IMAGE DATABASE AND IMAGE ANALYSIS OF CHROMOSOME INFORMATION SHIN-ICHI TOYABE . [ET AL.] pdf

1: Chromosome Nanoscience and Technology - CRC Press Book

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Especially when the image signals are faint to such an extent that the intensity of the luminance signal is based on the Poisson distribution, it is effective to perform a smoothing processing for each of the probability distributions of the signals and the noises by a test of a uniformity of the Poisson distribution, enabling a clear and denoised image to be obtained. The International Application was published in Japanese on Jul. As a result, pepper-and-salt noise patterns can be seen over the length and breadth of the image. In general, as a method for removing noises, a method for smoothing signals in the neighboring region of each pixel is available. A moving average method, a Gaussian-filter method, a median-filter method and so on are generally available as the conventional smoothing methods. In the moving average method, however, a smoothing quality varies depending on the number of neighboring pixels to be taken in averaging. If the neighboring pixels are taken in large number, a boundary line of a target signal becomes blurred, whereas if in small number, noises remain. In the Gaussian-filter method as well, a weighted average method is implemented by weighted averaging according to the Gaussian distribution with neighboring pixels of the pixel of interest included, and thus a boundary line of a target signal becomes also blurred if the neighboring pixels are adopted in large number, whereas noises still remain if adopted in small number. Similarly, the same problem as described above occurs in the median-filter method, because a median value of signals in neighboring pixels of a pixel of interest is adopted as a signal of the pixel of interest, and hence the smoothing quality is varied depending on the number of the neighboring pixels to be taken for the pixel of interest. According to the above-described smoothing method, it is necessary to preliminary determine the number of neighboring pixels to be taken for a pixel of interest, and denoising effect varies depending on target images and hence the appropriate number of the neighboring pixels is difficult to determine. As an alternative method, one method is disclosed in which a noise standard deviation is expected in advance, and if the absolute value of the difference between the value of the neighboring pixel and the value of the pixel of interest is less than a numerical constant set to two times the expected noise standard deviation, then the value of the neighboring pixel replaces the original value of the pixel of interest see Patent Document 1. This method does not require preliminarily determining the number of the neighboring pixels to be taken for the pixel of interest, yet it is necessary to expect the noise standard deviation in advance. Consequently, this method has a drawback that if the standard deviation is expected to be large, an image will lose its clearness, whereas if expected to be small, the noise reduction will become ineffective. Further, another method is proposed, in which the processing is executed such that all pixel signals on an image are converted into binary data to extract edges from each of image data in each bit and the image data of lower-order bits than a bit specified when the number of the edges extracted is found to be less than a predetermined value are determined as noises that are to be removed or to be replaced by a certain value see Patent Document 2. This method is effective only when the noise level is low and is uniform approximately over the length and breadth of the image. Besides, it is generally known that a low-pass filter processing to remove high-spatial-frequency components may be applied to such noises that are scattered in fines over the length and breadth of an image. According to this process, however, there is a possibility that even true components among the high-spatial-frequency components may be deleted together with the noise components. Japanese Unexamined Patent Publication No. It is another object of the present invention to provide a computer-readable recording medium on which an image processing program according to the method is recorded. According to a first aspect of the present invention, there is provided an image processing method having the steps of: In the first aspect of the invention, noises are not judged by a threshold value of a certain constant. Due to the luminance signal of a pixel having a stochastic fluctuation, if the

luminance signal in a certain region can be regarded as following the same probability distribution by testing whether it follows the same probability distribution or not, the region is determined as a range of the fluctuation to successively expand the region, thereby providing a method for determining the range of a uniformity of the distribution. Thus, the image processing method can be provided. Consequently, there is no need to preset the size of a neighboring region, thereby allowing for obtaining a noise-reduced clear image. According to a second aspect of the present invention, there is provided an image processing method, including the steps of: When pixel signals and noise signals are so extremely faint as to be at a level where the number of photons ranging from only several to several dozens is detected, intensities of luminance signals are in a discrete state. In such a case, the intensities of the luminance signals are regarded as following the Poisson distribution. Accordingly, the point of interest and its neighboring region that is regarded as following the same probability distribution can be estimated by applying a likelihood ratio test. As a result, a noise-reduced clear image can be obtained by implementing the process even if the image signals are faint. According to a third aspect of the present invention, there is provided an image processing method according to the first or second aspect, in which when said test region is expanded gradually from said point of interest toward a surrounding area, said expanded test region is rejected to set the last test region as said neighboring region if an average value of observed values for luminance signals of respective pixels belonging to said expanded test region exceeds or falls short of a given confidence limit value. When a difference between true luminance values of the point of interest and surrounding pixels is small, a type II error may occur. However, if the average value of the observed values has exceeded or fallen short of the predetermined confidence limit value when the test range has been expanded, the size of the tested range at that time is rejected to set the last tested range as the neighboring region, thus being capable of restraining the type II error. According to a fourth aspect of the present invention, there is provided an image processing device having: According to a fifth aspect of the present invention, there is provided an image processing device including: According to a sixth aspect of the present invention, there is provided an image processing device according to the fourth or the fifth aspect, wherein when said test region is expanded gradually from said point of interest toward a surrounding area, said expanded test region is rejected to set the last test region as said neighboring region if an average value of observed values for luminance signals of respective pixels belonging to said expanded test region exceeds or falls short of a given confidence limit value. According to a seventh aspect of the present invention, there is provided a computer-readable recording medium on which an image processing program is recorded, wherein said image processing program has the steps of: In order to implement the image processing method of the foregoing first aspect using a common computer, the image processing program is provided in the form of a computer-readable recoding medium. As a result, the image processing program is so convenient that a noise-reduced clear image can be obtained both online and offline. According to an eighth aspect of the present invention, there is provided a computer-readable recording medium on which an image processing program is recorded, wherein said image processing program having steps of: In the case of image signals comprising faint signals in which intensities of luminance signals are regarded as following the Poisson distribution, it is effective to discriminate a region of true image signals from a region of noises by the test of the Poisson distribution to implement the smoothing processing with different parameters for each of the regions, thereby leading to a remarkable effect of obtaining a noise-reduced clear image. According to a ninth aspect of the present invention, there is provided a computer-readable recording medium according to the seventh or eighth aspect, wherein when said test region is expanded gradually from said point of interest toward a surrounding area, said expanded test region is rejected to set the last test region as said neighboring region if an average value of observed values for luminance signals of respective pixels belonging to said expanded test region exceeds or falls short of a given confidence limit value. According to the present invention, it is tested by a statistical method whether luminance signals around a point of interest are distributed according to the same probability distribution as that of the point of interest or not, with respect to luminance signals of the respective pixels constituting an image, to thereby determine a region where the

luminance signals can be regarded as being distributed according to the same probability distribution and then the data within the region are smoothed. Hence, such effects are exerted that there is no need to preliminarily set parameters such as a size of a neighboring region and thus a noise-reduced clear image is obtainable. The resultant image, however, often remains unclear. Hereunder is a detailed description of an image processing method according to the present invention with reference to appended drawings. If not completed yet, a new pixel of interest is set in step ST2. In an initial condition, no pixel has undergone the image processing yet, and hence the image processing advances from the step ST1 to the step ST2, and a certain pixel such as the one located at a left-hand corner of the image is set as a pixel of interest. In step ST4, it is tested whether or not the intensities of the five signals described above are in accordance with the distribution function at a suitable significance level, e. Namely, in the present embodiment, the test is implemented, using a pixel range shown in FIG. The test implemented here is a so-called uniformity test of the Poisson distribution and is implemented using a likelihood ratio.

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2: OMIM Entry - * - ZETA-CHAIN-ASSOCIATED PROTEIN KINASE; ZAP70

We have constructed a database system named CHRONIS (CHROmosome and Nano-Information System) to collect images of animal chromosomes and related nanotechnological information. CHRONIS enables rapid sharing of information on chromosome research among cell biologists and researchers in other fields.

This article has been cited by other articles in PMC. We previously reported that bone fractures and intracranial haemorrhages were two major fall-related injuries and that risk assessment score for osteoporotic bone fracture was significantly associated not only with bone fractures after falls but also with intracranial haemorrhage after falls. Based on the results, we tried to establish a risk assessment tool for predicting fall-related severe injuries in a hospital. We found that fall risk score and fracture risk score were the two significant factors, and we constructed models to predict fall-related severe injuries incorporating these factors. When the prediction model was applied to another independent dataset, the constructed model could detect patients with fall-related severe injuries efficiently. The new assessment system could identify patients prone to severe injuries after falls in a reproducible fashion. Background Falls are very common adverse events in a hospital and can cause severe injuries. These injuries may lead to prolonged length of hospital stay and additional healthcare costs. This situation results in psychological distress for and complaints from the patients with possible litigation from the patients and their families. Several clinical characteristics have been shown to be associated with increased incidence of falls in a hospital, and various risk assessment tools for inpatient falls have been developed through integration of these risk factors. Thomas Risk Assessment Tool in Falling elderly inpatients tool is commonly used as a fall risk assessment tool in clinical practice. One of the most important reasons for preventing falls is to prevent serious injuries in patients at high risk for injuries after falls Gates, Risk assessments tools are needed to predict falls that are likely to be complicated with serious injuries. We previously reported that the most frequent serious injury after falls was bone fracture and the second most frequent serious injury was intracranial hemorrhage and that these two kinds of injuries accounted for almost all severe injuries after falls Toyabe, , On the basis of these findings, we tried to construct risk assessment models to predict serious injuries after falls by integrating various identified risk factors including risk assessment scores for falls and bone fractures. We then selected the most appropriate model by comparing the performances of the constructed prediction models and validated the performance of the model by using another independent dataset. There are 23 clinical departments and the service area of the hospital as a tertiary care hospital covers all districts in Niigata Prefecture, which has a population of 2 During that period, 29 patients were admitted to the hospital, but patients were excluded from the study because of missing data. Finally, data were obtained from 29 patients patient-days including 13 females and 15 males. The data warehouse includes data for gender, age, body weight, height, history of bone fractures, smoking habit, alcoholic consumption, prescriptions of various drugs, coexisting illness, admission day, discharge day, background disease based on ICD codings, admission ward, and diagnosis and treatment department. The drugs that may cause hemorrhagic tendency include anticoagulants and antiplatelets. Information on risk factors for falls was obtained from medical charts of the patients and fall assessment records completed by attending nurses at admission. A score of more than two was considered high risk for falls in a Japanese setting, when the score was calculated on the basis of the original method Toyabe, These risk factors include age, prior fragility fracture, parental history of hip fracture, smoking, use of systemic corticosteroids, excess alcohol intake and rheumatoid arthritis. Medical staff who find inpatients who have fallen are encouraged to report the events by using an online intra-institutional incident reporting system. The incident reports contain information on degree of injury, potential causative factors of the incident, type of events and essential information on the event such as the name of the patient involved in the event, the name of the medical staff involved, the exact time and place, detailed description of the course of the event, action against the event taken by medical staff and outcome of the event. It is easy to identify fall-related reports

among all reports according to information on the category of reports. When the physician who is responsible for the fallen patient finds signs or symptoms that suggest severe injuries such as bone fracture or intracranial hemorrhage, the physician orders an x-ray examination of the affected area or computed tomography scan of the head through image order entries. Therefore, text data of image order entries are expected to contain information on fall-related severe injuries in a more concentrated manner compared with incident reports and to contain information on fall events that are not reported in incident reports. The text data of image order entries contain information on possible diagnosis, short clinical course and purpose of the order. Severe injuries after falls correspond to cases in which the degree of harm is moderate, serious or fatal in terms of the framework of the international classification of patient safety, and they include bone fractures and intracranial hemorrhage WHO, Pain, bruises, isolated hematomas and superficial wounds were excluded from severe injuries. Peripheral bone fractures were included only when they were verified by radiographic examination. Vertebral compression fractures were included only when they were not detected by radiographic examination before the falls but were first detected by radiographic examination after falls. Diagnosis of intracranial hemorrhage was made by a computed tomography scan or magnetic resonance imaging. The first method was the difference in proportions test and multiple logistic analyses in which time between admission and falls was not considered in the analysis. In multiple logistic analyses, significant risk factors were detected by using the stepwise selection method. The second method was survival analyses in which time between admission and falls was considered as survival time. The reason why we used survival analysis is that length of stay in acute care hospitals in Japan is very long compared with that in other countries, and the length of hospital stay should affect frequency of inpatient falls OECD, Discharge from the hospital without falls was considered as censoring. The Kaplan-Meier method was used for the analyses, and the logrank test was used to examine whether each risk factor was significantly associated with falls. The stepwise selection method was used to select significant risk factors in the multivariate analyses. The regression coefficients were divided by the smallest coefficient and then rounded to the nearest integer. Each individual risk score was added to form a total risk score for severe injuries after falls. The cut-off value to differentiate high and low risks for severe injuries after falls was determined on the basis of the Youden index from the receiver operating characteristics ROC curve. In the second method, each risk factor was scored on the basis of the regression coefficient of multivariate logistic regression analyses and the subsequent procedure was the same as that in the first method. In the third method, cut-off values were set for all significant factors based on the Youden index from the ROC curve. When all significant factors exceed their cut-off values, the patient was considered as being at high risk for severe injuries after falls. The three models were applied to the development dataset, and the most appropriate model was selected in terms of sensitivity, specificity, positive predictive value PPV , negative predictive value NPV and F-measure. F-measure is a harmonic mean of sensitivity and PPV. Based on the results, we estimated necessary sample size for test dataset that was used to validate the selected model for the risk assessment tool. The selected model was then applied to the test dataset to ascertain whether the results obtained from analyses of the development dataset were reproducible. The incidences of severe injuries after falls were compared in high-risk and low-risk patients using the differences in proportions test and logrank test. A p-value less than 0. Rate of occurrence of severe injuries after falls was calculated as 0. The injuries included bone fractures 33 cases, The other three cases were disruption of surgical wounds, rupture of a liver tumor and facial laceration with fracture of the teeth. These three cases were excluded from subsequent analyses because number of patients who belonged to these categories of injury was small. Therefore, the 44 cases were considered as cases of fall-related severe injuries in the development dataset. Bone fractures included 28 cases of peripheral bone fracture Table 1 Results of univariate analysis of risk factors for severe injuries after falls Factors Non-fallers and fallers without severe injuries Logrank test.

IMAGE DATABASE AND IMAGE ANALYSIS OF CHROMOSOME INFORMATION SHIN-ICHI TOYABE . [ET AL.] pdf

3: JoVE | Peer Reviewed Scientific Video Journal - Methods and Protocols

[et al.] -- Dynamic and functional analysis of chromosomal proteins / Nobuko Ohmido [et al.] -- Development of a sustainable chromosome imaging database / Kenji Taniguchi [et al.] -- Image database and image analysis of chromosome information / Shin-ichi Toyabe.

Methods and kits for generating libraries of sequences are provided. Methods of using selectively enriched non-random polynucleotide sequences for detection of fetal aneuploidy are provided. No new matter has been added. Sequencing a large number of polynucleotides to generate sufficient data for fetal aneuploidy detection can be expensive. Methods for randomly enriching fetal nucleic acids in cell-free maternal sample have been described, including enriching nucleic acids based on size, formaldehyde treatment, methylation status, or hybridization to oligonucleotide arrays. There is a need for a means of selectively enriching non-random fetal and maternal polynucleotide sequences in a way that facilitates aneuploidy detection by massively parallel sequencing techniques and increases the sensitivity of aneuploidy detection. In one embodiment, said selectively enriching comprises performing PCR. In another embodiment, said selectively enriching comprises linear amplification. In another embodiment, said selectively enriching comprises enriching at least 1, 5, 10, 50, , or non-random polynucleotide sequences from a first chromosome. In another embodiment, said selectively enriching comprises enriching at least 1, 10, or polynucleotide sequences from one or more regions of a first chromosome, wherein each region is up to 50 kb. In another embodiment, said non-random polynucleotide sequences comprise sequences that are sequenced at a rate of greater than 5-fold than other sequences on the same chromosome. In another embodiment, said non-random polynucleotide sequences each comprise about bases. In another embodiment, said cell-free DNA sample is a maternal sample. In another embodiment, said maternal sample is a maternal blood sample. In another embodiment, said maternal sample comprises fetal and maternal cell-free DNA. In another embodiment, said cell-free DNA is from a plurality of different individuals. In another embodiment, said sequencing comprises Sanger sequencing, sequencing-by-synthesis, or massively parallel sequencing. In another embodiment, said aneuploidy is trisomy 21, trisomy 18, or trisomy In another embodiment, said aneuploidy is suspected or determined when the number of enumerated sequences is greater than a predetermined amount. In another embodiment, said predetermined amount is based on the amount of enumerated sequences from a control region. In another aspect, a method is provided comprising: In another embodiment, each of said oligonucleotides has a substantially similar thermal profile. In another embodiment, said polynucleotide sequences each comprise about bases. In another embodiment, said polynucleotide sequences are from a cell-free DNA sample. In another embodiment, said polynucleotide sequences are from a maternal sample. In another embodiment, said polynucleotide template is a chromosome suspected of being aneuploid. In another embodiment, said polynucleotide template is chromosome In another embodiment, the polynucleotide template is a chromosome not suspected of being aneuploid. In another embodiment, said polynucleotide template is chromosome 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 14, 15, 16, 17, 19, 20, or In another embodiment, said rate is at least 10 or fold. In another embodiment, there are at least 7, 10, 17, or 27 sequence reads for the sequences that were sequenced at a higher frequency rate. In another embodiment, said selectively enriching comprises performing PCR. In another embodiment, the method further comprises a step of determining the presence of absence of fetal aneuploidy based on said sequencing In another aspect, a method for identifying polynucleotide sequences for enrichment in a polynucleotide template is provided comprising: In one embodiment, said polynucleotide sequences are from a cell-free DNA sample. In another embodiment, said sequencing coverage rate is at least or fold. In another embodiment, there are at least 7, 10, 17, or 27 reads for the polynucleotide sequences that were sequenced at a higher frequency rate. In another embodiment, said identified polynucleotide sequences are used to determine the presence or absence of fetal aneuploidy. In another aspect, a kit comprising a set of oligonucleotides that selectively amplify one or more regions of a

chromosome is provided, wherein each of said regions is sequenced at a rate of greater than 5-fold than other regions of the chromosome. In one embodiment, each of said oligonucleotides in the kit is part of an oligonucleotide pair. In another embodiment, said set of oligonucleotides comprises at least oligonucleotides. In another embodiment, an oligonucleotide in each oligonucleotide pair comprises sequence identical to sequence in an oligonucleotide in the other pairs and sequence unique to that individual oligonucleotide. In another aspect, a method for sequencing cell-free DNA from a maternal sample is provided comprising: In one embodiment, said sequencing comprises sequencing-by-synthesis. In another embodiment, said method further comprises bridge amplification. In another embodiment, said sequencing comprises Sanger sequencing. In another embodiment, said sequencing comprises single molecule sequencing. In another embodiment, said sequencing comprises pyrosequencing. In another embodiment, said sequencing comprises a four-color sequencing-by-ligation scheme. In another embodiment, said sequenced enriched sequences are used to determine the presence or absence of fetal aneuploidy. In another embodiment, the isolated genomic DNA are sequenced by a method comprising bridge amplification, Sanger sequencing, single molecule sequencing, pyrosequencing, or a four-color sequencing by ligation scheme. In another embodiment, the isolated genomic regions comprise at least , , or 10, different sequences. In another embodiment, the regions are present at a rate greater than fold, fold, fold. In another embodiment, the sequence is a single amplicon. In one embodiment, the oligonucleotides hybridize to the sequences under mild hybridization conditions. In another embodiment, the oligonucleotides have similar thermal profiles. In one embodiment, the first set of oligonucleotide pairs comprises sequence that distinguishes polynucleotides in one sample from polynucleotides in another sample. In another embodiment, said first set of oligonucleotide pairs comprises sequence that distinguishes polynucleotides in one sample from polynucleotides in another sample and sequence that extends the length of the product. In another embodiment, said polynucleotide sequences are enriched sequences. In another aspect, a method for labeling enriched polynucleotides in two or more samples that allows identification of which sample the polynucleotide originated is provided, comprising: In another aspect, a kit is provided comprising a a first set of oligonucleotide primer pairs comprising: In one embodiment, the common region in the first set of primers comprises sequence that distinguishes polynucleotides in one sample from polynucleotides in another sample. In another embodiment, the common region in the first set of primers comprises sequence that distinguishes polynucleotides in one sample from polynucleotides in another sample and sequence that extends the length of the product. In another aspect, a kit is provided comprising: A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which: The non-random sequences can be enriched from a maternal sample for use in detecting a fetal abnormality, for example, fetal aneuploidy. In one embodiment, the selection of non-random polynucleotide sequences for enrichment can be based on the frequency of sequence reads in a database of sequenced samples from one or more subjects. In another embodiment, the selection of polynucleotide sequences for enrichment can be based on the identification in a sample of sequences that can be amplified in one or more regions of a chromosome. The selection of polynucleotide sequences to enrich can be based on knowledge of regions of chromosomes that have a role in aneuploidy. The selective enrichment of sequences can comprise enriching both fetal and maternal polynucleotide sequences. In another aspect, the provided invention includes methods for determining the presence or absence of a fetal abnormality comprising a step of enriching non-random polynucleotide sequences from a maternal sample. The non-random polynucleotide sequences can be both fetal and maternal polynucleotide sequences. In another aspect, the provided invention comprises a kit comprising oligonucleotides for use in selectively enriching non-random polynucleotide sequences. In another aspect, the provided invention includes methods for generating a library of enriched polynucleotide sequences. A library can be generated by the use of one or more amplification steps, which can introduce functional sequences in polynucleotide sequences that have been selectively enriched. In one aspect, a method for

determining the presence or absence of fetal aneuploidy is provided comprising selectively enriching non-random polynucleotide sequences e. The selectively enriching step can comprise amplifying nucleic acids. Amplification can comprise performing a polymerase chain reaction PCR on a sample of nucleic acids. Amplification can be linear amplification, wherein the number of copies of a nucleic acid increases at a linear rate in a reaction. The selectively enriching step can comprise a hybridization step. The hybridization can occur on a solid support. Some polynucleotide sequences from a sample comprising nucleic acids e. These sequences may be more likely to be enriched by, for example, amplification methods. Identifying and enriching these polynucleotide sequences can reduce the number of nucleic acids that need to be analyzed to determine the presence or absence of fetal aneuploidy. This enrichment can reduce the cost of aneuploidy determination. In one embodiment, the non-random polynucleotide sequences that are selectively enriched can comprise sequences that are sequenced at a frequency of greater than at least 2-, 3-, 4-, 5-, 6-, 7-, 8-, 9-, , , , , , , , , , , , , or fold than other sequences on the same chromosome in a database of sequence information. The sequencing rate data can be derived from a database of enumerated polynucleotide sequences, and the database of enumerated polynucleotide sequences can be generated from one or more samples comprising non-maternal samples, maternal samples, or samples from subjects that are pregnant, have been pregnant, or are suspected of being pregnant. The samples can be cell-free nucleic acid e. The subjects can be mammals, e. The enumerated sequences can be derived from random, massively parallel sequencing of samples, e. Patent Application Publication Nos. Techniques for massively parallel sequencing of samples are described below. The database can comprise sequence information from samples from at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 30, 40, 50, 60, 70, 80, 90, , , , , , , , , , , , , , , , 10,, ,, or 1,, different subjects. The data can be processed to indicate the overlap of individual polynucleotide sequences from the samples from the subjects FIGS. The database can indicate the frequency with which one or more nucleotides at a specific chromosome position is sequenced among the samples. The length of the sequence that can overlap can be at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, , , , , , , , , or bases. The frequency of sequencing of one or more nucleotides at a first position of a chromosome can be compared to the frequency of sequencing of one or more other nucleotides at a second position on the chromosome to determine the fold frequency at which the first position was sequenced relative to the second position. The sequence polynucleotide sequence or base that is sequenced at a higher frequency can be sequenced at least 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 35, 40, 45, 50, 60, 70, 80, 90, , , , , , , , , , , , , , , , 10,, ,, or 1,, times in one or more samples in the database. In one embodiment, a method for identifying polynucleotide sequences for enrichment in a polynucleotide template is provided comprising sequencing a plurality of polynucleotide sequences from the polynucleotide template, enumerating sequenced polynucleotide sequences, and identifying one or more sequenced polynucleotide sequences that are sequenced or that have a coverage rate at least 5-fold greater than a second set of polynucleotide sequences. In another aspect, one or more unique isolated genomic DNA sequences are provided, wherein said genomic DNA sequences comprise regions that are sequenced at a rate greater than 5-fold than other regions of genomic DNA.

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Comparison between their respective elasticity distributions e. In the SPM experiments, the force curves are obtained along whole single human chromosomes in culture medium. This method enables visualization of the topographic and elasticity images of the chromosomes, taking into account the effect of the finite thickness of the samples on the estimation of elasticity. Some ordered structure or a coarse nonhomogeneity is clearly visible in the elasticity image. It is considered that the domain structure reflects a robust higher-ordered structure such as the arrangement of the G-bands. The unfixed human chromosomes were stretched by a micromanipulator in hexylene glycol buffer. This enables, by stretching, elasticity mapping of the chromosome and examination of its morphology of a wound filament. Nucleic Acids Res 3: Eur Biophys J Arch Histol Cytol Phys Rev Lett Jpn J Appl Phys Cytogenet Genome Res Exp Cell Res Cell Motil Cytoskeleton J Electron Microsc During cell division, the mitotic chromosome forms a highly condensed structure, and distributes the genetic information to two daughter cells evenly and accurately. Therefore, the formation of a higher order chromosomal structure is an indispensable aspect of its vital activity. However, it has only been possible to observe the macro structure, because chromosome research has been largely carried out by optical or electron microscopy see also Part II. Recently, genomic research that centers on DNA has advanced prominently. Therefore, a new analytical technique that can include these spatially distributed elements is required for advanced research on chromosomes. For example, the chromosome could be finely fractionated by a probe for atomic force microscopy AFM , then these parts distributed to each chamber of an array, and DNA would be detected by using a suitable method, such as polymerase chain reaction PCR amplification see also Chapter 3. Since the development of AFM in , it has contributed to research within various fields in physics, chemistry and biology, as a powerful tool that enables the visualization and analysis of a specific region of a molecule, from micrometer to nanometer in scale [2,3]. In addition to collecting surface information of materials, through various improvements AFM is expected to develop as a nanoscale fabrication tool, in connection with dip-pen lithography and anodic oxidation [4]. To mechanically modify solid materials, such as semiconductors and resist films, the dynamic plowing technique using an AFM tip has been reported [5â€”7]. As an application for biological samples, dissections of chromosomes and DNA using a conventional pyramidal AFM probe have also been reported by several groups [8â€”15]. Thus, there is no longer any doubt that AFM has become an important device to aid research in nanotechnology. In our research, we focused on the possibility of nanoscale physical and mechanical operations using AFM. Several dissection and manipulation methods have been developed for analyzing the relationships between three-dimensional structure and chromosomal information. In this report, we attempted the physical dissection of a chromosome through AFM operation, as a first step toward developing our chromosome chip. As an initial step, we were able to achieve the physical dissection of a human metaphase chromosome with the conventional probe, which has a pyramidal wedge-shaped tip [15]. After dissection, the chromosomal inner structures were exposed around the dissected regions and topographic profiles in the section were then obtained with a carbon nanotube probe, under ambient conditions. A cross-sectional analysis revealed that nanoscale globular structures were observed in the gap of the dissected region. However, it has been problematic to apply a conventional probe to chromosome dissection because the chromosome surface was often scarified, with damage by the contact of the wedge-shaped probe tip. The conventional AFM probe limited our range of application as a result of its shape and material properties. Therefore, the development of a suitable and novel probe for AFM manipulation at the nanoscale has been in demand. Additionally, the novel probe would be required to simultaneously have both the functions of imaging and manufacturing. In

consideration of these points, we attempted to manufacture a knife-edged probe, as well as perform dissection of DNA and the chromosome [16]. It should be noted that it is desirable to collect the sample selectively after dissection with the knife-edged AFM probe. We made an attempt to develop a tweezer-type AFM probe, which has a high performance in imaging and collecting the biomolecules on the substrate under AFM operation [17,18]. In this chapter, the fabrication of AFM tweezers and their applications will be described [19]. The acute angle was The cantilever, which had the knife-edged probe, was joined with a silicon foundation to set on the cantilever holder for AFM operation. The actual measured values of the resonance frequency, Q value and free amplitude were The fabrication process was as follows: This device had two thin probes that were formed in the front of the silicon cantilever, with a vertical triangular shape. One functioned as an AFM imaging probe tip for the tapping mode, and was called the sensing probe. The other could be made to work as a tweezer, by closing the vertical face of the probe the movable probe. The principle of operation for the movable probe was based on the leverage of the thermal expansion actuator, which was assembled in the base of its cantilever and was actuated with DC electricity. Here, we assume the AFM tweezers are used in the tapping mode. If both of the resonance frequencies are the same, it is thought that the sample or substrate surface will be damaged by oscillation of the movable probe during the AFM imaging by the sensing probe. The resonance frequencies were therefore set to different values by making each probe a different length. This means that at the resonance frequency of the sensing probe, the amplitude of the movable probe will be smaller relative to that of the sensing probe. The sample surface can then be scanned using the sensing probe, without damage of the sample surface by contact with the movable probe. The resonance frequency of the sensing probe was set to be higher than that of the movable probe [17,18]. The starting material was a SOI wafer Si[]: Illustration of the design a and the principle of operation b of the AFM tweezers. The AFM image can be taken using the sensing probe. To capture the samples, the movable probe, which had the thermal expansion actuator, was operated by applying voltage. The actual measured values of the resonance frequencies of the sensing probe and the movable probe were The ohmic value of the thermal expansion actuator between the probe electrodes was 4. In addition, the displacement of the movable probe, which was actuated with the thermal expansion actuator, was magnified approximately 12 times. Human metaphase chromosomes were prepared from human lymphocytes, which were obtained from whole human peripheral blood according to standard protocols [21]. However, the chromosome samples adsorbed strongly to the substrate, and also included some elements of the cell other than the chromosomes. This chromosome sample was kindly donated by Prof. Uchiyama from Osaka University. After drying, the silicon substrate was rinsed with ultrapure water. First, procedures of imaging and dissection of dsDNA were attempted in order to investigate the properties of the knife-edged probe. The probe tip was withdrawn from the sample surface and while maintaining the same location, the operation mode was switched to contact mode without probe oscillation. The probe tip then again approached the same position of the sample surface. For determination of the dissection regions, the AFM probe was positioned using the Seiko vector scanning program. The probe tip was withdrawn once from the surface and again switched to the tapping mode, and the dissected DNA was then imaged. Several loading forces from to 0. From to 0. No dissection was observed at 0. Additionally, it was possible to continue imaging using the same probe after dissection [16]. After switching to the contact mode without probe oscillation, the dissection was performed at 0. The probe motion was controlled by the Seiko vector scanned program. After switching to the tapping mode again, the dissected DNA could be observed b. The same probe was used for the imaging and dissection procedures throughout this experiment. This value represents the probe amplitude reduction from the initial amplitude. For example, if the amplitude reference were set to â€”0. If the amplitude reference were set to â€”1. The calculation of the loading force in the tapping mode has been previously described by us [16]. After obtaining an AFM image of the chromosome, a series of single-line scans were performed to allow the use of several amplitude references during the scanning process. For the determination of the dissection regions, the AFM probe was positioned using the Seiko vector scanning program. No dissection was observed at amplitude references between â€”0.

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Below an amplitude reference of â€”1. The dissection was carried out, controlling amplitude reference, along the arrowed lines indicated in a. The oscillation amplitude of the probe was completely dampened to zero below an amplitude reference of â€”1. Then, the probe tip reached and touched the sample surface. The loading forces of each amplitude reference were 1 â€”0. After dissection, the dissected chromosome was observed with the same knife-edged probe. The cross-sectional analyses are shown in b. The depth of the dissection area was The dissection depths became greater as the amplitude reference was decreased below â€”1. Here, chromosome dissection was also achieved with the conventional AFM probe. However, chromosomal debris having a height of This debris, including DNA and several genes, was lost after the manipulation.

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5: Shinichi Morishita

Image Database and Image Analysis of Chromosome Information; Shin-ichi Toyabe, Takayuki Matsuto, Tatsuo Ushiki, and Kouhei Akazawa. Show More. Customer Reviews.

It is expressed predominantly in T and NK cells summary by Chan et al. The ZAP70 gene is expressed in T- and natural killer cells. They mapped the murine homolog to mouse chromosome 1 by the same method. They found that this phosphorylation site is distinct from the phosphorylation sites for other PTKs. Animals deficient in pre-TCR-alpha have few alpha-beta lineage cells but an increased number of gamma-delta T cells. These gamma-delta T cells exhibit more extensive TCR-beta rearrangement than gamma-delta T cells from wildtype mice. These observations are consistent with the idea that different signals emanating from the gamma-delta-TCR and pre-TCR instruct lineage commitment. Using confocal microscopy and biochemistry to analyze the initiation of signaling, Saint-Ruf et al. NK cells express both molecules, which associate with immunoreceptor tyrosine-based activation motifs ITAMs. Using mice deficient in both Zap70 and Syk, Colucci et al. The mutant cells expressed Nkg2d and were able to lyse targets with and without Nkg2d ligands in vitro and in vivo. However, wildtype cells, but not the double-deficient cells, responded to CD16 and Ly49d see cross-linking with increased cytotoxicity, suggesting that these 2 ITAM-bearing receptors are unable to signal in the mutant cells. Inhibitors of PI3K see or Src kinases blocked and, in combination, abrogated cytotoxic activity in the mutant cells, whereas inhibition of both kinases was required to reduce wildtype NK activity. Moreover, ZAP70 expression by itself can be used as a prognostic marker. The mutation was present in heterozygous state in the parents and 3 unaffected sibs. In 3 sibs, 2 boys and a girl, with IMD48, Chan et al. In a female infant with IMD48, Elder et al. The parents and unaffected sibs were heterozygous for the mutation. Chronic Lymphocytic Leukemia Rassenti et al. In studies of patients with CLL, Rassenti et al.

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6: Publications Authored by Akazawa Kouhei | PubFacts

We have constructed a database system named CHRONIS (CHROmosome and Nano-Information System) to collect images of animal chromosomes and related nanotechnological information.

This loop is not found in tissues where the gene is not expressed. Some TADs are transcriptionally active, while others are repressed. The result shows that the orientation of CTCF binding motifs in an enhancer-promoter loop should be facing to each other in order for the enhancer to find its correct target. Hi-C interactions among all chromosomes from G human kidney cells, as plotted by the my5C software. Heat map visualization illustrating the bipartite structure of the mouse X chromosome, as plotted by Hi-Browse. Heat map visualization of a 3 Mbp locus chr4: Circular plot of the bipartite mouse X chromosome, generated by the Epigenome Browser. As such, specific analysis packages exist for each experiment type. Fit-Hi-C [3] is a method based on a discrete binning approach with modifications of adding distance of interaction initial spline fitting, aka spline-1 and refining the null model spline The result of Fit-Hi-C is a list of pairwise intra-chromosomal interactions with their p-values and q-values. Hi-C data visualization tools are recently reviewed in Gurken et al. The 3-D organization of the genome can also be analyzed via eigendecomposition of the contact matrix. Each eigenvector corresponds to a set of loci, which are not necessarily linearly contiguous, that share structural features. An interaction between two loci must be confirmed as specific through statistical significance testing. Currently, regulatory motifs on the long-range chromatin interactions have not been studied extensively. Several studies have focused on elucidating the impact of DNA motifs in promoter-enhancer interactions. For genome-scale motif analysis, in , Wong et al. In the next year, Wong published another article reporting 18, motif pairs in 6 human cell lines. Cancer genome analysis[edit] The 3C-based techniques can provide insights into the chromosomal rearrangements in the cancer genomes. Specifically, they found a bifurcation of a single TAD normal into 2 distinct smaller TADs cancer caused by a common deletion on 17p Ferhat Ay et al.

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7: Chromosome conformation capture - Wikipedia

CHRONIS: an animal chromosome image database CHRONIS enables rapid sharing of information on chromosome research among cell biologists and researchers in other fields via the Internet. CHRONIS is also intended to serve as a liaison tool for researchers who work in different centers.

Researcher, IBM Japan Algorithm and Software for Biology Graduate courses: Efficient computer programs have made it possible to elucidate and analyze large-scale genomic sequences. Fundamental tasks, such as the assembly of numerous whole-genome shotgun fragments, the alignment of complementary DNA sequences with a long genome, and the design of gene-specific primers or oligomers, require efficient algorithms and state-of-the-art implementation techniques. We have been developing basic software implementation techniques for processing large-scale genome sequences. Primary results include the assembly of the medaka Mb and silkworm Mb genomes, an online tool for designing highly effective, target specific siRNA for human, mouse, rat, dog, and chicken genes siDirect , and a web site for multiplex genomic PCR primers on the human genome PrimerStation. The latter two software programs are widely used and incorporated into a couple of commercial products. Masahiro Kasahara and Shinichi Morishita. Large-scale genome sequence processing. Imperial College Press, pp. Teleosts comprise more than half of all vertebrate species and have adapted to a variety of marine and freshwater habitats. Their genome evolution and diversification are important subjects for the understanding of vertebrate evolution. Although draft genome sequences of two pufferfishes have been published, analysis of more fish genomes is desirable. We reported a high-quality draft genome sequence of a small egg-laying freshwater teleost, medaka Oryzias latipes. Medaka is native to East Asia and an excellent model system for a wide range of biology, including ecotoxicology, carcinogenesis, sex determination and developmental genetics. We found single nucleotide polymorphisms SNPs at an average rate of 3. Analyses based on the dense SNP information show a strict genetic separation of 4 million years Myr between the two populations, and suggest that differential selective pressures acted on specific gene categories. Four-way comparisons with the human, pufferfish Tetraodon , zebrafish and medaka genomes revealed that eight major interchromosomal rearrangements took place in a remarkably short period of 50Myr after the whole-genome duplication event in the teleost ancestor and afterwards, intriguingly, the medaka genome preserved its ancestral karyotype for more than Myr. The medaka genome browser is freely accessible on the Internet at http: Basic steps of genome assembly Chromosome Evolution in Vertebrates: Although several vertebrate genomes have been sequenced, little is known about the genome evolution of early vertebrates and how large-scale genomic changes such as the two rounds of whole-genome duplications 2R WGD affected evolutionary complexity and novelty in vertebrates. Reconstructing the ancestral vertebrate genome is highly nontrivial because of the difficulty in identifying traces originating from the 2R WGD. To resolve this problem, we developed a novel method capable of pinning down remains of the 2R WGD in the human and medaka fish genomes using invertebrate tunicate and sea urchin genes to define ohnologs, i. We validated the reconstruction using the chicken genome, which was not considered in the reconstruction step, and observed that many ancestral proto-chromosomes were retained in the chicken genome and had one-to-one correspondence to chicken microchromosomes, thereby confirming the reconstructed ancestral genomes. Our reconstruction revealed a contrast between the slow karyotype evolution after the second WGD and the rapid, lineage-specific genome reorganizations that occurred in the ancestral lineages of major taxonomic groups such as teleost fishes, amphibians, reptiles, and marsupials. Ten reconstructed proto-chromosomes in the vertebrate ancestor shown at the top are assigned distinct colors, and their daughter chromosomes in the gnathostome ancestor are distinguished by their respective vertical bars. In the genomes of the osteichthyan, teleost, and amniote ancestors, and human, chicken, and medaka genomes, genomic regions are assigned colors and vertical bars that represent correspondences of individual regions to the proto-chromosomes in the gnathostome ancestor from which respective regions originated. Unassigned blocks

are shown in the rightmost chromosome Un in the osteichthyan and amniote ancestors. Phenome for Budding Yeast: For comprehensive understanding of precise morphological changes resulting from loss-of-function mutagenesis, a large collection of 1 cell images was assembled from 91 micrographs of budding yeast disruptants of non-lethal genes. All the cell images were processed computationally to measure morphological parameters in individual mutants. We have recently made this morphological quantitative data available to the public through the Saccharomyces cerevisiae Morphological Database SCMD. Inspecting the significance of morphological discrepancies between the wild type and the mutants is expected to provide clues to uncover genes that are relevant to the biological processes producing a particular morphology. To facilitate such intensive data mining, a suite of new software tools for visualizing parameter value distributions was developed to present mutants with significant changes in easily understandable forms. In addition, for a given group of mutants associated with a particular function, the system automatically identifies a combination of multiple morphological parameters that discriminates a mutant group from others significantly, thereby characterizing the function effectively. These data mining functions are available through the World Wide Web at http: Image processing and data mining. B Superimposition of three micrographs for individual cells. D Several examples of morphological parameters. E Data mining processes. The medaka draft genome and insights into vertebrate genome evolution. Genome Research 17 9: High-dimensional and large-scale phenotyping of yeast mutants. Accelerated off-target search algorithm for siRNA. Avoiding Cartesian Products for Multiple Joins. Journal of the ACM, 44 1 , pp. Messages to Students Our primary interest is the research and development of fundamental theory and software for analyzing large-scale biological and medical data.

8: USB2 - Methods of fetal abnormality detection - Google Patents

The book consists of four main parts with 18 chapters: (1) devices for chromosome handling, (2) visualization of chromosomes at nano- and microlevels, (3) chromosomes as nanomaterials and (4) informatics of chromosome images.

9: OMIM Entry - # - IMMUNODEFICIENCY 48; IMD48

Shin-ichi Toyabe, Takayuki Matsuto, Tatsuo Ushiki and Kohei Akazawa: Image database and image analysis of chromosome information. Chromosome Nanoscience and Technology, CRC Press, FL, USA, pp,

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