of new digitized image tiles to be transmitted from the central station and the central station responding by sending the subset of digitized image tiles to both the first and second stations; and

communicating over a common communication channel between the first and second viewers about the virtual microscope slide views being displayed simultaneously to both of the first and second viewers.

59. A method in accordance with claim 58 further comprising:

the first user initiating requests for changes in views and resolutions and of the specimen slide images; and

-90-

the central station receiving the requested changes and transmitting a packet of image tiles to both the first user and second user for the change resolution and changed views.

60. A method in accordance with claim 58 further comprising:

moving a pointer on the virtual microscope slide image to a new location;

transmitting the pointer's new location from the first station to a central station;

transmitting from the central station to the second station the new location of the pointer; and

moving the pointer at the second station to the same new location on the slide image.

61. A method in accordance with claim 58 further comprising:

providing a central station with a central repository having a stored, plurality of digitized tiles for substantially the entire image of the specimen; and

selecting from the stored digitized image tiles a subset of the digitized image tiles and transmitting the subset of digitized image tiles to both the first and second users for viewing of the same image simultaneously at their respective stations.

62. A method in accordance with claim 61 further comprising providing a digitized image tile comprising an image analysis digitized image that corresponds substantially to a single field of view taken through an objective view of a microscope.

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63. A method in accordance with claim 61 further comprising using a reduced percentage of the corresponding microscope single field of view for transmission as a digitized image tile for transmission from the central station.

-91-

64. A method of using a filing structure for organizing virtual microscope slide images to be requested by and transmitted to a requester from a server at a server station over a common carrier, comprising:

transmitting a request from a requester at requesting station to the server station;

transmitting a slide tray request to the server station;

transmitting slide tray information from the server station to the requesting station;

displaying to the requester slide tray information comprising a list of virtual microscope slide names on a display device at the requesting station;

selecting from the slide tray information a microscope slide name to cause an image request for the selected slide to be sent to the server station; and

transmitting from the server station a set of tiled digitized images comprising the slide specimen or a portion thereof for viewing on the display device at the requesting station.

65. A method of providing virtual microscope slides each having at least a portion of a specimen associated therewith and identified by name from a central station to remote stations comprising:

storing data at a central location for use in

for use in providing and assembling digitized image tiles for viewing a virtual microscope slide at multiple resolutions;

connecting one or more remote stations over a common communication channel to the central station;

transmitting a request from the remote station for information about the virtual microscope slides available for transmission to the requesting remote station;

transmitting from the central station a list of names of virtual microscope slides in response to the request form the remote station;

selecting a virtual microscope slide from the list of names by a viewer at the remote station;

displaying a thumbnail image of the specimen on the virtual microscope slide to the viewer at the remote station;

selecting a region from the thumbnail image to be displayed at higher resolution; and

assembling the digitized image tiles at the higher resolution and making them available for viewing at the higher resolution the selected region of the specimen.

- 66. A method in accordance with claim 65, wherein the selecting of a region from thumbnail image comprises displaying at the remote station a preview image larger in size than the thumbnail image and selecting from the preview image the region to be viewed at the higher resolution.
- 67. A method in accordance with claim 66 further comprising indicating on the preview image those regions where digitized image tiles are available for assembling into the higher resolution view.
 - 68. A method in accordance with claim 67 further

-93-

as a dynamic display such that the selection thereof activates a request to the central station to transmit the thumbnail image tiles to the remote station.

- 69. A method in accordance with claim 65, wherein selecting of a region on the thumbnail image causes a request to the central station and a responsive transmission of a larger preview slide image and a list of tiles for the higher magnification image in an X, Y coordinate system.
- 70. A method in accordance with claim 66 further comprising overlaying on the display device the thumbnail image, the preview image, and the higher magnification view.
- 71. A method in accordance with claim 65 further comprising:

changing the size and position of a viewing window for the selected region; and

zooming between several resolutions of the specimen when analyzing the specimen on the selected virtual microscope slide.

72. A method in accordance with claim 66 further comprising:

transmitting from the central station multiple image tiles at a higher resolution than the thumbnail image for viewing as a slide view image at the remote station; and

selecting from the slide view image and requesting from the central station multiple image tiles at a resolution higher than the side view image to provide a field view of specimen.

-94-

73. A method in accordance with claim 65 further comprising overlaying on the virtual specimen an overlay showing the regions of the specimen actually scanned and available for viewing and showing the regions of the specimen that have not been scanned and are not available for viewing.

- 74. A method in accordance with claim 65 wherein the selecting of a virtual microscope slide from the list of names comprises sending a request to the central station which results in transmission of a dynamic self-executing control program having stored multiple resolution tiles for the selected slide to the receiving station.
- 75. A method in accordance with claim 74 further comprising sending and assembling the stored multiple resolution tiles from the dynamic, self-executing program at a viewer to provide the higher resolution view of the region.
- 76. A method in accordance with claim 74 further comprising adding descriptive text for the microscope slide by a user at a remote station for use by another viewer.
- 77. A method in accordance with claim 76 further comprising storing the descriptive text on a computer separate from the stored image tiles so that different users at different stations may access the slides with respectively associated, descriptive texts and update their separate texts.
- 78. A method in accordance with claim 75 further comprising using the self-executing program to provide multiple resolution tiles to show substantially the entire specimen at each of the predetermined resolutions.

-95**-**

- 79. A method in accordance with claim 78 further comprising transmitting from the central station a prestored thumbnail image slide for the specimen and prestored preview images for each of the resolutions that are available.
 - 80. A method in accordance with claim 79 further comprising digitally reducing from the highest resolution the other resolutions for the respective prestored image tiles.
 - 81. A method in accordance with claim 78 further comprising:

transmitting a thumbnail view of substantially the entire specimen to the requesting station for display; and

selecting from the thumbnail view a region to be viewed at a higher magnification and sending a select slide request to the server station to obtain a high-magnification set of digitized image tiles of the selected region.

- 82. A method in accordance with claim 81 further comprising transmitting from the server station a high-magnification preview image in response to the select slide request.
- 83. A method in accordance with claim 82 further comprising:

selecting from the higher-magnification preview image an area thereon for viewing at higher magnification; and displaying the selected areas as a field view.

84. A method in accordance with claim 83 further comprising the viewer changing the resolution of the field view images to zoom back and forth there between during a

-96-

diagnosis by a pathologist of the specimen on the virtual microscope slide.

85. A method in accordance with claim 81 further comprising:

providing a dynamic display of virtual microscope names and the thumbnail view; and

using a control device to select the name and region from these dynamic displays.

- 86. A method in accordance with claim 64 wherein the displaying to the requester of slide tray information comprises displaying a file folder tree display in a window of the requester's display device.
- 87. A method of operating a display drive to display sets of tiled digitized images of portions or of a specimen to a viewer comprising:

storing at a central location sets of tiled digitized images at different resolutions;

displaying to the viewer a thumbnail view of the specimen at a first resolution;

selecting by the viewer from the thumbnail view an area to be viewed at a second resolution higher than the first resolution of the thumbnail view;

displaying to the viewer a set of tiled digitized images of the selected area at the second resolution;

selecting by the viewer from the set of digitized, tiled images at the second resolution an area for viewing at a third resolution higher than the second resolution; and

displaying simultaneously to the viewer another set of digitized, tiled images at the third higher resolution and

-97-

- 88. A method in accordance with claim 87 further comprising forming and displaying the thumbnail view form a plurality of digitized, tiled images at the first resolution.
- 89. A method in accordance with claim 87 further comprising providing a grid on at least one of the sets of digitized, tiled images showing the tile boundaries for selecting a tile as an area for viewing at a higher resolution.
- 90. A method in accordance with claim 87 further comprising:

providing a grid on the thumbnail view to aid in selecting the area to be viewed at the second resolution; and providing a grid on the second resolution digitized tiled image to aid in selecting the area to be viewed at the third resolution.

- 91. A method in accordance with claim 87 wherein each of the three views shown simultaneously with there being an overlapping of the views being shown simultaneously.
- 92. A method in accordance with claim 87 further comprising:

changing the size and locations of the displayed views on the display device; and

changing the magnification to allow zooming between different magnifications for viewing a suspicious area of a specimen.

93. A method in accordance with claim 87 further comprising:

-98-

providing a first window on the display device for viewing the thumbnail view;

providing a second window on the display device for viewing a set of digitized tiled images which are filling the second window; and

providing a third window on the display device for viewing at the third resolution a set of digitized tiled images, which are filling the third window.

94. A method of providing tiled, digitized image tiles of specimens over a common communication channel to viewers at remote locations, comprising:

storing at a central location data for sets of digitized image tiles of a plurality of specimens;

requesting over the common communication channel access to the data for the stored, digitized image tiles of at least one specimen of the stored image tiles;

sending back over the common communication channel information to the remote location to aid in the selection of a digitized image tile for viewing by the remote user;

using the sent information for selecting at the remote location and requesting a transmission of specific digitized image tiles from those stored at the central location;

sending from the central station the stored data for the selected, digitized image tiles over the common communication channel to the remote location;

providing an applet for transmitting from the central station to a browser at a remote location for viewing, manipulating and reconstructing the digitized image tiles into a composite view;

-99-

using a previously-installed control program at the remote station for viewing, manipulating and reconstructing the digitized image tiles into a composite view; and

making available at the remote location the digitized, image tiles requested for viewing the specimen or a portion thereof while using one of the applet or previously-installed control program.

95. A method of providing a text file created by a first user for a second user of a virtual microscope slide comprised of a set of digitized image tiles comprising:

providing a common communication channel having a provider station that provides virtual microscope slides;

transmitting a virtual microscope slide to the first user at a first station connected to the common communication channel;

creating text at the first station for instructing the second user with respect to evaluating the virtual microscope slide transmitted to the first station from the provider station; and

transmitting the text over the common communication channel from the first station to the second user at the second station to provide instructions to the second user to aid in the second user's review of the virtual microscope slide.

96. A method in accordance with claim 95 further comprising:

identifying the virtual microscope slide to the second user in the transmitted text; and

the user requesting and receiving the identified virtual microscope slide over the common communication channel

-100-

97. A method in accordance with claim 95 further comprising:

instructing in the text the second user as to a region of the virtual microscope slide to view; and instructing the second user as to what to observe in the selected region.

- 98. A method in accordance with claim 95 further comprising providing instructions in the text as to resolutions to be used in viewing a region on the virtual microscope slide.
- 99. A method in accordance with claim 95 further comprising providing a virtual microscope slide to the first and second users wherein each of the digitized image tiles corresponds substantially to a view shown through an objective lens of a microscope.
- 100. A method in accordance with claim 95 further comprising using a reduced percentage of a corresponding original microscope image for transmission as a digitized image tile.
- 101. A method for viewing a virtual microscope slide specimen views comprised of sets of digitized image tiles . transmitted over a common communication channel comprising:

providing a transmitting station connected to the common communication channel and accessible by a number of remote receiving stations connected to the common communication channel;

storing virtual microscope digitized image tiles at the transmitting station;

-101-

transmitting a control program to the requesting computer for use in obtaining and aligning the transmitted sets of digitized image tiles to form a composite, coherent, seamless digitized, virtual microscope, slide view from a set of digitized tiled images;

selecting by the user of a region at a desired resolution of the slide specimen for viewing;

requesting by the control program of the specific tiles needed for a tiled, image view of the specimen region at the desired resolution;

transmitting from the remote station the requested tiles for the region to the receiving station; and

assembling and displaying the transmitted tiles for the region using the control program to form the view of the region of the specimen at the desired resolution without having transmitted all of the sets of tiles for the specimen to the receiving station.

- 102. A method in accordance with claim 101 further comprising transmitting a group of requested tiles to the receiving station.
- 103. A method in accordance with claim 101 further comprising:

caching the transmitted tiles under the control of the control program; and

first searching the user's cached tiles for tiles to be used to satisfy the user's request and, secondly, requesting from the transmitting station those tiles not found in the cache, to satisfy the request.

104. A method in accordance with claim 103 further

-102-

storing at the transmitting station a large quantity of tiles for a substantive portion of one specimen at several resolutions; and

transmitting only the tiles requested which may be a small portion of the total stored quantity of tiles for the one specimen.

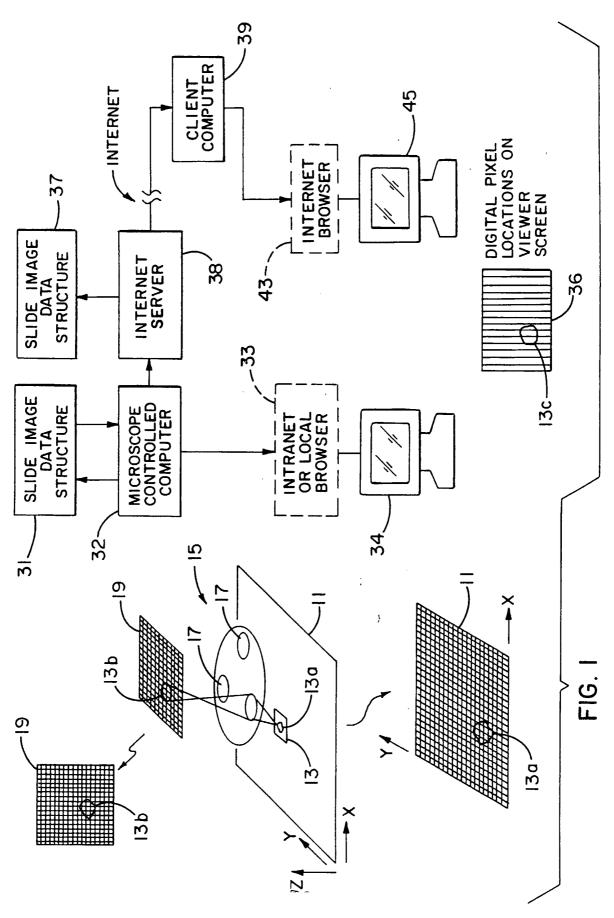
105. A method in accordance with claim 104 further comprising:

 $\mbox{identifying the tiles using an X, Y stage coordinate} \\ \mbox{system;}$

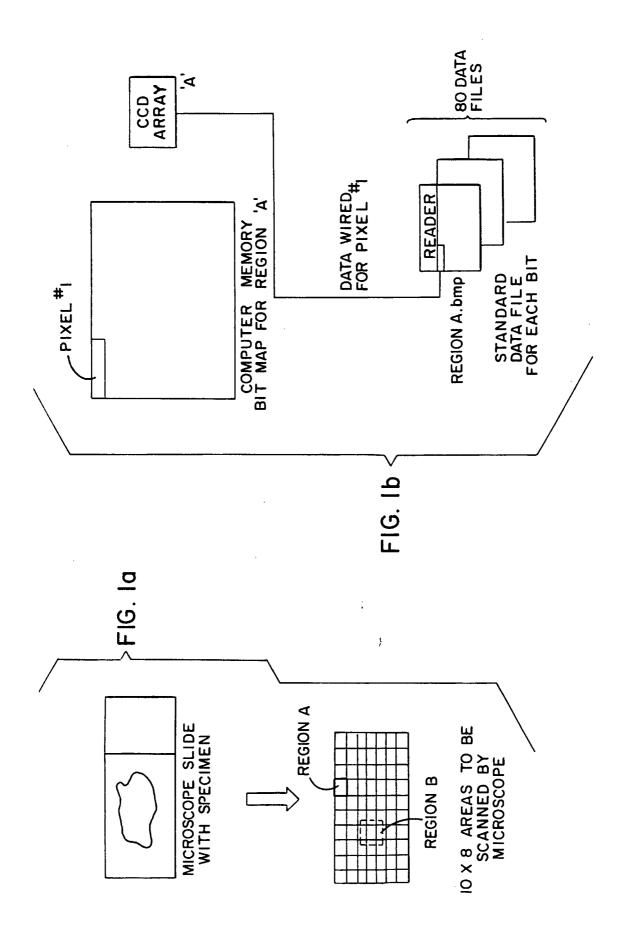
providing a list of the identified tiles; and searching the list for the requested tiles to be used to display the requested region.

106. A method in accordance with claim 101 further comprising:

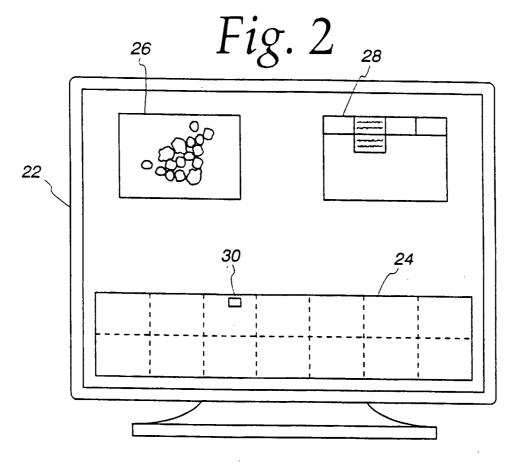
providing tiles that are represented by data acquired by scanning and digitizing a field of view of the specimen through a microscope; and compressing the data to provide the digitized image tile used for transmission.

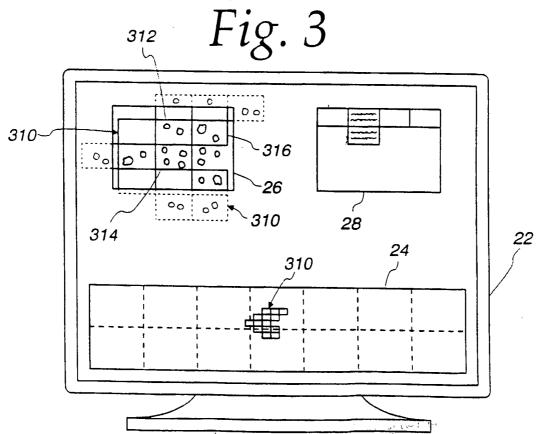


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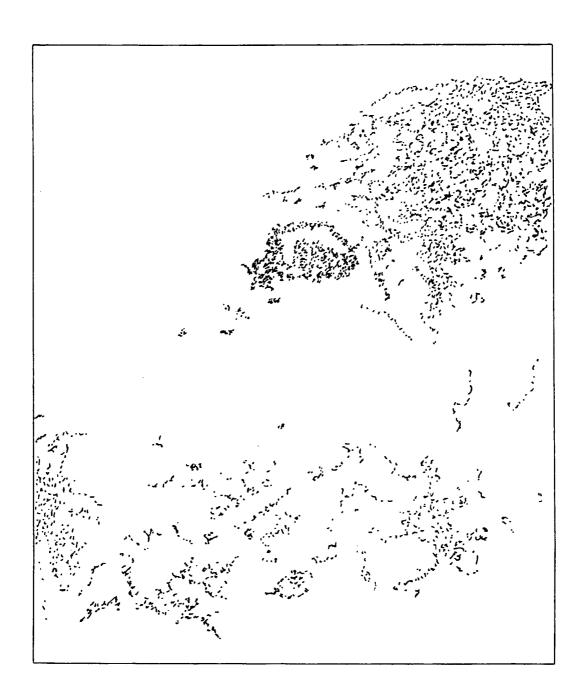


FIG. 4

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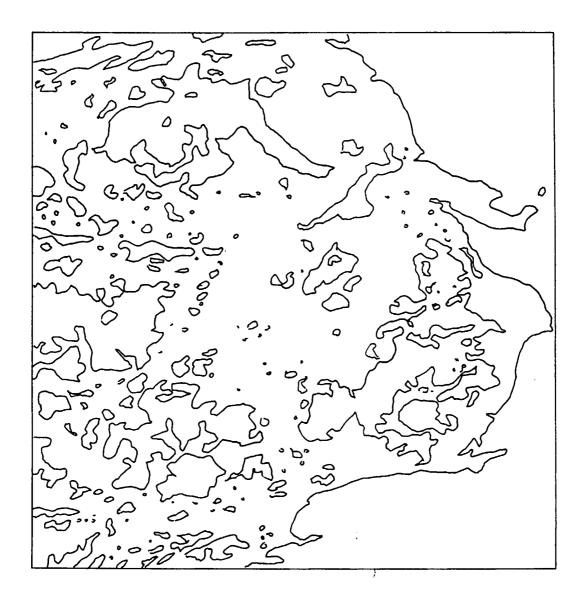
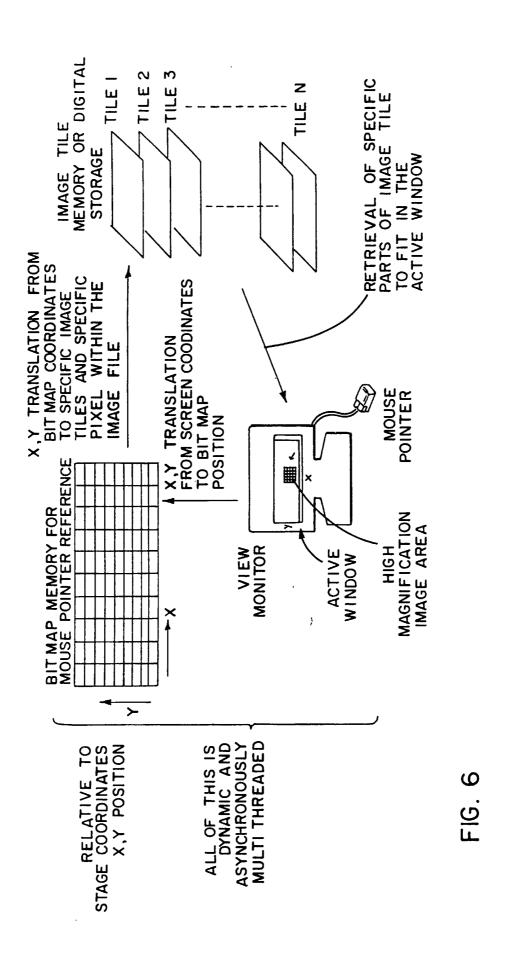
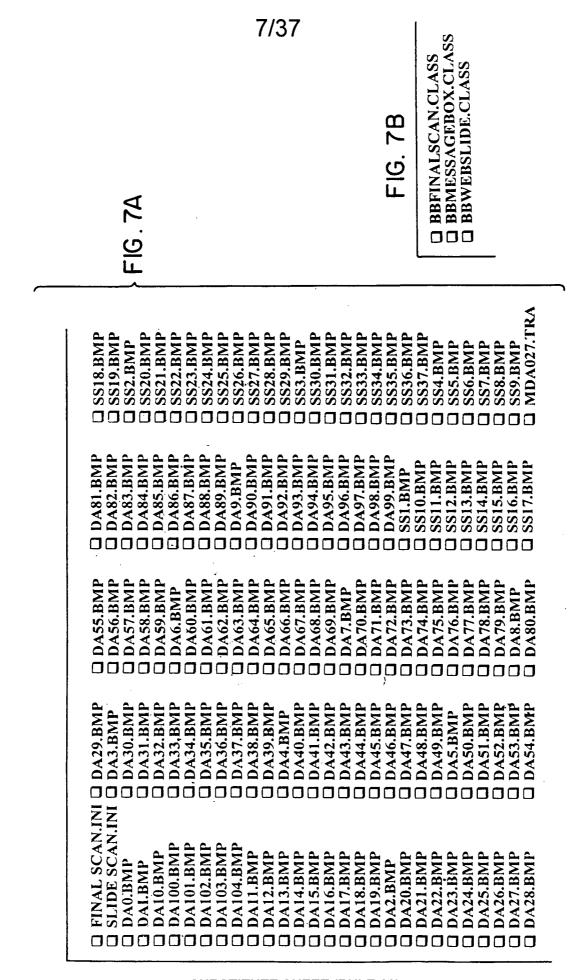


FIG. 5





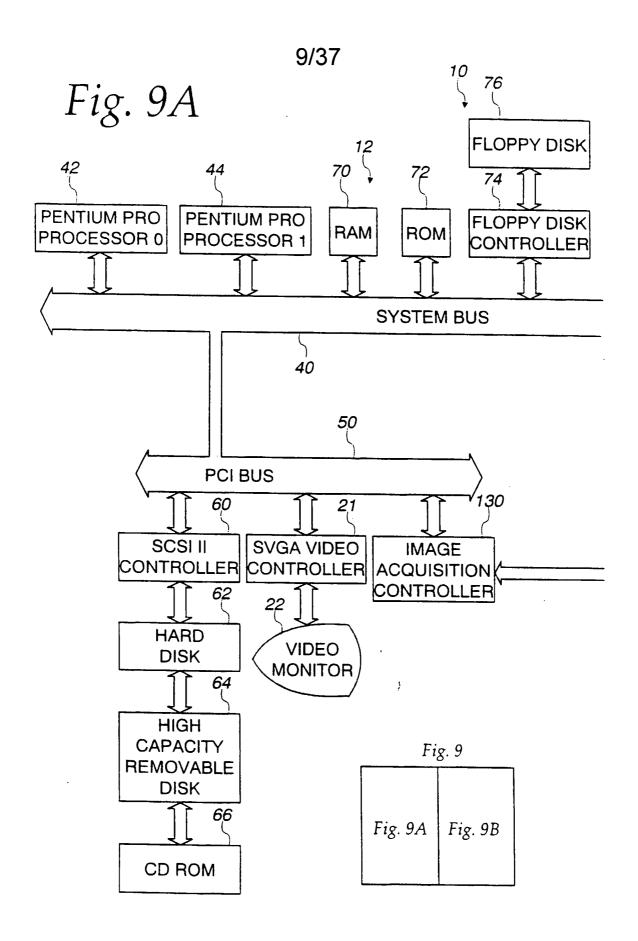
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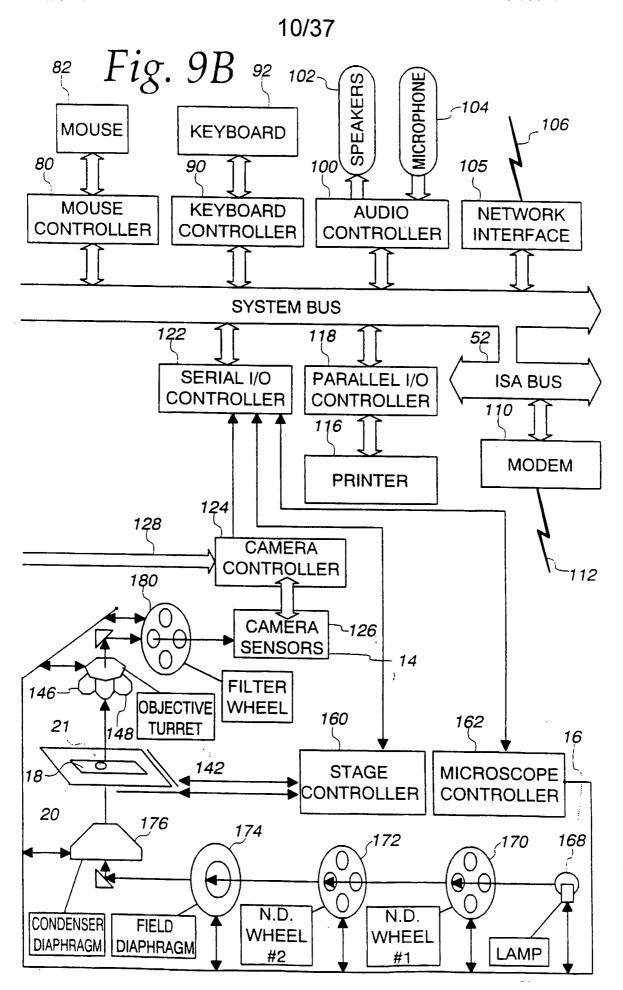
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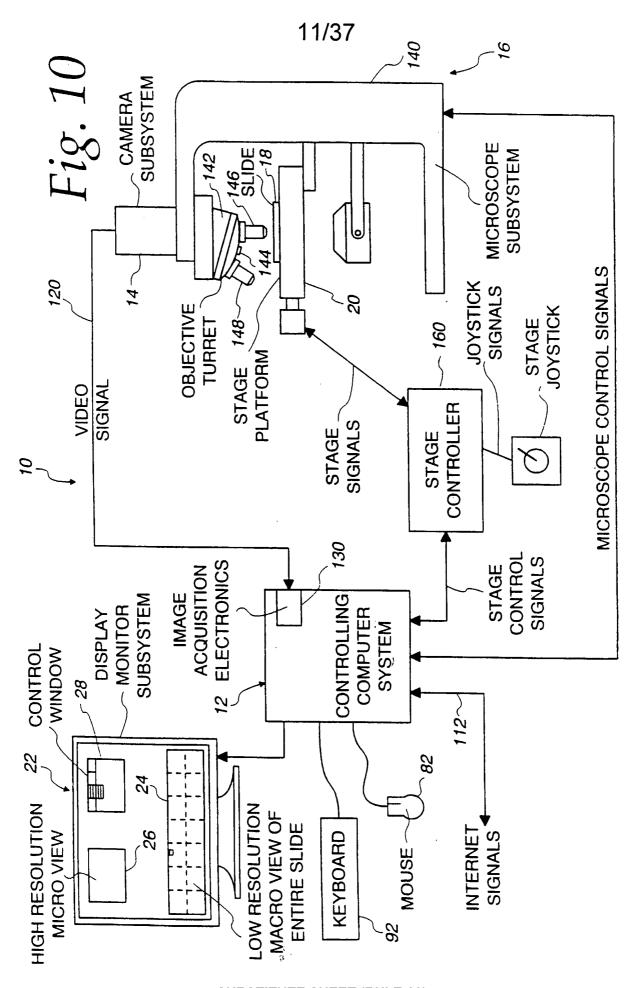
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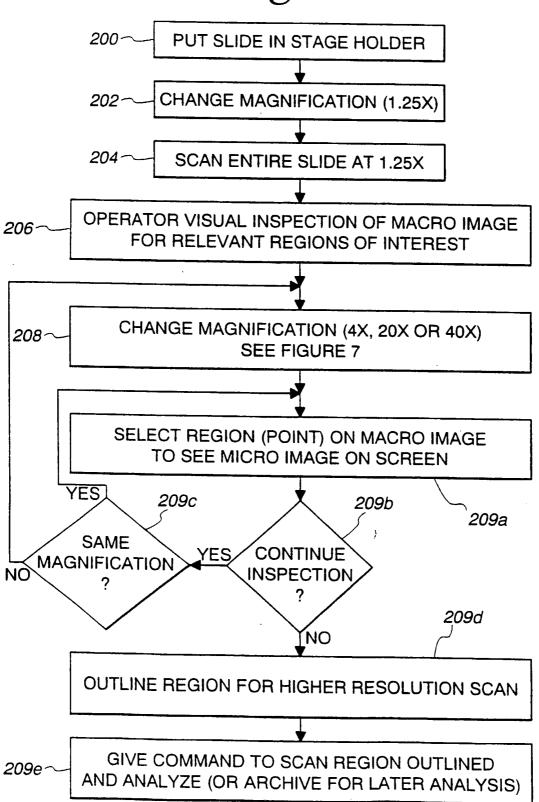
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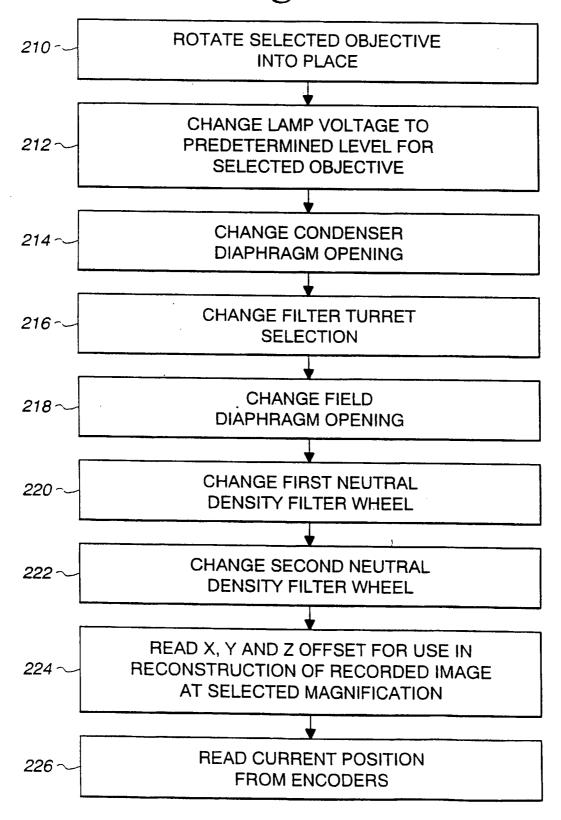
12/37

Fig. 11



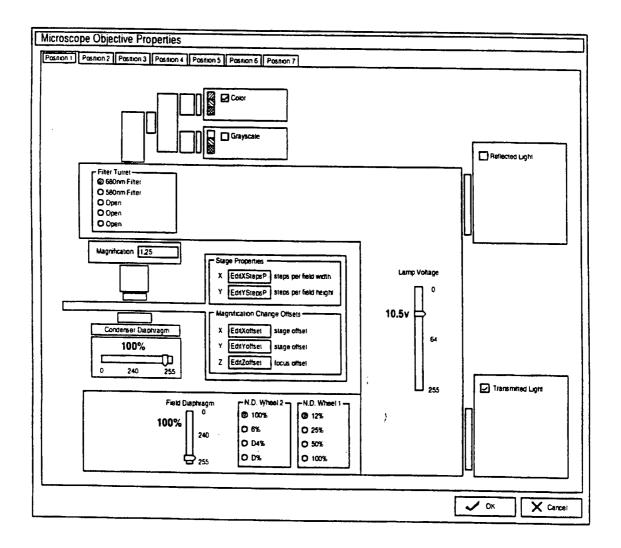
13/37

Fig. 12



14/37

Fig. 13



15/37

Fig. 14



POINT MOUSE TO SCREEN PIXEL AND 240 -DRAW BOX FOR REGION SELECTED

COMPLETE X, Y SCREEN POINTS FOR EDGES OF REGION SELECTED AND TRANSLATE POINTS TO 242 X. Y STAGE COORDINATE POINTS

MAKE LIST OF ALL X, Y FIELDS TO POSITION STAGE TO, FOR THE OBJECTIVE. USE INFORMATION FOR FIGURE ON X, Y OFFSETS FOR THE OBJECTIVE, AND 244 ~ FOR STAGE OFFSETS, AND SIZE OF FIELD FOR OBJECTS.

Fig. 15

SCAN AND ANALYZE REGION

MOVE STAGE TO POSITION OF EACH X, Y COORDINATE IN LIST OF X, Y COORDINATES FOR FIGURE 9

ACQUIRE IMAGE AND ANALYZE NOTE: IF NECESSARY AS A RESULT OF ANALYSIS CHANGE OBJECTIVE AND ALL LIGHT PROPERTIES TO DIFFERENT MAGNIFICATION.

OPTIONALLY STORE FOR ARCHIVAL OR VIEWING PURPOSES ENTIRE REGION OR AREAS SELECTED AS A RESULT OF ANALYSIS

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252 ~

254 -

Fig. 16

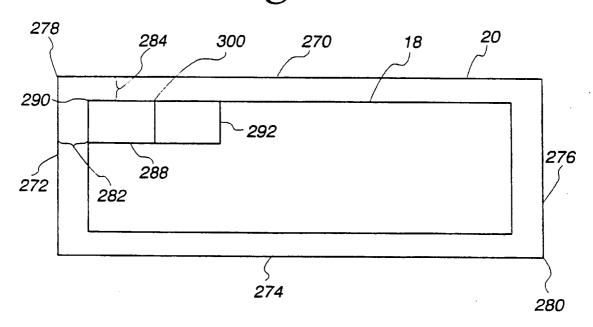
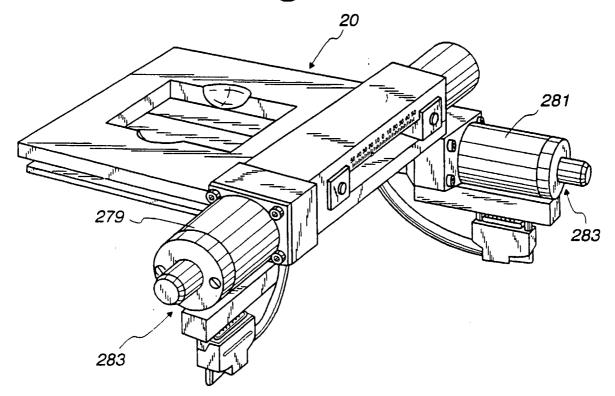
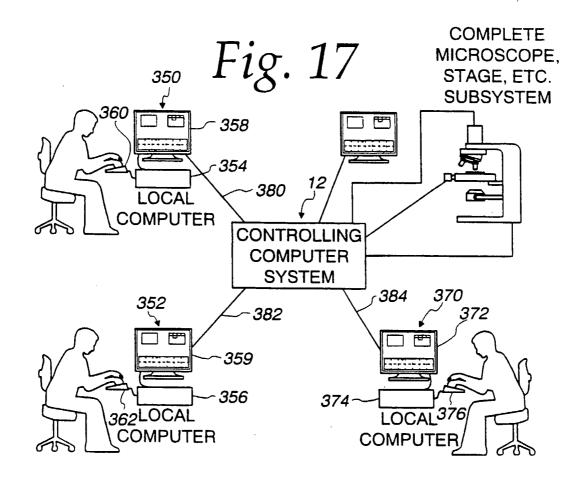


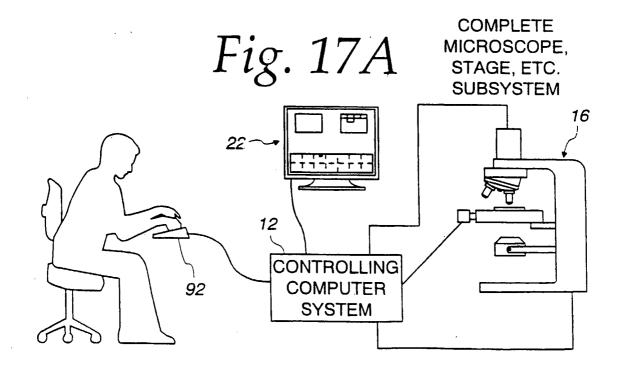
Fig. 16A

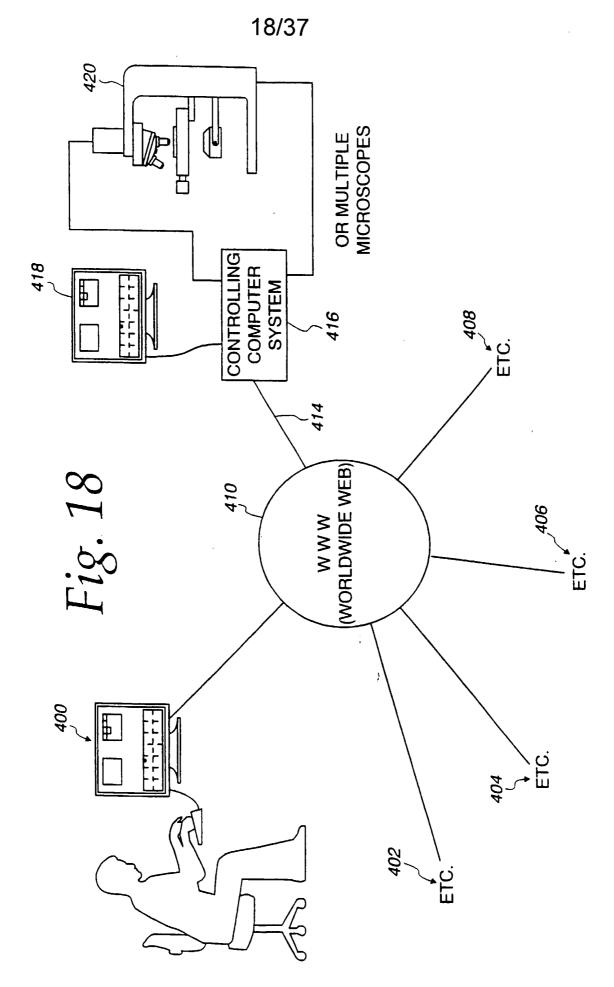


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17/37







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19/37

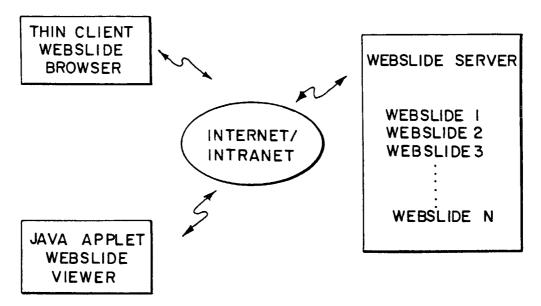


FIG. 19

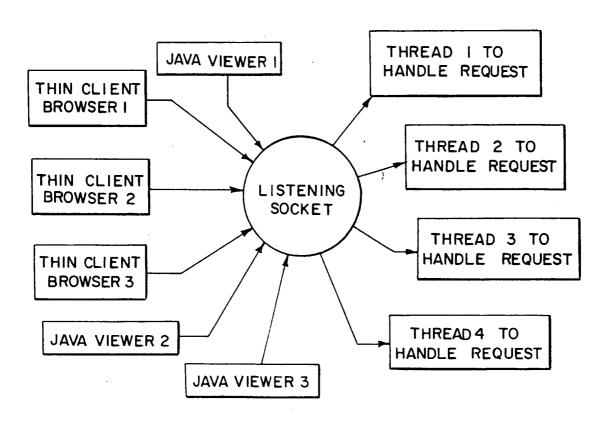
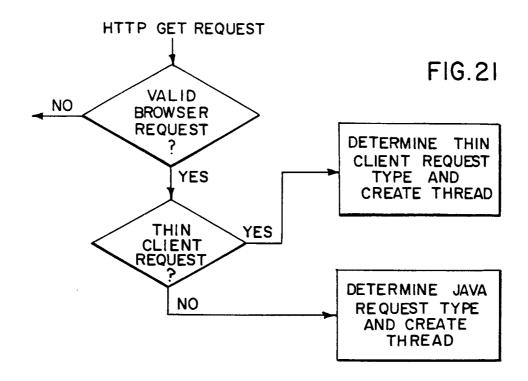
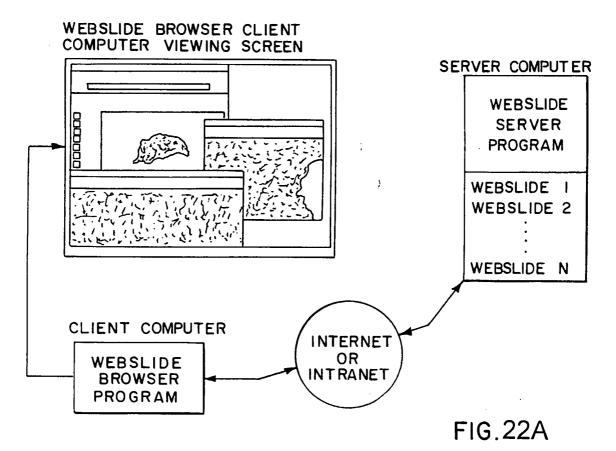


FIG.20

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21/37

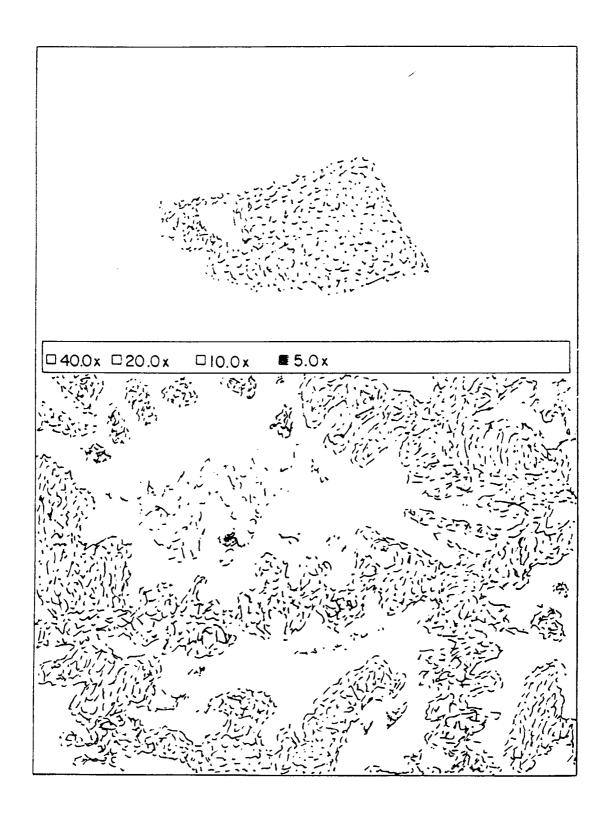


FIG.22B

22/37

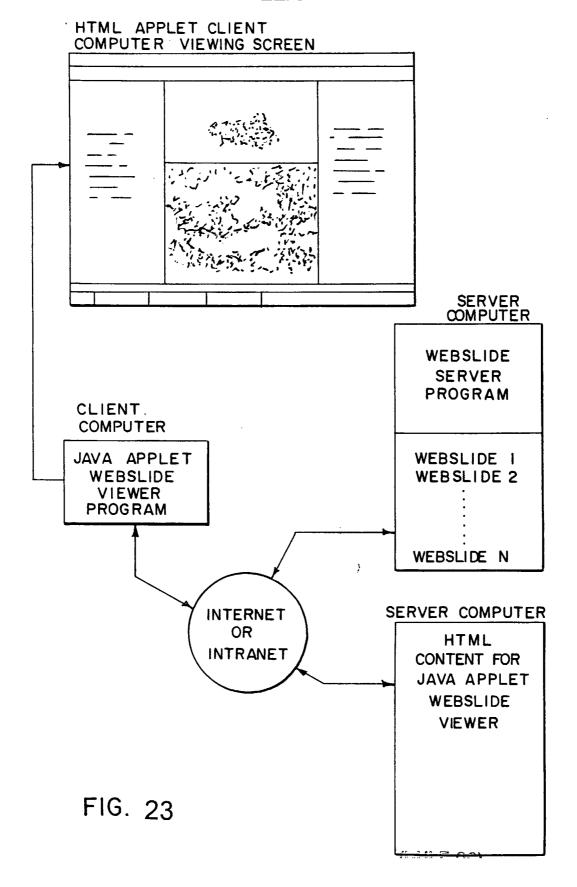
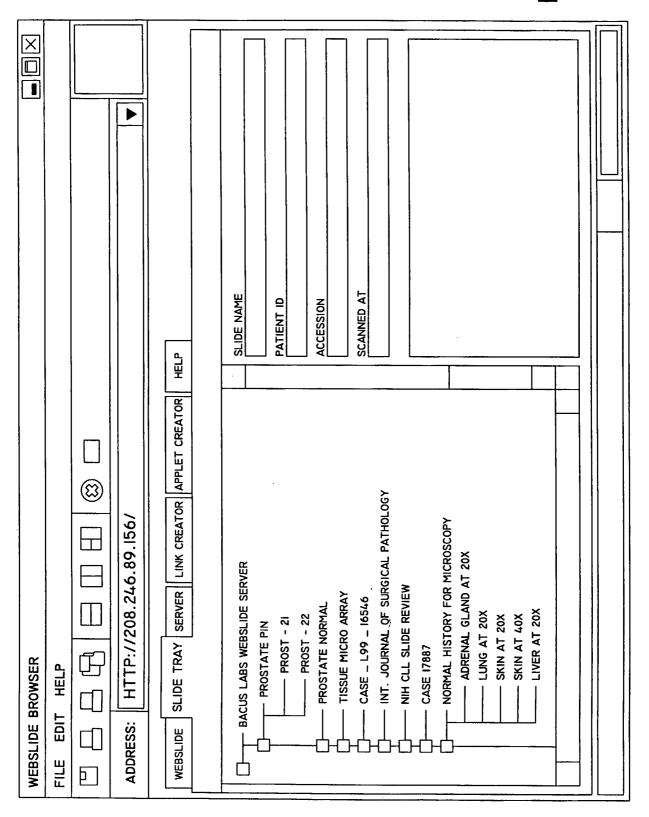


FIG. 24

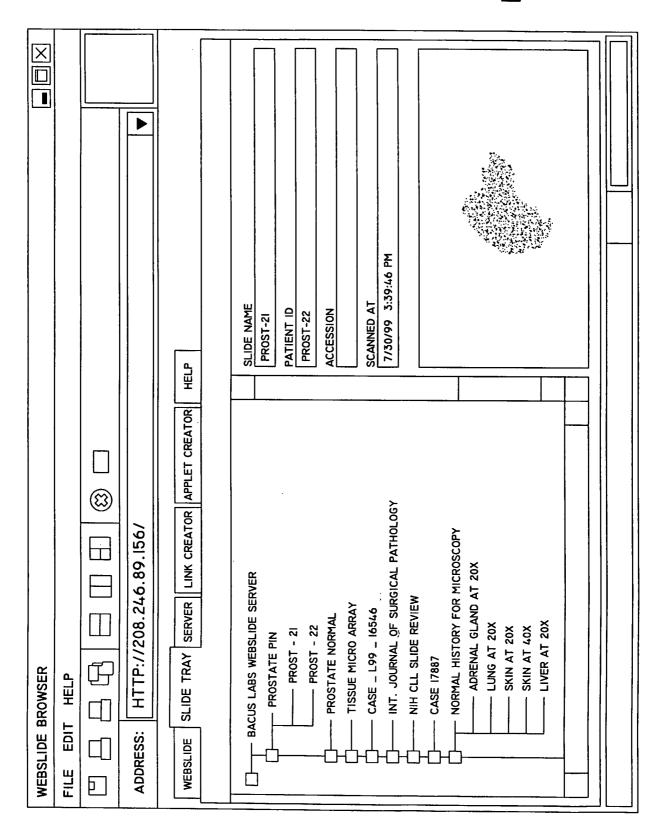
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F16. 2



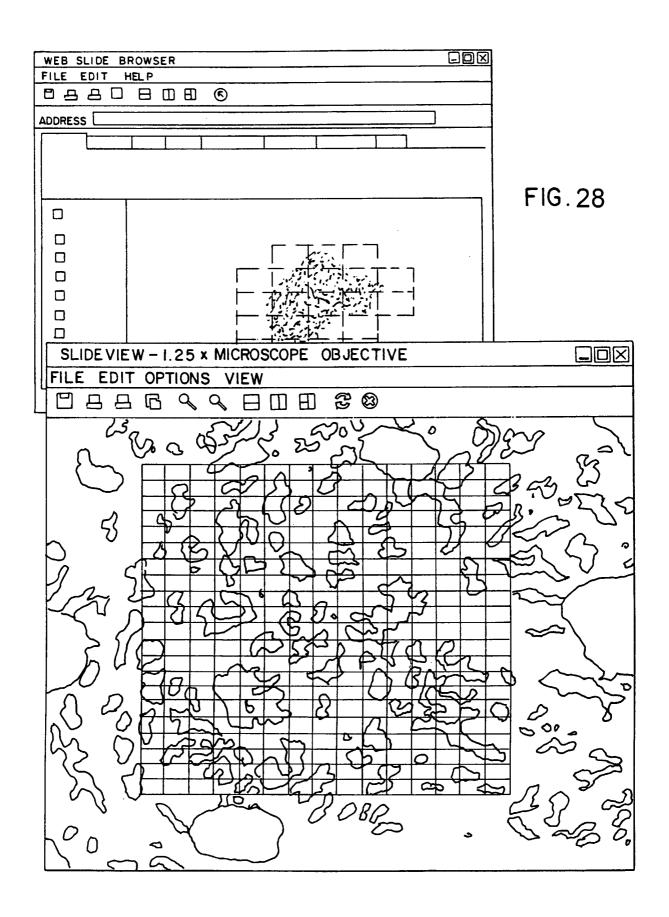
F16._2@

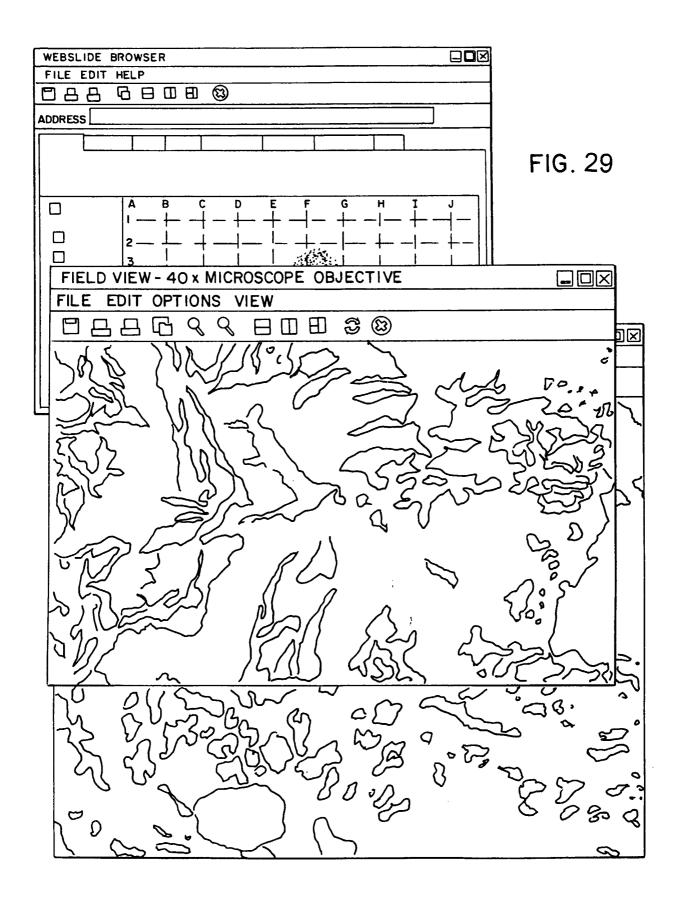


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GLATICLES SCAN AREA MULTI MAG TILE LOCATION SLIDE VIEW FIELD VIEW		





29/37

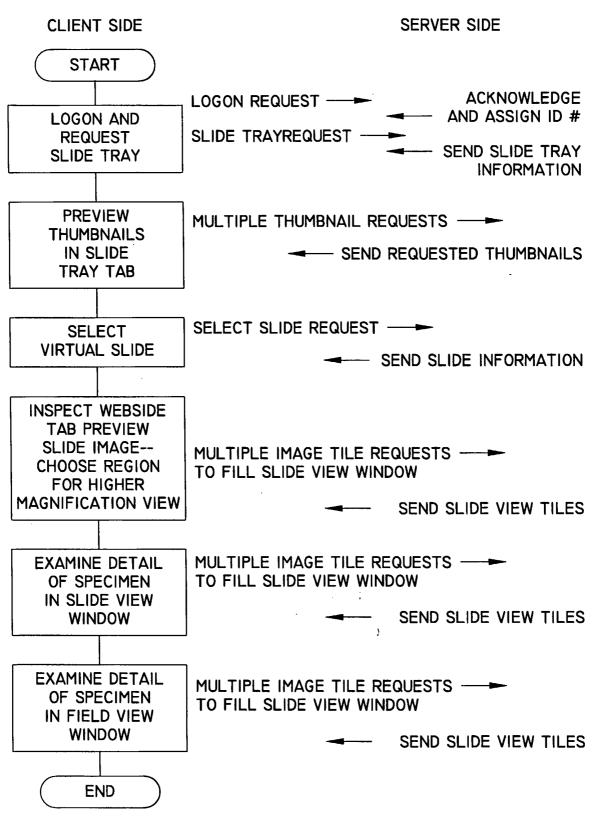
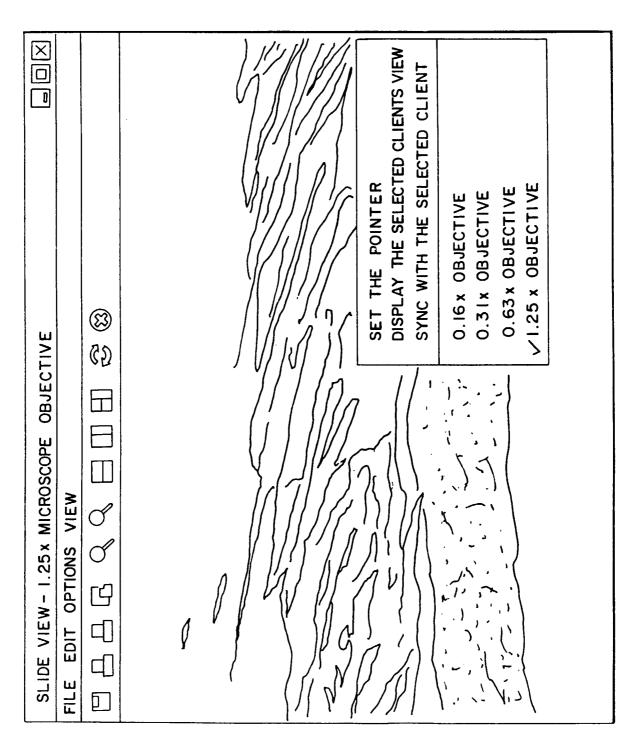


FIG. 30

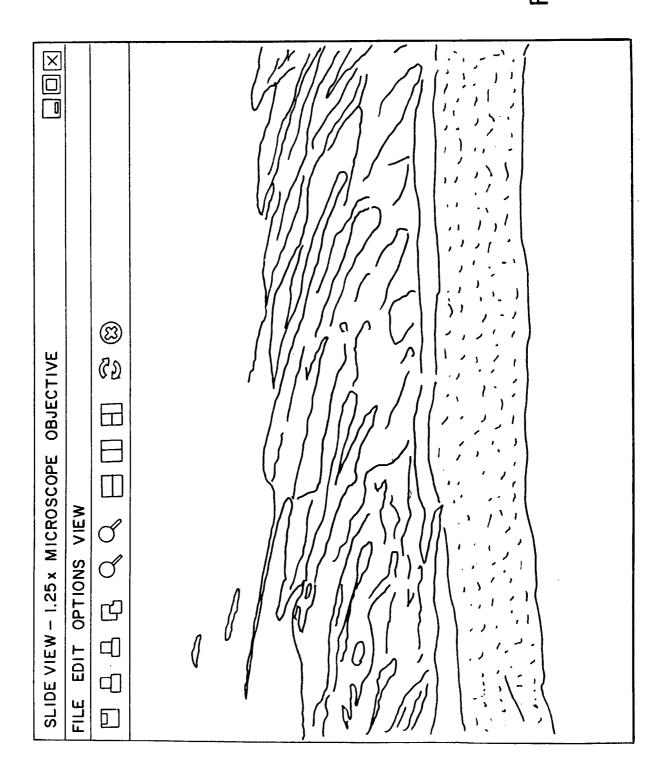
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FIG. 32



-16. 33



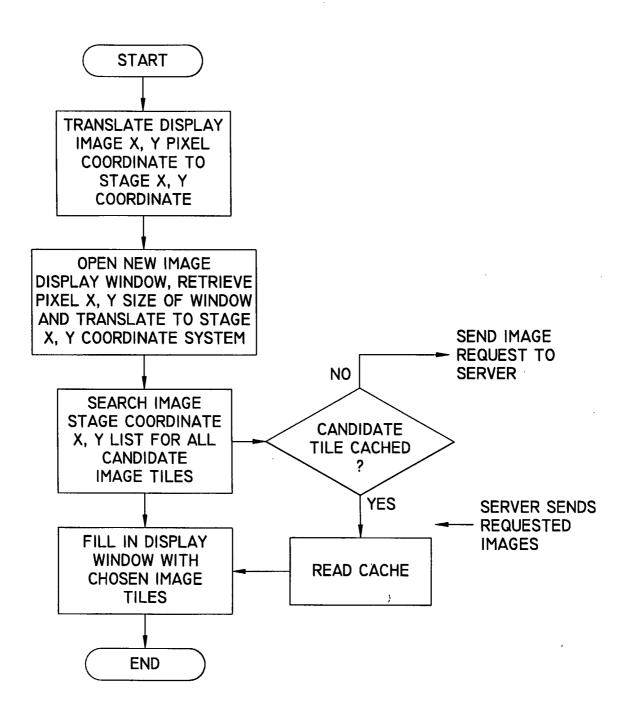
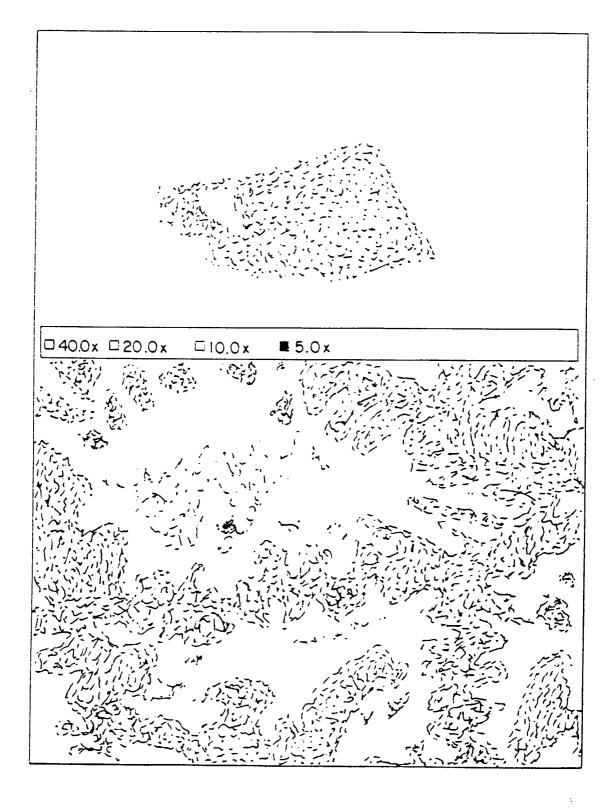
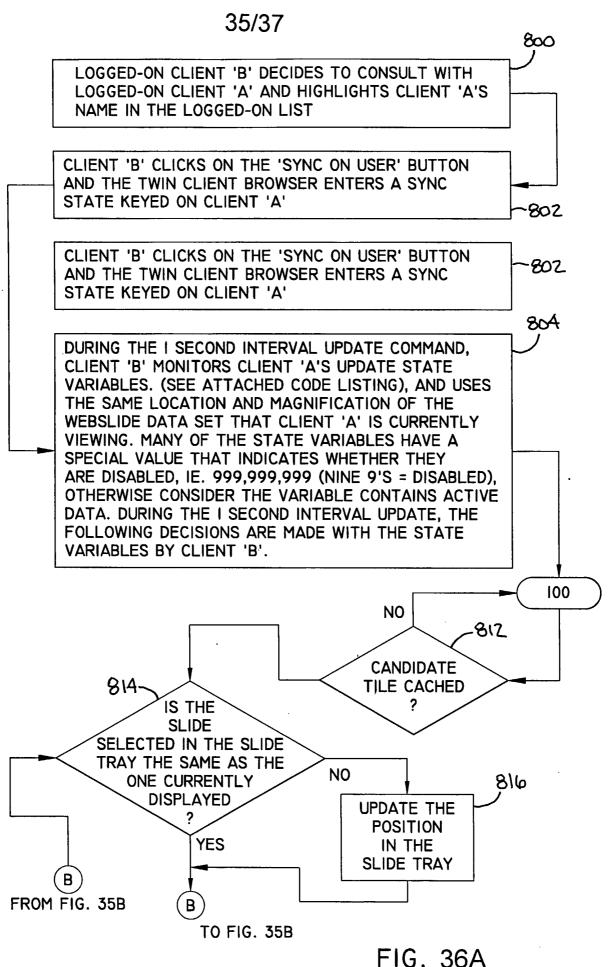


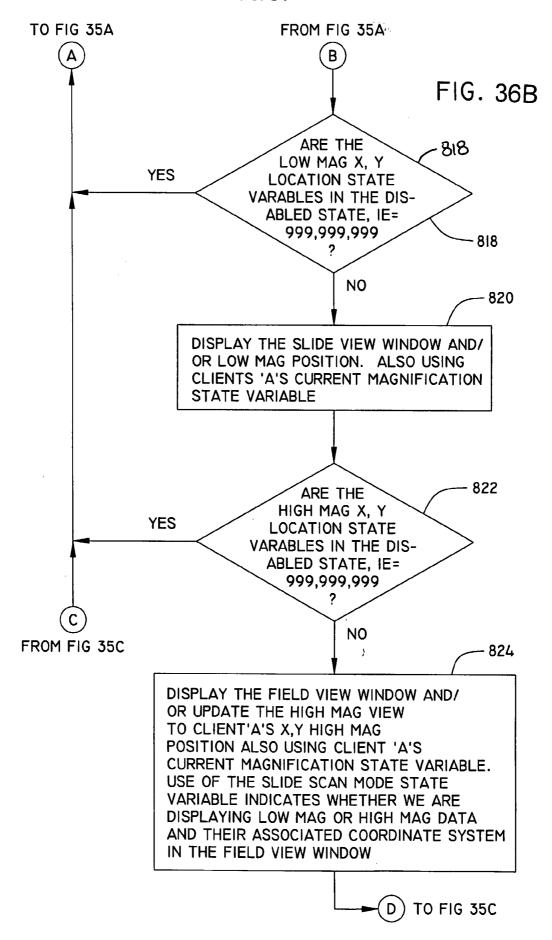
FIG. 34

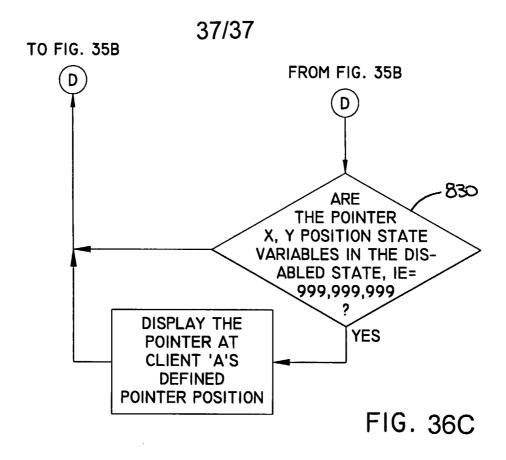
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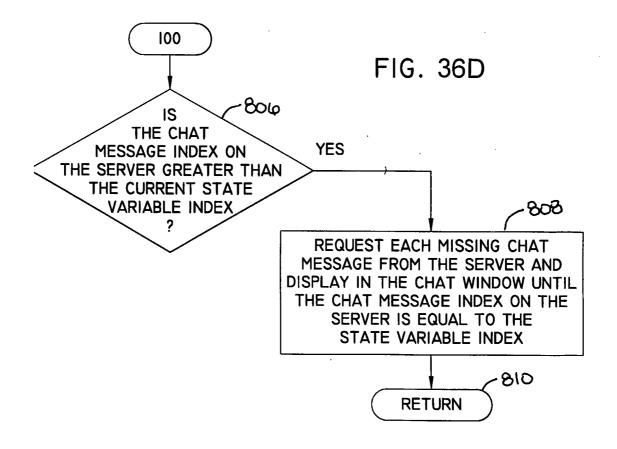




36/37







INTERNATIONAL SEARCH REPORT

International application No. **
PCT/US01/01782

A. CLASSIFICATION OF SUBJECT MATTER								
IPC(7) : Please See Extra Sheet								
US CL: Please See Extra Sheet. According to International Patent Classification (IPC) or to both national classification and IPC								
	DS SEARCHED							
Minimum d	ocumentation searched (classification system followed	by classification symbols)						
U.S. : 382/128, 129, 133, 134; 348/79; 359/109, 363, 368, 381, 391; 396/56, 429, 432								
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched								
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)								
C. DOC	UMENTS CONSIDERED TO BE RELEVANT							
Category*	Citation of document, with indication, where app	propriate, of the relevant passages	Relevant to claim No.					
X	US 5,297,034 A (WEINSTEIN) 22 document.	March 1994, the whole	1-28					
X	US 5,793,969 A (KAMENTSKY ET whole document.	AL) 11 August 1998, the	1-14, 29-50, 87- 94, 101-106					
X	US 5,993,001 A (BURSELL ET AL) 30 document.	0 November 1999, the whole	1-14, 29-50, 101-106					
X,P	US 6,091,930 A (MORTIMER ET AL document.	L) 18 JULY 2000, the whole	64, 86, 65-84, 95- 106					
X,P	US 6,148,096 A (PRESSMAN ET A whole document.	L) 14 November 2000, the	1-14, 29-50, 51- 63, 87-93					
X Purther documents are listed in the continuation of Box C. See patent family annex.								
	pecial categories of cited documents:	"T" later document published after the int date and not in conflict with the app the principle or theory underlying th	lication but cited to understand					
to	be of particular relevance relier document published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step						
"L" do	necument which may throw doubts on priority claim(s) or which is ted to establish the publication date of another citation or other	when the document is taken alone "Y" document of particular relevance, the	ne claimed invention cannot be					
"O" do	pecial reason (as specified) Document referring to an oral disclosure, use, exhibition or other eans	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						
"P" do	ocument published prior to the international filing date but later than se priority date claimed	"&" document member of the same patent family						
Date of the	c actual completion of the international search CH 2001	Date of mailing of the international se 20 APR2						
Name and Commission	mailing address of the ISA/US oner of Patents and Trademarks	Authorized officer SHERVIN NAKHJANANUGENIO JOGAN. Telephone No. (703) 305 3960						
Box PCT	on, D.C. 20231	SHERVIN NAKHJATANIGENIA SMALA						
Egosimile 1	No. (703) 305-3230	Telephone No. (703) 305 3990	10 900					

INTERNATIONAL SEARCH REPORT

International application No. PCT/US01/01782

claim No

INTERNATIONAL SEARCH REPORT

International application No. PCT/US01/01782

A. CLASSIFICATION OF SUBJECT MATTER: IPC (7):
G06K 9/00; H04N 7/18; G02F 1/00; G02B 21/36, 21/00, 21/26; G03B 17/00; G01N 11/00
A. CLASSIFICATION OF SUBJECT MATTER: US CL :
382/128, 129, 133, 134; 348/79; 359/109, 363, 368, 381, 391; 396/56, 429, 432