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Introducción

A grosso modo:

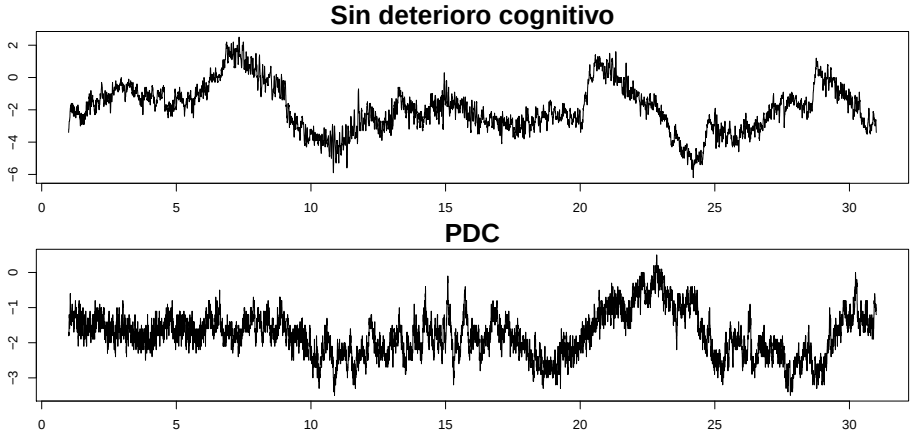
El objetivo de este trabajo es explorar la hipótesis de estacionariedad en registros polisomnográficos (EEG durante el sueño) en adultos mayores con Deterioro Cognitivo y de un grupo control.

Se describen diferencias entre [lo que arrojan los análisis para] registros de ambos grupos, que sugieren su posible utilización como marcadores de uso clínico.

El estudio y diagnóstico de una gran cantidad de enfermedades depende de nuestra habilidad para registrar y analizar señales electrofisiológicas.

Se suele asumir que estas señales son complejas: no lineales, no estacionarias y sin equilibrio por naturaleza. Pero usualmente no se comprueban formalmente estas propiedades.

Correlación inter-hemisférica durante el sueño MOR del Adulto Mayor con Deterioro Cognitivo.



Adaptado de Vázquez-Tagle y colaboradores (2016)

Capítulo 1

"Parte fisiológica"

Esta parte tiene partes copiadas del protocolo de Génesis: es temporal. Tiene mucho sentido que, como la tesis tiene enfoque matemático, deba citar el trabajo de personas enfocadas al área de fisiología. Dentro de poco escribiré mi propia revisión, aunque sea de la misma bibliografía.

1.1. Adulto mayor

Un adulto mayor, de acuerdo a la Organización Mundial de la Salud [2,4], son aquellas personas de 60 a 74 años y son considerados de edad avanzada, de 75 a 90 viejas o ancianas, y las que sobrepasan los 90 se les denomina grandes viejos o longevos. A todo individuo mayor de 60 años se le llamará indistintamente persona de la tercera edad. Un adulto mayor es un individuo que tenga de edad 60 años o más que viva en países en vías de desarrollo y de 65 años o más en los que viven en países desarrollados (3)

1.1.1. Envejecimiento

El envejecimiento es un proceso biológico que se caracteriza por la disminución de las funciones que hacen más susceptible al ser humano de padecer enfermedades y morir a consecuencia de ellas [1]. Durante esta etapa ocurren cambios biológicos,

psicológicos y sociales, normales e inherentes a todo individuo debido a que el organismo va perdiendo la habilidad para responder ante el estrés y mantener la regulación homeostática y metabólica, teniendo como consecuencia la disminución de las capacidades cognitivas y de sobrevivencia, reflejándose en la imposibilidad de adaptarse a situaciones de restricción o sobrecarga de cualquier tipo [4,9,10] A pesar de ser un proceso natural, no todos los individuos envejecen de la misma forma debido a que la calidad de vida y funcionalidad durante la vejez está relacionada con los aprendizajes adquiridos durante la infancia, adolescencia y edad adulta [11]. Los estilos de vida, los factores de riesgo, la accesibilidad a la educación y la promoción de la salud adoptados a lo largo de la vida son fundamentales al momento de llegar a esta etapa para que en el presente de esta se logre autonomía, a pesar de la edad y los padecimientos que se tengan [1]. En lo que concierne al ser humano se reconocen tipos diferentes de envejecimiento, entre los que sobresalen el individual y el demográfico o poblacional. El envejecimiento individual es el proceso de evolución que experimenta cada persona en el transcurso de su vida mientras que el envejecimiento poblacional es el incremento del número de adultos mayores con respecto al conjunto de la población a que pertenecen. Esta dualidad de interpretaciones hace que el análisis del envejecimiento deba hacerse en 2 planos diferentes: el social (con implicaciones y dimensiones del micromundo y macromundo) y el individual[12]. En este sentido, factores como el descenso de la mortalidad general, el aumento de la esperanza de vida y la reducción de la natalidad, dan lugar a un proceso conocido como envejecimiento poblacional, es decir, un proceso que implica una creciente participación de los adultos mayores en la estructura poblacional. Sin embargo, la población de jóvenes y adultos en edad productiva atraviesa por una etapa de crecimiento heredada de periodos de alta fecundidad del pasado.

1.2. Morfologá neuronal y cambios en la anatomía cerebral con la vejez (fisiología)

El envejecimiento considerado normal viene determinado por una serie de procesos moleculares, celulares, fisiológicos y psicológicos que conducen directamente al deterioro de funciones cognitivas, específicamente en la atención y memoria [19, 20].

En un principio se consideraba que el envejecimiento cerebral ocurría fundamentalmente por una muerte neuronal programada [8], sin embargo, estudios realizados con tejido cerebral post mortem de adultos mayores que en vida fueron sanos, mostraron que dicha muerte neuronal no alcanza un 10 % en su totalidad [10]. En este sentido, los cambios morfolgicos que sufren las neuronas durante el envejecimiento son abundantes, observándose una importante disminución de la arborizaciń dendrítica así como en la densidad y volumen [14]. La disminución en la arborización dendrítica y de las espinas dendríticas de las neuronas piramidales de la corteza prefrontal, temporal superior, pre central y occipital [14]. Dichas alteraciones morfológicas conducen durante el envejecimiento a una disminución de la densidad sináptica y a una desmielinización axónica en neuronas de la neocorteza [25].

Con el paso del tiempo, la organización anátomo-funcional del cerebro sufre modificaciones que traen como consecuencia la afectación de diferentes capacidades cognitivas, sin embargo, la vulnerabilidad de los circuitos neuronales ante los procesos que ocurren durante el envejecimiento no suceden de forma homogénea en todo el cerebro [14].

Por otro lado, la relevancia del estudio de los cambios anatómicos asociados al envejecimiento fisiológico ha ido aumentando al permitir evaluar como dichos cambios se correlacionan con el deterioro funcional y cognitivo que caracteriza a las personas mayores, facilita la identificación de estadios tempranos de diferentes patologías neurodegenerativas estableciendo diferencias entre estas y los cambios asociados al envejecimiento fisiológico [14].

Durante el envejecimiento, el cerebro sufre una afectaciń progresiva del peso [9] y volumen [15] cambios atribuidos a la reducción de sustancia gris y blanca en las

regiones córtico-subcorticales [14].

Consecuencia de la disminución de la sustancia gris cortical, se produce una reducción de la girificación en las circunvoluciones, así como un incremento de la profundidad y expansión de los surcos de la corteza, siendo estos fenómenos ms acentuados en los lóbulos frontales, temporales y parentales, y mucho menos evidentes en la corteza occipital [22].

Los cambios de presión externa producidos por la dilatación de las astas frontales y por la disminución de la sustancia blanca peri ventricular durante la etapa del envejecimiento provocan también un aumento del espacio ventricular que conduce a la expansión del líquido cerebroespinal [14, 22]. Durante el envejecimiento se reduce significativamente el volumen de estructuras subcorticales como la amígdala [2], el núcleo caudado [22], el tálamo [7] y el cerebelo [14].

1.3. El sueño (fisiolía)

(Esta sección también es copiada, por el momento)

El sueño se define como un proceso vital cíclico complejo y activo, compuesto por varias fases y que posee una estructura interna característica, con diversas interrelaciones en los sistemas hormonales y nerviosos [11]. Una suspensión fácilmente reversible de la interacción sensoriomotriz con el medio ambiente, por lo general asociados con el decúbito y la inmovilidad.

El sueño se determina por cuatro dimensiones diferentes: tiempo circadiano (esto es la hora del día en que se localiza); factores intrínsecos del organismo (edad, sexo, patrones de sueõ, estado fisiológico o necesidad de dormir, entre otros); conductas que facilitan o inhiben el sueño; y el ambiente. Las dos últimas dimensiones se relacionan con la higiene del sueño, que incluye las prácticas necesarias para mantener un sueño nocturno y una vigilancia diurna normales [24].

Las características conductuales que se asocian con el sueño en el ser humano pueden enumerarse de la siguiente forma [7]

1. Disminución de la conciencia y reactividad a los estímulos externos

2. Se trata de proceso fácilmente reversibles (lo cual lo diferencia de otros estados patológicos como el estupor y el coma)

3. Se asocia a inmovilidad y relajación muscular

4. Suele presentarse con una periodicidad circadiana (diaria)

5. Durante el sueño los individuos adquieren una postura estereotipada

6. La ausencia de sueño (privación), induce distintas alteraciones conductuales y fisiológicas, además de que genera una "deuda" acumulativa de sueño que eventualmente deberá recuperarse

1.3.1. Fisiología del sueño

Los organismos vivos tienen su propio ritmo de actividad y reposo, mismos que desencadenan en la percepción de ciclos naturales tales como la sucesión del día y la noche. En este sentido, el sustrato neurológico relacionado con la ritmicidad del sueño se encuentra en el hipotálamo, estructura que tiene diversidad de conexiones en el Sistema Nervioso Central, con el fin de ejercer una función o funciones capaces de sincronizar el organismo [6, 11].

Diversos y muy importantes procesos fisiológicos y cerebrales, están estrechamente relacionados o determinados por el sueño o la periodicidad del mismo. A este respecto, existen diversas teorías acerca de las funciones del sueño, por ejemplo:

1. Restablecimiento o conservación de la energía

2. Eliminación de radicales libres acumulados durante el día

3. Regulación y restauración de la actividad eléctrica cortical

4. Regulación térmica

5. Regulación metabólica y endocrina

6. Homeostasis sináptica

7. Activación inmunológica

8. Consolidación de la memoria

Las estructuras límbicas, tales como la amígdala y el hipotálamo, también estarían activadas, lo que explicaría los fenómenos emotivos durante la fase de sueño REM ya que las emociones están directamente vinculadas con estas zonas cerebrales [4].

1.3.2. Función del sueño

Los efectos del sueño no se limitan al propio organismo (necesidad de restauración neurológica y la salud), sino que influyen en el desarrollo y funcionamiento normal de un individuo en la sociedad, afectando el rendimiento laboral o escolar [3, 17, 23, 24], el bienestar psicosocial [5, 13, 26], la seguridad vial, entre otras [12].

Dentro de los factores que se pueden ver afectados por la disminución de las horas de sueño se encuentra la calidad del sueño, la cual no sólo se refiere al hecho de dormir bien durante la noche, sino que incluye también un buen funcionamiento diurno.

1.4. Etapas del sueño

El sueño normal se divide en dos etapas: sueño REM (Rapid-eyemovement) o también conocido como sueño MOR (movimiento-ocular-rápido) y sueño no-REM, los cuales se diferencian fundamentalmente por sus rasgos electroencefalográficos y una serie de características fisiológicas 51 Una herramienta tecnológica que ha sido de vital importancia para el estudio de la fisiología del sueño es el electroencefalograma (EEG). De forma muy simplificada, el EEG es el la representación gráfica y digital de las oscilaciones que muestra la actividad eléctrica del cerebro, al ser registrada mediante electrodos colocados encima de la piel cabelluda en distintas regiones de la cabeza 4 El sueño MOR se caracteriza por la presencia de ondas de bajo voltaje y alta frecuencia en el electroencefalograma, atonía muscular y movimientos oculares rápidos, además es donde se presentan la mayoría de los sueños. El sueño no- MOR se compone de cuatro fases, 1 y 2, que son de sueño ligero, y 3 y 4 de sueño profundo, las

mismas que transcurren de manera secuencial desde la primera hasta la cuarta fase, que es la fase reparadora del sueño, aquella que produce en la persona la sensación de haber descansado cuando se levanta 13,22,43. Las características de las fases del sueño no-MOR incluyen cuatro etapas, la primera que corresponde a la transición de la vigilia al sueño; la etapa 2 es la intermedia (mayor porcentaje del tiempo de sueño) y en el EEG aparecen husos de sueño y los complejos K. La etapa 3 es la del sueño relativamente profundo, representado en el electroencefalograma por ondas lentas de gran amplitud, y la etapa 4o de sueño profundo con más del 50 % de ondas lentas de gran amplitud13. Durante el estado de alerta, mientras se mantienen los ojos cerrados, en el EEG se observan oscilaciones de la actividad eléctrica que suelen encontrarse entre 8-13 ciclos por segundo (Hz), principalmente a nivel de las regiones occipitales (ritmo alfa). Durante el sueño ocurren cambios característicos de la actividad eléctrica cerebral que son la base para dividir el sueño en varias fases. Como ya se mencionó, el sueño suele dividirse en dos grandes fases que, de forma normal, ocurren siempre en la misma sucesión: todo episodio de sueño comienza con el llamado sueño sin movimientos oculares rápidos (No MOR), que tiene varias fases, y después pasa al sueño con movimientos oculares rápidos (MOR). La nomenclatura acerca de las fases del sueño ha sido recientemente modificada por la Academia Americana de Medicina del Sueño (2007)52. Quedó de la siguiente manera:

1.4.1. Sueño No MOR

Fase 1 (ahora denominada N1): esta fase corresponde con la somnolencia o el inicio del sueño ligero, en ella es muy fácil despertarse, la actividad muscular disminuye paulatinamente y pueden observarse algunas breves sacudidas musculares súbitas que a veces coinciden con una sensación de caída (mioclonías hípnicas), en el EEG se observa actividad de frecuencias mezcladas, pero de bajo voltaje y algunas ondas agudas (ondas agudas del vértex). Fase 2 (ahora denominada N2): en el EEG se caracteriza por que aparecen patrones específicos de actividad cerebral llamados husos de sueño y complejos K; físicamente la temperatura, la frecuencia cardiaca y respiratoria comienzan a disminuir paulatinamente. Fases 3 y 4 o sueño de ondas lentas (en conjunto

llamadas fase N3): esta es la fase de sueño No MOR más profunda, y en el EEG se observa actividad de frecuencia muy lenta (¡2 Hz)53.

1.4.2. Sueño MOR

Ahora es llamado fase R y se caracteriza por la presencia de movimientos oculares rápidos; físicamente el tono de todos los músculos disminuye (con excepción de los músculos respiratorios y los esfínteres vesical y anal), así mismo la frecuencia cardiaca y respiratoria se vuelve irregular e incluso puede incrementarse y existe erección espontánea del pene o del clítoris. Durante el sueño MOR se producen la mayoría de las ensoñaciones (lo que conocemos coloquialmente como sueños), y la mayoría de los pacientes que despiertan durante esta fase suelen recordar vívidamente el contenido de sus ensoñaciones53. Por otro lado, las necesidades de sueño son muy variables según la edad y las circunstancias individuales 43,54: Un niño recién nacido duerme casi todo el día, con una proporción próxima al 50 % del denominado sueño «activo», que es el equivalente del sueño MOR. A lo largo de la lactancia los períodos de vigilia son progresivamente más prolongados y se consolida el sueño de la noche; además, la proporción de sueño MOR desciende al 25-30 %, que se mantendrá durante toda la vida. Entre el 1er y 3er año de vida el niño ya sólo duerme una o dos siestas. Entre los 4 y 5 años y la adolescencia los niños son hipervigilantes, muy pocos duermen siesta, pero tienen un sueño nocturno de 9-10 horas bien estructurado en 5 ciclos o más. Por lo que se refiere a los individuos jóvenes, en ellos reaparece en muchos casos la necesidad fisiológica de una siesta a mitad del día43,55. La necesidad de sueño en un adulto puede oscilar entre 5 y 9 horas. Asimismo, varía notablemente el horario de sueño entre noctámbulos y madrugadores. En épocas de mucha actividad intelectual o de crecimiento o durante los meses del embarazo, puede aumentar la necesidad de sueño, mientras que el estrés, la ansiedad o el ejercicio físico practicado por la tarde pueden reducir la cantidad de sueño. Los estudios efectuados en individuos aislados de influencias exteriores han mostrado que la tendencia fisiológica general es a retrasar ligeramente la fase de sueño con respecto al ciclo convencional de 24 horas y a dormir una corta siesta “de mediodía” 43,56. Un adulto joven pasa aproximadamente entre

70-100 min en el sueño no MOR para después entrar al sueño MOR, el cual puede durar entre 5-30 min, y este ciclo se repite cada hora y media durante toda la noche de sueño. Por lo tanto, a lo largo de la noche pueden presentarse normalmente entre 4 y 6 ciclos de sueño MOR 22 Por otro lado, en los ancianos se va fragmentando el sueño nocturno con frecuentes episodios de despertar y se reduce mucho el porcentaje de sueño en fase IV y no tanto el de sueño MOR, que se mantiene más constante a lo largo de la vida. Las personas de edad avanzada tienen tendencia a aumentar el tiempo de permanencia en la cama. Muchas de ellas dormitan fácilmente durante el día varias siestas cortas43.

1.4.3. Alteraciones del ciclo vigilia-sueño

La relevancia que tiene el sueño para para la supervivencia de un individuo es la cantidad de horas que este duerme a lo largo de su vida, mismas que depende fundamentalmente de sus necesidades fisiológicas y de las demandas del ambiente al que está expuesto 4,57 En el caso de los humanos, es posible establecer una clasificación de patrones de sueño en función de su duración (corta, intermedia y larga) 4. Las personas que muestran un patrón de sueño intermedio, es decir, duración aproximada de entre 7-8 horas, presentan un mejor estado de salud a lo largo de su vida, comparado con los individuos de duración de sueño corta o excesivamente larga que frecuentemente tienen de problemas de salud y/o laborales 42,45,46 . La estabilidad del sueño nocturno es otro factor a tener en cuenta debido a que es razonable pensar que un sueño muy fragmentado no cumplirá con sus funciones fisiológicas de igual forma que un patrón de sueño estable a lo largo de la noche. Al respecto, los adultos mayores informan que duermen menos durante la noche, y se acuestan y se despiertan más temprano de lo habitual. Además, tardan más tiempo en conciliar el sueño, se despiertan con más frecuencia durante la noche y la duración de estos despertares es más prolongada 58,59. La disminución del tiempo de sueño asociada a un incremento de la somnolencia diurna incide negativamente en la función cerebral del día siguiente 60 Por otro lado, existen diversas formas de pérdida de sueño13,25,46: a) la privación de sueño, que quiere decir la suspensión total del sueño por un periodo ($>$ 24

h), b) la restricción del sueño, que significa una disminución del tiempo habitual de sueño, generalmente de forma crónica, y c) la fragmentación del sueño, que significa la interrupción repetida (despertares) de la continuidad del sueño14. Todos estos tipos de alteraciones del sueño han demostrado afectar distintas funciones cognitivas y variedades de memoria en mayor o menor grado. Las alteraciones de sueño específicamente en personas mayores se han asociado con la presencia de enfermedades crónicas, problemas físicos y de salud mental 3

1.5. El electroencefalograma

[Esta parte esta copiada y pegada de "The origin of biopotentials" de John William Clark (2008), bajo las mismas consideraciones que el marco teorico del protocolo de investigacion de genesis: deberia ser capaz de escribir mi propio resumen, y solo es cuestion del tiempo que tardare en escribirlo PERO por lo mientras pondre esto aqui]

The background electrical activity of the brain in unanesthetized animals was described qualitatively in the nineteenth century, but it was first analyzed in a systematic manner by the German psychiatrist Hans Berger, who introduced the term electroencephalogram (EEG) to denote the potential fluctuations recorded from the brain. Conventionally, the electrical activity of the brain is recorded with three types of electrodes—scalp, cortical, and depth electro- des. When electrodes are placed on the exposed surface (cortex) of the brain, the recording is called an electrocorticogram (ECoG). Thin insulated needle electrodes of various designs may also be advanced into the neural tissue of the brain, in which case the recording is referred to as a depth recording. (There is surprisingly little damage to the brain tissue when electrodes of appropriate size are employed.) Whether obtained from the scalp, cortex, or depths of the brain, the recorded fluctuating potentials represent a superpo- sition of the field potentials produced by a variety of active neuronal current generators within the volume-conductor medium. Unlike the relatively simple bioelectric source considered in Section 4.2 (the nerve trunk with its enclosed bundles of circular cylindrical nerve axons), the sources gener- ating these field potentials are aggregates of neuronal ele-

ments with complex interconnections. The neuronal elements mentioned previously are the dendrites, cell bodies (somata), and axons of nerve cells. Moreover, the architecture of the neuronal brain tissue is not uniform from one location to another in the brain. Therefore, prior to undertaking any detailed study of electroencephalography, we first discuss necessary background information regarding (1) the gross anatomy and function of the brain, (2) the ultra- structure of the cerebral cortex, (3) the field potentials of single neurons leading to an interpretation of extracellular potentials recorded in the cerebral cortex, and (4) typical clinical EEG waveforms recorded via scalp electrodes. We shall then focus on the general volume-conductor problem in electroencephalography and briefly discuss abnormal EEG waveforms (Sherman and Walterspacher, 2006).

1.5.1. INTRODUCTION TO THE ANATOMY AND FUNCTION OF THE BRAIN

The central nervous system (CNS) consists of the spinal cord lying within the bony vertebral column and its continuation, the brain, lying within the skull [Figure 4.24]. The brain is the greatly modified and enlarged portion of the CNS, surrounded by three protective membranes (the meninges) and enclosed within the cranial cavity of the skull. The spinal cord is likewise surrounded by downward continuations of the meninges, and it is encased within the protec- tive bony vertebral column. Both brain and spinal cord are bathed in a special extracellular fluid called cerebral spinal fluid (CSF). Division of the brain into three main parts—cerebrum, brainstem, and cerebellum—provides a useful basis for the study of brain localization and function (Figure 4.24). The brainstem (medulla, pons, midbrain, diencephalon) is the oldest part of the brain. It is actually a short extension of the spinal cord and

serves three major functions: (1) a connecting link between the cerebral cortex, spinal cord, and cerebellum; (2) an integrative center for several visceral functions (e.g., control of blood pressure and ventilation); and (3) an integration center for various motor reflexes. The diencephalon is the most superior portion of the brainstem;

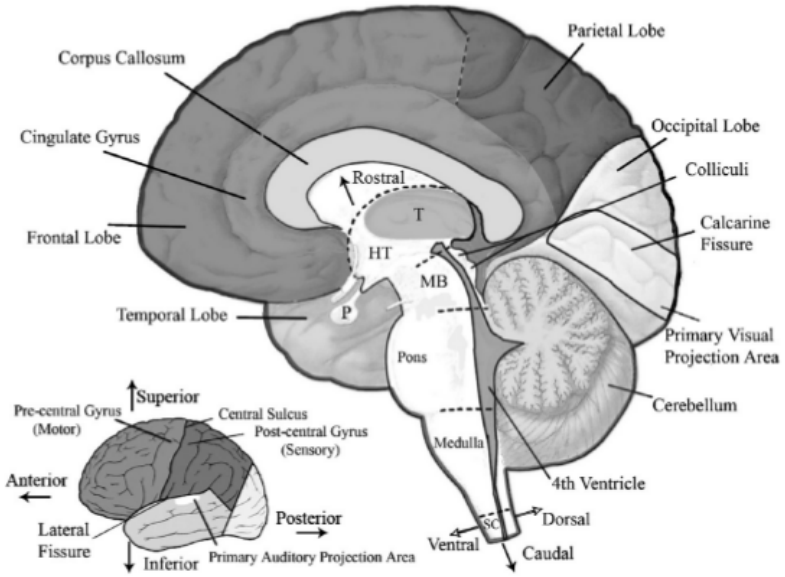


Figura 1-1: Anatomical relationship of brainstem structures [medulla oblon- gata, pons, midbrain, and diencephalon (thalamus and hypothalamus)] to the cerebrum and cerebellum. General anatomic directions of orientation in the nervous system are superimposed on the diagrams. Here the terms rostral (toward head), caudal (toward tail), dorsal (back), and ventral (front) are associated with the brainstem; remaining terms are associated with the cerebrum. The terms medial and lateral imply nearness and remoteness, respectively, to or from the central midline axis of the brain. Symbols: T (thalamus), HT (hypo- thalamus), MB (midbrain), SC (spinal cord), P pituitary gland). (Adapted from John H. Martin, Neuroanatomy: Text and Atlas, 2nd ed., 1996, pp 14–15, with permission of Appleton and Lange, a Simon and Schuster Company.)

its chief component and largest structure is the thalamus. The thalamus serves as a major relay station and integration center for all of the general and special sensory systems, sending information to their respective cortical reception areas. It serves as the gateway to the cerebrum. Another major component of the diencephalon is the hypothalamus, which integrates functions of the autonomic nervous system and along with the pituitary gland, regulates functions of the thyroid, adrenal, and reproductive glands. The cerebellum is a coordinator in the voluntary (somatic) muscle system and acts in conjunction with the brainstem and cerebral cortex to maintain balance and provide harmo- nious muscle movements. The larger cerebrum occupies a special dominant position in the central nervous system, and conscious functions of the nervous system are localized within this structure. Within the CNS there are ascending (sensory) nerve tracts that run from the spinal cord or brain stem to various areas of the brain, conveying information regarding changes in the external environment of the body that are reported by various peripheral biological sensors. There are a variety of such sensors, including the general sensors of temperature, pain, fine touch, pressure, as well as the special senses of vision, audition, equilibrium, taste, and olfaction. Figure 4.25 shows the basic plan associated with the general sense pathways from the periphery (e.g., skin, muscles) to the cortex. A three-neuron chain is involved in conveying information to the cortex where the primary neuron has its cell body in a ganglion outside the CNS and makes synaptic contact with a secondary neuron whose cell body is located in a nucleus within

either the spinal cord [e.g., the dorsal horn or the brain stem (Figure 4.25)]. Note from Figure 4.25 that the axon of the secondary neuron crosses (decus- sates) to the other side of the cord and joins a nerve fiber tract bound for the thalamus. The tertiary neuron in the pathway is located in a thalamic nucleus, and its axon travels in the thalamocortical radiations to the postcentral gyrus, which is located just posterior to the central sulcus [Figure 4.24 (inset)]. Thus, the postcentral gyrus is the cortical projection area for the general senses. Neural pathways for the special senses, particularly audition and vision, follow the same general ground plan; however, there are notable deviations from the scheme depicted in Figure 4.25. Usually, more than

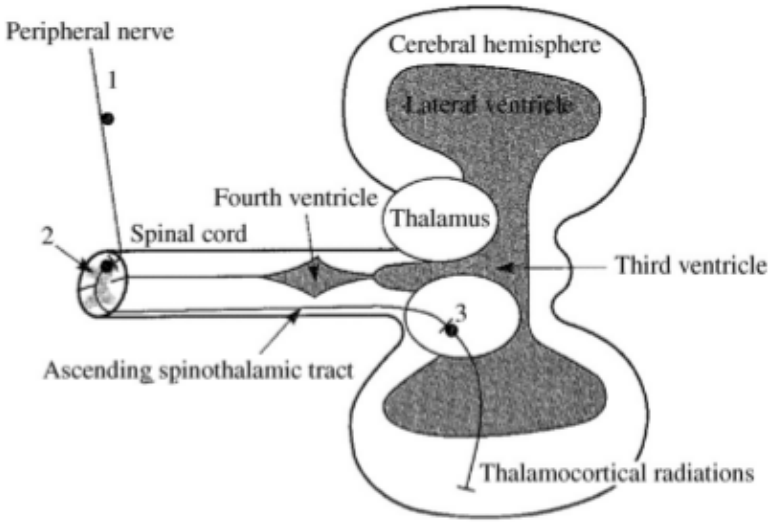


Figura 1-2: A simplified diagram of the CNS showing a typical general sense pathway from the periphery (neuron 1) to the brain (neuron 3). Note that the axon of the secondary neuron (neuron 2) in the pathway decussates (crosses) to the opposite side of the cord. Descending (motor) pathways are also crossed (see text).

three neurons are involved in the pathway and not all of the "secondary neurons" decussate. Most of the neurons cross to the opposite (contralateral) side of the body, however a significant number ascend to the thalamus on the same (ipsilateral) side of the body. The auditory and visual pathways have their own special thalamic relay centers—the medial and lateral geniculate bodies, respectively, as well as their own cortical projection areas (Figure 4.24). Likewise, within the CNS there are descending (motor) nerve tracts that originate in various brain structures such as the cerebrum and cerebellum (Figure 4.24) and terminate ultimately on motor neurons in the ventral horn of the spinal cord (Figure 4.10). These motoneurons, in turn, control the con- tractile activity of the skeletal musculature. For example, the corticospinal tract is a bundle of axons from the primary motor cortex [precentral gyrus, Figure 4.24 (inset)], which projects directly to motor neurons in the spinal cord. Since the ascending general sensory pathways are crossed, the descending corticospinal tracts each cross to the opposite side of the body prior to making synaptic contact with the spinal motor neurons. Thus, two-way communication links exist between the brain and spinal cord that allow higher centers in the brain to control or modify the behavior

of the elemental spinal reflex arc at a given spinal level. By means of these links, the brain is not only informed of a peripheral event but can also modify the response of the spinal reflex to that environmental stimulus. Information is transmitted to the brain by means of a frequency-modulated train of nerve impulses that, upon reaching specific areas of the brain, stimulates the activity of resident neurons. Similarly, the decision to implement a motor action in response to the initial stimulus is manifested in the electrical activity of cortical neurons in specific areas of the brain [e.g., precentral gyrus (primary motor cortex); premotor cortex in frontal lobe]. The pattern of activity is specific to the type of motor action to be taken. Electrical activity in either ascending or descending nerve fiber tracts may be represented to a first approximation by an action current dipole oriented in the direction of propagation (bioelectric source model). One should be aware that the properties (e.g., size, bulk conductivity) of the volume-conductor medium can change along the length of a particular fiber tract between the spinal cord and the cortex, and the volume-conductor model adopted should be based on the particular measurement considered. The volume-conductor-field potential solutions can be used to both fit and interpret body surface

potential measurements obtained clinically. Recording field potentials non- invasively from the relatively small volume of active nerve trunks, invariably requires the use of cumulative signal averaging techniques. In Figure 4.8, the median nerve was stimulated and compound action potentials were recorded from the subject's forearm. Although not shown in this figure, sensory fibers in the median nerve thus activated, initiate activity in the general sense pathways to the brain. Averaged field potential recordings can be taken at a variety of points along the ascending pathways [e.g., from spinal cord and brain stem tracts taking note of the crossed nature of the pathway, and finally at the cortex itself (postcentral gyrus)]. The field potentials associated with long nerve tracts depends to a large extent on (a) whether the tract is straight or bent and (b) the resistance (geometry and specific conductivity) of the surrounding volume- conductor media. This important subject is discussed later; however, for the present, these different types of averaged field potentials are called collectively somato- sensory evoked potentials. The subject of nerve tracts has been discussed pre-

viously; however, the activity of both nuclei in the ascending pathway and clusters of cells in the cortex, depends not only on the ensemble of neurons there, but also on the geometry of the ensemble and the different types of synaptic connections involved. Averaged sensory evoked potentials in response to brief auditory "clicks" or flashes of light are also routinely recorded as the auditory evoked response (AER) and the visual evoked response (VER), respectively (Jacobson, 1994; Heckenlively and Arden, 1991). Using an electromagnetic stimulating device held over the primary motor cortex (just anterior to the central sulcus), it is also possible to induce currents that activate the corticospinal tract, making possible the recording of averaged field potentials from the descending motor pathways (York, 1987; Geddes, 1987; Esselle and Stuchly, 1992). The same volume-conductor principles are applicable to the analysis of these different types of evoked potential recordings. The cerebrum is a paired structure, with right and left cerebral hemispheres, each relating to the opposite side of the body. That is, voluntary movements of the right hand are "willed" by the left cerebral hemisphere. The surface layer of the hemisphere is called the cortex; it receives sensory information from skin, eyes, ears, and other receptors located generally on the opposite side of the body. This information is compared with previous experience and produces movements in response to these stimuli. Each hemisphere consists of several layers. The outer layer is a dense collection of nerve cells that appear gray in color when examined in a fresh state. It is consequently called gray matter. This outer layer, roughly 1 cm thick, is called the cerebral cortex. It has a highly convoluted surface consisting of gyri (ridges) and sulci (valleys), the deeper sulci being termed fissures. The deeper layers of the hemisphere (beneath the cortex) consist of myelinated axons (or white matter) and collections of cell bodies termed nuclei. Some of the integrative functions of the cerebrum can be localized within certain regions of the cortex; others are more diffusely distributed.

A major dividing landmark of the cerebral cortex is the lateral fissure (Figure 4.24), which runs on the lateral (side) surface of the brain from the open end in front, posteriorly and dorsally (backward and upward). The lateral fissure defines a side lobe of cortex inferior to (below) it that is called the temporal lobe [Figure 4.24 (inset)].

The superior (upper) part of this lobe contains the primary auditory cortex, which is the part of the cortex that receives auditory impulses via neural pathways leading from the auditory receptors in the inner ear. The visual system is another example of the projection of the senses onto the cerebral cortex. The occipital lobe at the back of the head is the primary visual cortex. Light flashed into the eye evokes large electrical potentials from electrodes placed over this area of the cortex. Another major landmark of the cerebral cortex is the central sulcus [Figure 4.24 (inset)]. However, it is not so prominent and unvarying an anatomical landmark as the lateral fissure. The central sulcus runs from the medial surface (surface along the midline of the brain) over the convexity of the hemisphere to the lateral fissure. It also represents the posterior border of the frontal lobe. The gyrus lying just anterior (forward) to the central sulcus is the precentral gyrus, which functions as the primary motor cortex. From this gyrus, nerve signals run down through the brainstem to the spinal cord for control of skeletal muscles via neural control of motoneurons in the ventral horn of the spinal cord (Figure 4.10). Lesions (destruction) of part of the precentral gyrus cause partial paralysis on the opposite side of the body. Immediately posterior to the central sulcus [Fig. 24 (inset)] is the primary somatosensory cortex, the postcentral gyrus. This region receives impulses from all the general sense receptors from the skin (such as pressure, touch, and pain receptors). Each little area along this gyrus is related to a particular part of the body (for example, the legs on the medial end, the hand in the center, and the face on the end next to the lateral fissure). If a recording electrode is placed appropriately during a neurosurgical procedure, a cortical response can be evoked by tactile stimuli delivered to the contralateral (opposite) hand. Likewise, if a stimulus is applied through the same electrode, the subject reports a tingling sensation in the contralateral hand. Higher-order sensory discrimina- tion, such as the ability to recognize a number drawn on the palm of the hand, is organized solely in the parietal lobe of which the postcentral gyrus is a part. Destruction of the parietal lobe results in a loss of this discriminative ability. For example, a subject may still know that he or she is being touched but cannot tell where or what is being drawn on the palm of the hand. The parietal lobe is also responsible for a person's awareness

of the general position of the body and its limbs in space.

1.5.2. ULTRASTRUCTURE OF THE CEREBRAL CORTEX

The functional part of the cerebrum is the cerebral cortex (bark, outer covering), a relatively thin layer of gray matter (1.5 to 4.0 mm in thickness) covering the outer surface of the cerebrum, including its intricate convolutions.

Because it is the most recent phylogenetic acquisition of the brain, the cerebral cortex has undergone a relatively greater development than other parts of the brain. The greatest advance in relative growth has been the neocortex, which is present on the superior and lateral aspects of the cerebral hemispheres. The distinctly different type of cortex located on the medial surface and base of the brain is known as the paleocortex. We shall use the term cortex in this chapter to refer specifically to the neocortex. Cortical architectures in vertebrates share several common features: (1) stratified layers containing cell bodies and fiber bundles; (2) an outermost layer that lacks neurons (layer I); (3) at least one inner layer containing neurons that give rise to large dendrites, which rise vertically to layer I and travel in that layer forming multiple branches (arborization). The human cortex is generally arranged in six such cortical layers. The neurons are of two main types: pyramidal and nonpyramidal (many subtypes have been identi- fied). There are also a large number of horizontally oriented layers of nerve fibers that extend between adjacent regions of the cortex, as well as vertically oriented bundles that extend from the cortex to more distant regions of the cortex or downward to the brainstem and spinal cord. Figure 4.26 shows a schematic drawing of a typical cortical pyramidal cell. The bodies of this type of cell are commonly triangular in shape, with the base down and the apex directed toward the cortical surface. (Pyramidal

cell bodies vary greatly in size, from axial dimensions of 15 x 10 mm up to 120 x 90 mm or more for the giant pyramids of the motor cortex, which are called Betz cells after their discoverer.) These cells usually consist of the following parts: (1) a long apical

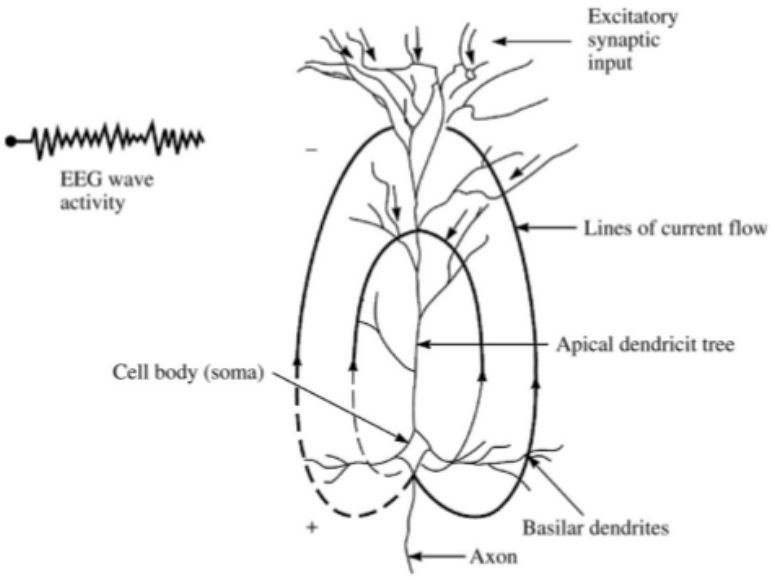


Figura 1-3: Electrogenesis of cortical field potentials for a net excitatory input to the apical dendritic tree of a typical pyramidal cell. For the case of a net inhibitory input, polarity is reversed and the apical region becomes a source (nose). Current flow to and from active fluctuating synaptic knobs on the dendrites produces wavelike activity. (See text.)

dendrite (up to 2 mm in length) that ascends from the apex of the cell body through the overlaying cellular layers, and which frequently reaches and branches terminally within the outermost layer of the cortex; (2) dense dendritic arborization occurring at the base of the pyramid-shaped cell (largely horizontally—basilar dendrites); and (3) a single pyramidal cell axon which can emerge from the inner surface of the cortex as projection fibers to other areas of the cortex, or to other structures (e.g., the thalamus, cerebellum, or spinal cord). Frequently these axons send recurrent collateral (feedback) branches back on the cellular regions from which they sprang. Axons of some pyramidal cells turn back toward the cortical surface (never leaving the gray matter) to end via their many branches on the dendrites of other cells. Nonpyramidal cells of the neocortex differ remarkably from pyramidal cells. Their cell bodies are small, and dendrites spring from them in all directions to ramify in the immediate vicinity of the cell. The axon may arise from a large dendrite; it commonly divides repeatedly to terminate on the cell bodies and dendrites of immediately adjacent cells.

The axons of other non- pyramidal cells may turn upward toward the cortical surface, or they may leave the motor cortex (though this is not common). For a detailed exposition of the various cells, layers, cellular interconnec- tions, inputs, and outputs of the neocortex, see Kandel et al. (1991).

1.5.3. BIOELECTRIC POTENTIALS FROM THE BRAIN

Unipolar recordings of the cortical surface potential relative to that of a remote reference potential may be viewed as a measurement of the integrated field potential at a boundary of a large volume conductor that contains an array of action current sources. Under normal conditions, action potentials con- ducted by axons in the cortical medium contribute very little to the integrated surface potential, since there are many axons in the cortex which run in many directions relative to the surface and which fire asynchronously. Consequently, their net spatial and temporal influence on the field potential at the surface is negligible. An exception occurs, of course, in the case of a response evoked by the simultaneous (synchronous) stimulation of a cortical input (e.g., direct electrical stimulation of thalamic nuclei or their afferent pathways, which project directly to the cortex via thalamocortical axons—the cortical input). These synchronous responses are called evoked potentials, and they are of relatively large amplitude. Synchronicity of the underlying fiber and cortical neuron activity is a major factor influencing surface potential magnitude. Unipolar field potentials recorded within the cortical layers have shown that the cortical surface potential is largely due to the net effect of local postsynaptic potentials of cortical cells (Figure 4.26). These may be of either sign (excitatory or inhibitory) and may occur directly underneath the electrode

or at some distance from it. A potential change recorded at the surface is a measure of the net potential (current resistance iR) drop between the surface site and the distant reference electrode. It is obvious, however, that if all the cell bodies and dendrites of cortical cells were randomly arranged in the cortical medium, the net influence of synaptic currents would be zero. This would result in a “closed field” situation that produces relatively small far-field potentials (Lorente de No, 1947).

Thus, any electrical change recorded at the surface must be due to the orderly and symmetric arrangement of some class of cells within the cortex. Pyramidal cells of the cerebral cortex are oriented vertically, with their long apical dendrites running parallel to one another. Potential changes in one part of the cell relative to another part create "open" potential fields in which current may flow and potential differences can be measured at the cortical surface. Figure 4.26 illustrates this concept in diagrammatic fashion. Synaptic inputs to the apical dendritic tree cause depolarization of the dendritic membrane. As a result, subthreshold current flows in a closed path through the cytoplasmic core of the dendrites and cell body of the pyramidal cell, returning ultimately to the surface synaptic sites via the extracellular bathing medium. From the indicated direction of the lines of current flow, the extracellular medium about the soma behaves as a source (nose), while the upper part of the apical dendritic tree behaves as a sink (). The influence of a particular dendritic postsynaptic potential (PSP) on the cortical surface recording depends on its sign [excitatory () or inhibitory ()] and on its location relative to the measurement site. The effect of each PSP may be regarded as creating a radially oriented current dipole. Therefore, continuing synaptic input creates a series of potential dipoles and resulting current flows that are staggered but overlapped in space and time. Surface potentials of any form can be generated by one population of presynaptic fibers and the cells on which they terminate, depending on the proportion that are inhibitory or excitatory, the level of the postsynaptic cells in the cortex, and so forth. Nonpyramidal cells in the neocortex, on the other hand, are unlikely to contribute substantially to surface records. Their spatially restricted dendritic trees are radially arranged around their cell bodies such that charge differences between the dendrites and the cell body produce fields of current flow that sum to zero when viewed from a relatively great distance on the cortical surface (closed-field situation). Thus, to summarize, the apical dendrites of pyramidal cells constitute a meshwork of similarly oriented, densely packed units in the outer layers of the cortex. As multiple synaptic endings on the dendritic tree of each cell become active, current can flow in either direction between the dendritic process depending on whether the synapses are excitatory or inhibitory. The sour-

ce–sink relationship between dendrite and cell is that of a constantly shifting current dipole, where variations in dipole orientation and strength produce wavelike fluctuations in the surface field potential (Figure 4.26). When the sum of dendritic activity is negative relative to the cell, the cell

is depolarized and quite excitable. When it is positive, the cell is hyper- polarized and less excitable.

1.5.4. RESTING RHYTHMS OF THE BRAIN

Electric recordings from the exposed surface of the brain or from the outer surface of the head demonstrate continuous oscillating electric activity within the brain. Both the intensity and the patterns of this electric activity are determined to a great extent by the overall excitation of the brain resulting from functions in the brainstem reticular activating system (RAS). The undulations in the recorded electric potentials (Figure 4.27) are called brain waves, and the entire record is called an electroencephalogram (EEG).

relative to an indifferent electrode such as the earlobe) may be as large as 10 mV, whereas those recorded from the scalp have a smaller amplitude of approximately 100 mV. The frequencies of these brain waves range from 0.5 to 100 Hz, and their character is highly dependent on the degree of activity of the cerebral cortex. For example, the waves change markedly between states of wakefulness and sleep. Much of the time, the brain waves are irregular, and no general pattern can be observed. Yet at other times, distinct patterns do occur. Some of these are characteristic of specific abnormalities of the brain, such as epilepsy (discussed later). Others occur in normal persons and may be classified as belonging to one of four wave groups (alpha, beta, theta, and delta), which are shown in Figure 4.27(a). Alpha waves are rhythmic waves occurring at a frequency between 8 and 13 Hz. They are found in EEGs of almost all normal persons when they are awake in a quiet, resting state of cerebration. These waves occur most intensely in the occipital region but can also be recorded, at times, from the parietal and frontal regions of the scalp. Their voltage is approximately 20 to 200 mV. When the subject is asleep, the alpha waves disappear

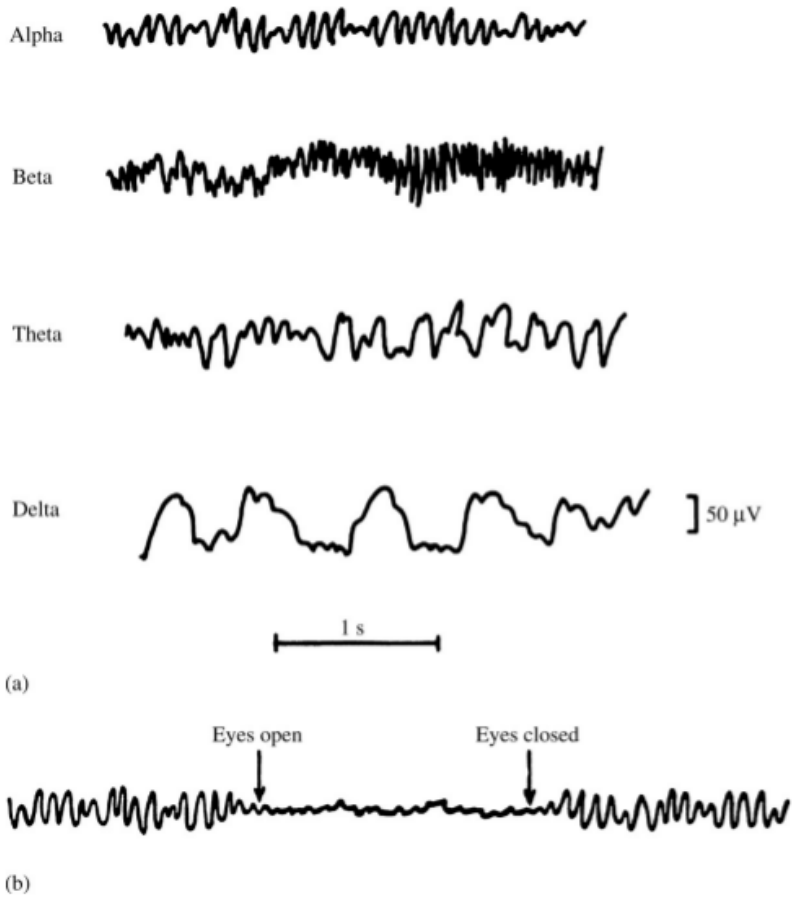


Figura 1-4: (a) Different types of normal EEG waves. (b) Replacement of alpha rhythm by an asynchronous discharge when patient opens eyes. (c) Representative abnormal EEG waveforms in different types of epilepsy. (From A. C. Guyton, Structure and Function of the Nervous System, 2nd ed., Philadelphia: W.B. Saunders, 1972; used with permission.)

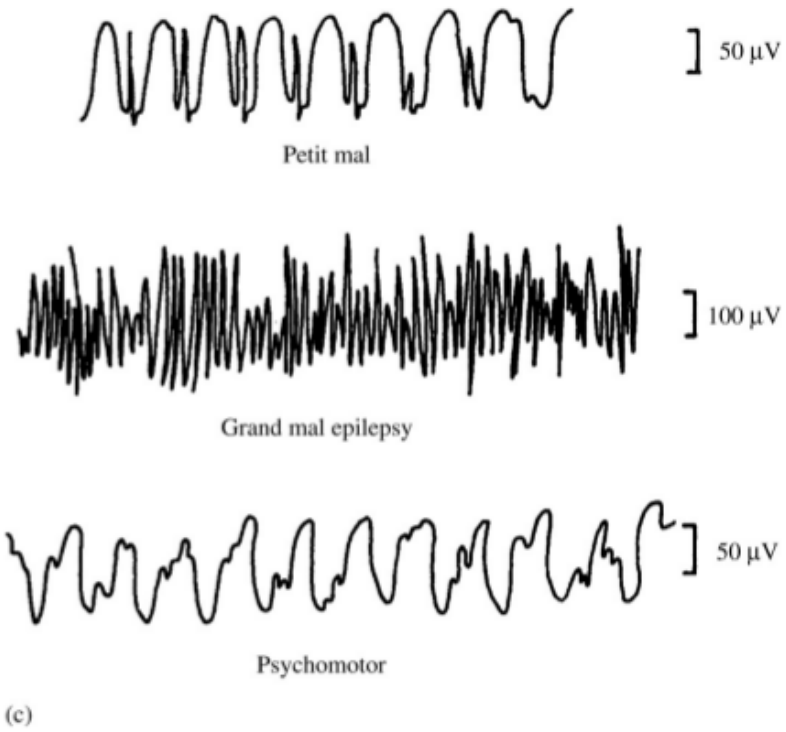


Figura 1-5: (Continuation)

completely. When the awake subject's attention is directed to some specific type of mental activity, the alpha waves are replaced by asynchronous waves of higher frequency but lower amplitude. Figure 4.27(b) demonstrates the effect on the alpha waves of simply opening the eyes in bright light and then closing them again. Note that the visual sensations cause immediate cessation of the alpha waves; these are replaced by low-voltage, asynchronous waves.

Beta waves normally occur in the frequency range of 14 to 30 Hz, and sometimes—particularly during intense mental activity—as high as 50 Hz. These are most frequently recorded from the parietal and frontal regions of the scalp. They can be divided into two major types: beta I and beta II. The beta I waves have a frequency about twice that of the alpha waves. They are affected by mental activity in much the same way as the alpha waves (they disappear and in their place appears an asynchronous, low-voltage wave). The beta II waves, on the other hand, appear during intense activation of the central nervous system and during tension. Thus one type of beta activity is elicited by mental activity, whereas the other is inhibited by it.

Theta waves have frequencies between 4 and 7 Hz. These occur mainly in the parietal and temporal regions in children, but they also occur during emotional stress in some adults, particularly during periods of disappointment and frustration. For example, they can often be brought about in the EEG of a frustrated person by allowing the person to enjoy some pleasant experience and then suddenly removing the element of pleasure. This causes approxi- mately 20 s of theta waves. Delta waves include all the waves in the EEG below 3.5 Hz. Sometimes these waves occur only once every 2 or 3 s. They occur in deep sleep, in infancy, and in serious organic brain disease. They can also be recorded from the brains of experimental animals that have had subcortical transections producing a functional separation of the cerebral cortex from the reticular activating system. Delta waves can thus occur solely within the cortex, independent of activities in lower regions of the brain. A single cortical cell can give rise only to small extracellular current, so large numbers of neurons must be synchronously active to give rise to the potentials recorded from the cerebral surface. The individual waves of the EEG are of long duration (for example, 30 to 500 ms), and one might well ask how they are produced. They can be long-lasting depolarizations of the cell membranes (for example, of the apical dendrites of pyramidal cells) or a summation of a number of shorter responses. In any event, a sufficiently large number of neurons must discharge together to give rise to these cortical potentials. The term synchroni- zation is used to describe the underlying process that acts to bring a group of neurons into unified action. Synaptic interconnections are generally thought to bring about synchronization, although extracellular field interaction between

cells has been proposed as a possible mechanism. Rhythmically firing neurons are very sensitive to voltage gradients in their surrounding medium. Besides the synchronization required for each wave of resting EEG, the series of repeated waves suggests a rhythmic and a trigger or pacemaker process that initiates such rhythmic action. By means of knife cuts below the intact connective- tissue covering (meningeal layer or pia matter) of the brain, one may prepare chronic islands of cortex—with all neuronal connections cut, but with the blood supply via surface vessels intact. Only a low level of EEG activity remains in such islands. Though the isolated islands of

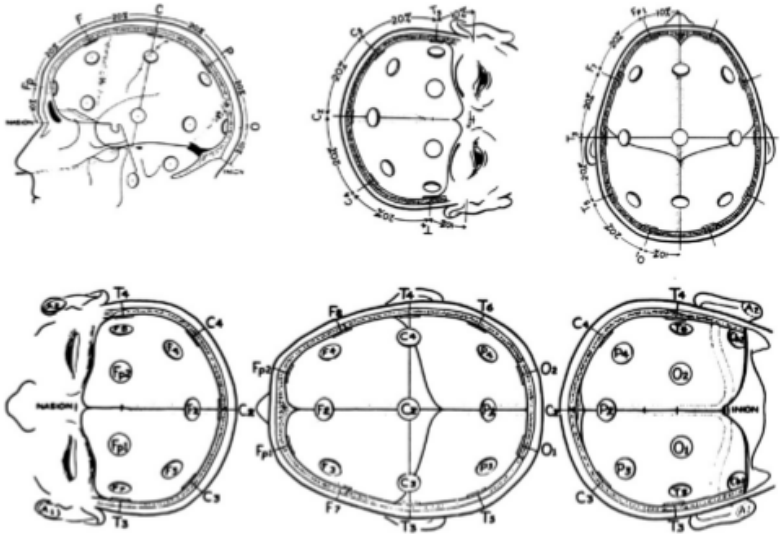


Figura 1-6: The 10–20 electrode system This system is recommended by the International Federation of EEG Societies. [From H. H. Jasper, "The ten– twenty electrode system of the International Federation in Electroencepha- lography and Clinical Neurophysiology." EEG Journal, 1958, 10 (Appendix), 371–375.]

cortex may not show spontaneous EEG activity, they still have the ability to respond rhythmically, which may be readily demonstrated by the rhythmic responses that are elicited by applying a single electrical stimulus. The inference is that various regions of the cortex, though capable of exhibiting rhythmic activity, require trigger inputs to excite rhythmic- ity. The RAS, mentioned earlier, appears to provide this pacemaker function.

1.5.5. THE CLINICAL EEG

The system most often used to place electrodes for monitoring the clinical EEG is the International Federation 10–20 system shown in Figure 4.28. This system uses certain anatomical landmarks to standardize placement of EEG electrodes. The representation of the EEG channels is referred to as a montage. In the bipolar montage, each channel measures the difference between two adjacent electrodes. In the referential montage, each channel

measures the diffference between one electrode and a reference electrode, such as on the ear. In the average reference montage, each channel measures the difference

between one electrode and the average of all other electrodes. In the Laplacian montage, each channel measures the difference between one electrode and a weighted average of the surrounding electrodes. The differ- ential amplifier requires a separate ground electrode plus differential inputs to the electrode connections. The advantage of using a differential recording between closely spaced electrodes (between successive pairs in the standard system, for example) is cancellation of far-field activity common to both electrodes; one thereby obtains sharp localization of the response. Although the same electric events are recorded in each of the ways, they appear in a different format in each case. The potential changes that occur are amplified by high-gain, differential, capacitively coupled amplifiers. The output signals are recorded and displayed. In the routine recording of clinical EEGs, the input electrodes are a problem. They must be small, they must be easily affixed to the scalp with minimal disturbance of the hair, they must cause no discomfort, and they must remain in place for extended periods of time. Technicians prepare the surface of the scalp, degrease the recording area by cleaning it with alcohol, apply a conducting paste, and glue nonpolarizable Ag/AgCl electrodes to the scalp with a glue (collodion) and hold them in place with rubber straps, or use a rubber cap that contains all electrodes. The EEG is usually recorded with the subject awake but resting recumbent on a bed with eyes closed. With the patient relaxed in such a manner, artifacts from electrode-lead movement are significantly reduced, as are contaminating signals from the scalp. Muscle activity from the face, neck, ears, and so on is perhaps the most subtle contaminant of EEG records in the recording of both spontaneous ongoing activity in the brain and activity evoked by a sensory stimulus (evoked response). For example, the frequency spectrum of the field produced by mildly contracted facial muscles contains frequency components well within the nominal EEG range (0.5 to 100 Hz). After technicians have achieved resting, quiescent conditions in the normal adult subject, the subject's scalp recordings show a dominant alpha rhythm in the parietal-occipital areas, whereas in the frontal areas, there is a low-amplitude, higher-frequency beta rhythm in addition to the alpha rhythm. In the normal subject there is symmetry between the recordings of the right and left hemispheres. There can be a wide range of EEG measurement

artifacts. In general there is a relationship between the degree of cerebral activity and the average frequency of the EEG rhythm: The frequency increases progressively with higher and higher degrees of activity. For example, delta waves are frequently found in stupor, surgical anesthesia, and sleep; theta waves in infants; alpha waves during relaxed states; and beta waves during intense mental activity. However, during periods of mental activity, the waves usually become asynchronous rather than synchronous, so that the magnitude of the summed surface potential recording decreases despite increased cortical activity.

1.5.6. SLEEP PATTERNS

When an individual in a relaxed, inattentive state becomes drowsy and falls asleep, the alpha rhythm is replaced by slower, larger waves (Figure 4.29). In deep sleep, very large, somewhat irregular delta waves are observed. Inter- spersed with these waves—during moderately deep sleep—are bursts of alpha- like activity called sleep spindles. The alpha rhythm and the patterns of the drowsy and sleeping subject are synchronized, in contrast with the low-voltage desynchronized, irregular activity seen in the subject who is in an alert state. The high-amplitude, slow waves seen in the EEG of a subject who is asleep are sometimes replaced by rapid, low-voltage irregular activity resembling that obtained in alert subjects. However, the sleep of a subject with this irregular pattern is not interrupted; in fact, the threshold for arousal by sensory stimuli is elevated. This condition has therefore come to be called paradoxical sleep. During paradoxical sleep, the subject exhibits rapid, roving eye movements. For this reason, it is also called rapid-eye-movement sleep, or REM sleep. Conversely, spindle or synchronized sleep is frequently called nonrapid-eye- movement (NREM), or slow-wave sleep. Human subjects aroused at a time when their EEG exhibits a paradoxical (REM) sleep pattern generally report

that they were dreaming, whereas individuals wakened from spindle sleep do not. This observation and other evidence indicate that REM sleep and dreaming are closely associated. It is interesting that during REM sleep, there is a marked reduction in muscle tone, despite the rapid eye movements.

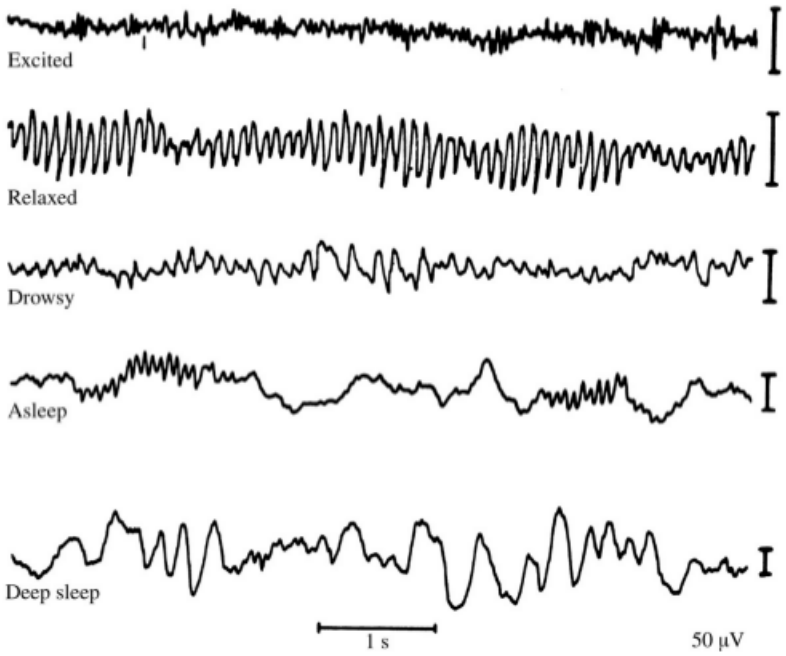


Figura 1-7: The electroencephalographic changes that occur as a human subject goes to sleep The calibration marks on the right represent 50 mV. (From H. H. Jasper, "Electrocephalography." In Epilepsy and Cerebral Localization, W. G. Penfield and T. C. Erickson (eds.). Springfield, IL: Charles C. Thomas, 1941.)

1.5.7. THE VOLUME-CONDUCTOR PROBLEM IN ELECTROENCEPHALOCRAPHY

Geometrically speaking, the brain approximates a sphere surrounded by concentric shells that differ in impedance and comprise the meninges (connec- tive tissue coverings of the brain), cerebral spinal fluid, skull, and scalp. This model is inaccurate to the extent that the brain is not really a true sphere, and its coverings are irregular in shape and thickness. Such irregularities are insignificant for the upper half of the brain, but complications are introduced by the marked departure of the lower parts of the brain from a spherical shape, as well as by variations in impedance produced by the openings (to the spinal column) through the base of the shell. Various cerebral structures differ somewhat in specific resistivity. Resistivity also varies in relation to the predominant direction of the fibers within the white matter. Thus the brain is neither a homogeneous nor an isotropic conducting medium. In practice, neurological generators do not correspond precisely to simple, one-dimensional dipoles. Any source of activity large enough to manifest itself in the EEG constitutes at least a small area of the cortex containing synchro- nously active neurons. This source may be regarded as a three-dimensional sheet polarized across its thickness. If it is small enough, it may still be conveniently represented as an equivalent dipole per unit volume. A larger area of the cortex may be curved, or even convoluted, and the equivalent dipole then becomes a complex vector sum of the whole. When there are many widely scattered active-current generators, an infinite number of combinations may give rise to the same pattern of surface potentials. Determining the equivalent dipole of cerebral activity is therefore of practical value only when EEG sources are highly "focal." Fortunately, this condition occurs frequently in the brain's response to sensory stimulation, as well as in pathological conditions. For example, Nunez (1981) considers in some depth the subject of the calculation of field potentials from equivalent current sources in inhomogeneous media. Particularly in Chapter of his book, Nunez provides an introduction to the equivalent source models that have been used in the field of theoretical electroencephalography to interpret scalp potentials. Exam-

ples of these models include the simple dipole at the center of a spherical conducting medium, the radially oriented dipole not at the center of a sphere (the radially oriented eccentric dipole), the freely oriented eccentric dipole in a sphere, the dipole in a three-concentric spherical shell model, and a dipole current source below a multilayered planar conducting medium. Considerable interest has arisen in determining the location of intra- cerebral sources of the potentials that are measured on the scalp. In general, nonuniqueness of this inverse problem is well known in that different

configurations of sources can lead to the same surface distribution. The usual approach taken to obtaining an approximate solution to the inverse problem is as follows: 1. 2. 3. 4. Assume a model (such as the eccentrically located dipole in a uniform, homogeneous spherical conducting medium. Assume that the electric field is quasistatic). After obtaining a solution to the associated boundary-value problem (the forward problem), produce model-generated potential values at measure- ment points on the cortical surface. Compare these theoretical potential values with particular discrete-time values of EEG waveforms measured at the same surface sites, and form a general least-squares reconstruction error function wherein the error is defined as the difference between predicted and measured potential at several selected cortical measurement sites. Iteratively adjust the EEG dipolar source parameters at each discrete- time instant to obtain the best fit to sampled EEG waveforms in a least- squares sense. The optimal dipole location is assumed to be the dipole location obtained when the reconstruction error function is so minimized. The influence of anisotropy on various EEG phenomena has been studied using models [Henderson et al. (1975); Cuffin (1991); Haueisen et al. (2002)]. These investigations, together with various in vivo studies, substantially agree that the presence of tissue anisotropy tends to attenuate and smear the pattern of scalp-recorded EEGs. However, this type of amplitude-related degradation apparently does not affect the model's ability to predict the locus of the EEG equivalent-dipole generator (although the dipole moment might be under- estimated). This is important in the sense that one of the major objectives of electroencephalography is determination of source location—for localized or focal activity—because in case of evoked cortical potentials and deep-brain

pathologies, this concept of an equivalent-dipole generator is of clinical value.

1.5.8. THE ABNORMAL EEG

One of the more important clinical uses of the EEG is in the diagnosis of different types of epilepsy and in the location of the focus in the brain causing the epilepsy. Epilepsy is characterized by uncontrolled excessive activity by either a part or all of the CNS. A person predisposed to epilepsy has attacks when the basal level of excitability of all or part of the nervous system rises above a certain critical threshold. However, as long as the degree of excitability is held below this threshold, no attack occurs. There are two basic types of epilepsy, generalized epilepsy and partial epilepsy. Generalized epilepsy involves the entire brain at once, whereas partial epilepsy involves a portion of the brain—sometimes only a minute focal spot and at other times a fair amount of the brain. Generalized epilepsy is further divided into grand mal and petit mal epilepsy.

Grand mal epilepsy is characterized by extreme discharges of neurons originating in the brainstem portion of the RAS. These discharges then spread throughout the cortex, to the deeper parts of the brain, and even to the spinal cord to cause generalized tonic convulsions of the entire body. They are followed near the end of the attack by alternating muscular contractions, called clonic convulsions. The grand mal seizure lasts from a few seconds to as long as 3 to 4 min and is characterized by postseizure depression of the entire nervous system. The subject may remain in a stupor for 1 min to as long as a day or more after the attack is over. The middle recording in Figure 4.27(c) shows a typical EEG during a grand mal attack. This response can be recorded from almost any region of the cortex. The recorded potential is of a high magnitude, and the response is synchronous, with the same periodicity as normal alpha waves. The same type of discharge occurs on both sides of the brain at the same time, indicating that the origin of the abnormality is in the lower centers of the brain that control the activity of the cerebral cortex, not in the cortex itself. Electrical recordings from the thalamus and reticular formation of experimental animals during an induced grand mal attack indicate typical high-voltage synchronous activity in these

areas, similar to that recorded from the cerebral cortex. Experiments on animals have further shown that a grand mal attack is caused by intrinsic hyperexcitability of the neurons that make up the RAS structures or by some abnormality of the local neural pathways of this system. Petit mal epilepsy is closely allied to grand mal epilepsy. It occurs in two forms, the myoclonic form and the absence form. In the myoclonic form, a burst of neuronal discharges, lasting a fraction of a second, occurs throughout the nervous system. These discharges are similar to those that occur at the beginning of a grand mal attack. The person exhibits a single violent muscular jerk involving arms or head. The entire process stops immediately, however, and the attack is over before the subject loses consciousness or stops what he or she is doing. This type of attack often becomes progressively more severe until the subject experiences a grand mal attack. Thus the myoclonic form of petit mal is similar to a grand mal attack, except that some form of inhibitory influence promptly stops it. The absence type of petit mal epilepsy is characterized by 5 to 20 s of unconsciousness, during which the subject has several twitchlike contractions of the muscles, usually in the head region. There is a pronounced blinking of the eyes, followed by a return to consciousness and continuation of previous activities. This type of epilepsy is also closely allied to grand mal epilepsy. In rare instances, it can initiate a grand mal attack. Figure 4.27(c) shows a typical spike-and-dome pattern that is recorded during the absence type of petit mal epilepsy. The spike portion of the record is almost identical to the spikes occurring in grand mal epilepsy, but the dome portion is distinctly different. The spike-and-dome pattern can be recorded over the entire cortex, illustrating again that the seizure originates in the RAS. Partial epilepsy can involve almost any part of the brain, either localized regions of the cerebral cortex or deeper structures of both the cerebrum and

brainstem. Partial epilepsy almost always results from some organic lesion of the brain, such as a scar that pulls on the neuronal tissue, a tumor that compresses an area of the brain, or a destroyed region of the brain tissue. Lesions such as these can cause local neurons to fire very rapid discharges. When the rate exceeds approximately 1000/s, synchronous waves begin spreading over adjacent cortical regions. These

waves presumably result from the activity of localized reverberating neuronal circuits that gradually recruit adjacent areas of the cortex into the "discharge," or firing, zone. The process spreads to adjacent areas at rates as slow as a few millimeters per minute to as fast as several centimeters per minute. When such a wave of excitation spreads over the motor cortex, it causes a progressive "march" of muscular contractions throughout the opposite side of the body, beginning perhaps in the leg region and marching progressively upward to the head region, or at other times marching in the opposite direction. This is called Jacksonian epilepsy or Jacksonian march. Another type of partial epilepsy is the so-called psychomotor seizure, which may cause (1) a short period of amnesia, (2) an attack of abnormal rage, (3) sudden anxiety or fear, (4) a moment of incoherent speech or mumbling, or (5) a motor act of rubbing the face with the hand, attacking someone, and so forth. Sometimes the person does not remember his or her activities during the attack; at other times the person is completely aware of, but unable to control, his or her behavior. The bottom tracing of Figure 4.27(c) represents a typical EEG during a psychomotor seizure showing a low-frequency rectangular-wave response with a frequency between 2 and 4 Hz with superimposed 14 Hz waves. The EEG frequently can be used to locate tumors and also abnormal spiking waves originating in diseased brain tissue that might predispose to epileptic attacks. Once such a focal point is found, surgical excision of the focus often prevents future epileptic seizures. The EEG is also used to monitor the depth of anesthesia. The EEG is also used as a brain–computer interface to enable disabled persons to communicate with a computer.

Capítulo 2

"Parte matemática"

Me temo que pasará algún tiempo antes que esta parte sea totalmente coherente y comprensible a un grado aceptable. Cabe mencionar que esta fuertemente inspirada por el libro Spectral Analysis and Time Series, de M. Priestley [21] porque está explícitamente dirigida a un público sin trasfondo matemático.

Debo citar los trabajos de Cohen, Nason, Adak, Dahlhaus, Gabor, Fryzelwicz, entre otros. En discusiones más modernas, se mencionan temas que aun no se han explorado: ciclo-estacionariedad, procesos harmonizables, estacionariedad local y por partes, diferencias entre memoria larga y memoria corta, espectros de ondaletas, espectros de Wigner-Ville, Wold-Cramér, Gabor. Debo mencionarlos, pero no he trabajado en ello y no se suficiente sobre ello.

La informalidad de la redacción se debe al tiempo: en versiones futuras debería mejorar.

Nota: no es prioritario, pero será una buena idea incluir una discusión sobre por qué tiene sentido revisar si los EEG son estacionarios, y es que un proceso estacionario es básicamente un ruido.

2.1. Estacionariedad débil

El ingrediente básico de las series de tiempo son los procesos estocásticos; para ello, se supone dada la defínción de variables aleatorias, espacios de probabilidad, y

espacios L^p; si es necesario los defino, y si no me conformaré con citar un libro sobre series de tiempo que cubra estos temas, como el de Chatfield (The Analysis of Time Series: An Introduction, 2003).

Una muy buena razón para empezar a describir **desde** procesos estocásticos es tener las definiciones a la mano, evitar conflictos con la notación $X(t)$ en lugar de X_t, y enfatizar detalles sobre el tiempo continuo.

Definición 1 (Proceso estocástico) *Un proeso estocástico* $\{X(t)\}$ *es una familia de variables aleatorias indexadas por el símbolo* t *que pertenece a algún conjunto* $T \in \mathbb{R}$

Matemáticamente se permitirá que t, referido como **tiempo**, tome valores en todo $\mathbb{R}$; las observaciones, en cambio, sólo pueden ser tomadas en un conjunto discreto y finito de instantes en el tiempo. Adicionalmente, en algunas secciones se considerarán procesos estocásticos complejos, si bien la mayor parte del texto sólo usará valores reales.

Esta definición particular de proceso estocástico debería enfatizar que para cada tiempo t, $X(t)$ es una variable aleatoria con su función de densidad de probabilidad, sus momentos [sólo se consideran va's con al menos segundos momentos finitos], etc.

Otro concepto clave de este texto es el de **estaionareidad débil**; quizá la mejor forma de motivar el adjetivo 'débil' es como contraposición a la **estacionariedad fuerte o total**. Para ello, sea $F(X;\cdot)$ la función de densidad de probabilidad de X, es decir, la probabilidad de que $X \leq x$ puede expresarse como $F(X;x) = P(X \leq)$ bajo el entendido que X y x pueden ser vectores en $\mathbb{R}^d$.

Definición 2 (Estacionariedad fuerte) *Un proceso estocástico* $\{X(t)\}$ *es fuertemente estacionario si, para cualquier conjunto de tiempos admisibles* $t_1, t_2, \ldots, t_n$ *y cualquier* $\tau \in \mathbb{R}$ *se cumple que*

$$F\left(X(t_1), X(t_2), \ldots, X(t_n); \cdot\right) \equiv F\left(X(t_1+\tau), X(t_2+\tau), \ldots, X(t_n+\tau); \cdot\right)$$

La estacionariedad fuerte depende de las funciones de densidad de probabilidad

conjunta para diferentes tiempos. Si un proceso es estacionario en el sentido fuerte, entonces todas las variables $X(t)$ son idénticamente distribuidas.

Con viene definir versiones menos fuertes de estacionariedad según sea posible deducirse de las mediciones de un fenómeno y/o sean relevantes en su modelación.

Definición 3 (Estacionariedad de orden m) *Un proceso estocástico se dice estacionario de orden m si, para cualquier conjunto de tiempos admisibles $t_1, t_2, \ldots, t_n$ y cualquier $\tau \in \mathbb{R}$ se cumple que*

$$E\left[X^{m_1}(t_1)X^{m_2}(t_2)\cdots X^{m_n}(t_n)\right] = E\left[X^{m_1}(t_1+\tau)X^{m_2}(t_2+\tau)\cdots X^{m_n}(t_n+\tau)\right]$$

Para cualesquiera enteros $m_1, m_2, \ldots, m_n$ tales que $m_1 + m_2 + \cdots + m_n \leq m$

Hay una especie de consenso según el cual la estacionariedad de orden 2, también llamada **estacionariedad débil** es suficiente para que se cumplan los teoremas más comunes sobre medias y varianzas. Algunas consecuencias que un proceso sea estacionario debilmente son las siguientes:

- Para todo t, $E[X(t)] = \mu$, una constante
- Para todo t, $\mathrm{Var}\left(X(t)\right) = \sigma^2$, una constante
- Para cualesquiera t, τ, $\mathrm{Cov}\left(X(t+\tau), \mathrm{Cov}\left(X(t)\right)\right) = E[X(t+\tau)X(t)] - \mu^2$, una función de τ pero no de t

El recíproco también es cierto: si un proceso cumple las tres condiciones anteriores, entonces es estacionario de orden 2. A su vez tres condiciones son más usuales en la literatura y tienen una intepretación más clara como modelo, pues se exige que el proceso tenga media y varianza constante, y que la función de autocorrelación no dependa de dónde se mida –lo cual simplifica la estimación de estas cantidades.

Antes de proseguir, cabe mencionar que la estacionariedad fuerte se define en términos de las funciones de densidad de probabilidad conjunta, mientras que la estacionariedad se define según los momentos; luego, la estacionariedad débil excluye procesos cuyos momentos no estén definidos. Por ejemplo, una colección de variables

independientes idénticamente distribuidos –con distribución de Cauchy– será fuertemente estacionario, pero no estacionario de orden m para ningún m.

Por el momento se asumirán procesos con segundos momentos finitos **debido a que** hay motivaciones en el modelo para ello: energía finita, cambios finitos de energía, respuestas suaves, etc.

2.2. El espectro de una serie de tiempo

Quiero y me siento obligado a citar la excelente discución filosófica de Loynes [16], resaltando la frase "Los espectros instantáneos no existen". También quiero citar una discusión más moderna de Mélard [18], donde una frase a favor es "El supuesto de estacionariedad ha sido válido previamente debido a la corta duración de las series y la baja capacidad de cómputo".

Pues la mayor parte de mi trabajo se ha centrado en el concepto de **espectro** de una serie de tiempo. La mejor forma de introducir el espectro evolutivo –en el sentido que estoy usando– es presentar un proceso estacionario de orden 2, $\{X(t)\}$, en su representación de Cramér [21] [la existencia de esta representacion esta garantizada por el teorema de Khinchin-Wiener –para procesos a tiempo continuos– y por una extension del mismo por Wold –para procesos a tiempo discreto. por ahora solo cito el resultado, pero quiza sea buena idea escribir la demostracion como apendice, una demostracion citada ya que es bastante tecnica]

$$X(t) = \int_{\Lambda} A(\omega) e^{i2\pi\omega t} dZ(\omega)$$

Donde el proceso $\{Z(\omega)\}$ tiene incrementos ortogonales, es decir

$$\text{Cov}\left(dZ(\omega_1, dZ(\omega_2))\right) = \delta(\omega_1, \omega_1) d\omega$$

Con δ la función delta de Dirac. Cabe mencionar que es suficiente si los incrementos son independientes, pero se puede debilitar ese requerimiento; incluso es de notarse que no se exige que el proceso sea al menos continuo –en el sentido estocástico.

El espectro de potencia de $\{X(t)\}$ se define como

$$f(\omega) = |A(\omega)|^2$$

Citaré de Adak [1] una tabla donde compara varias definiciones de espectro, para procesos no-estacionarios.

Table 1: Cohen's class of time-frequency distributions

Author	Definition of $f(t,\lambda)$	$G(t,\tau)$: time - lag kernel
Wigner-Ville	$\int_{-\infty}^{\infty} R_X(t+\tau/2, t-\tau/2)e^{-i2\pi\lambda\tau}d\tau$	$G(t,\tau) = \delta(t)$
Page(1952)	$\int_0^{\infty} R_X(t,t-\tau)e^{-i2\pi\lambda\tau}d\tau$ + $R_X(t,t+\tau)e^{-i2\pi\lambda\tau}d\tau$	$G(t,\tau) = \delta(t-\tau/2)$ if $\tau \geq 0$. $G(t,\tau) = \delta(t+\tau/2)$ if $\tau \leq 0$.
Levin(1967)	$\int_0^{\infty} \frac{1}{2}R_X(t,t-\tau)e^{-i2\pi\lambda\tau}d\tau +$ $\int_0^{\infty} \frac{1}{2}R_X(t,t+\tau)e^{-i2\pi\lambda\tau}d\tau$	$G(t,\tau) = \frac{1}{2}\delta(t-\tau/2) +$ $\frac{1}{2}\delta(t+\tau/2)$
Spectrogram — Windowed Spectral Analysis	$E[\mid \int w(t-u)X(u)e^{-i2\pi\lambda u}du \mid^2]$	$G(t,\tau) =$ $w(t-\tau/2)w^*(t+\tau/2)$
Priestley(1965)	$\mid A(t,\lambda) \mid^2$, where $R_X(t+\tau/2, t-\tau/2)$ $= \int A(t+\tau/2,\theta)\ A^*(t-\tau/2,\theta)e^{i2\pi\theta\tau}d\theta$	Relation to Cohen's class shown in Hammond(1992)
Choi-Williams(1989)	$\int_{-\infty}^{\infty}\int_{-\infty}^{\infty} R_X(u+\tau/2, u-\tau/2).$ $\frac{1}{\sqrt{4\pi\tau^2\sigma}} exp\left[\frac{-(t-u)^2}{4\tau^2\sigma}\right] .e^{-i2\pi\lambda\tau}dud\tau$	$G(t,\tau) =$ $\frac{1}{\sqrt{4\pi\tau^2\sigma}} exp\left[\frac{-t^2}{4\tau^2\sigma}\right]$

Dos identidades muy importantes para estimar el espectro son la *equivalencia* entre el espectro y la función de autocorrelación

$$f(\omega) = \int R_X(\tau)e^{-i2\pi\omega t}d\tau$$

Donde función de autocorrelación se ha definido como

$$R_X(\tau) = E\left[X(t)X(t+\tau)\right] = \int_0^{\infty} X(t)X(t+\tau)dt$$

[la demostracion es corta, batsa con reescribir una composicion de integrales como convolucion, la incluire mas tarde]

Por otro lado, se tiene la Identidad de Parseval

$$\int X^2(t)dt = \int f(\omega)d\omega$$

[esta demostracion se basa en la convergencia dominada del modulo de la integral de X^2 por la integral del modulo (...), la incluire mas tarde]

2.3. Test Priestley-Subba Rao (PSR)

(seccion en proceso de re-redaccion)

A muy grosso modo, el test PSR estima localmente el espectro evolutivo y revisa si estadísticamente cambia en el tiempo.

Para ello, usa un estimador para la función de densidad espectral que es aproximadamente (asintóticamente) insesgado y cuya varianza está determinada aproximadamente. La estimación se lleva a cabo en puntos en el tiempo y la frecuencia tales que en conjunto son aproximadamente no-correlacionados. Se aplica logaritmo para que la varianza de todos los estimadores sea aproximadamente la misma (el logaritmo ayuda a), amen que los errores conjuntos tengan una distribución cercana a una multinormal con correlación cero. Finalmente se aplica una prueba ANOVA de varianza conocida.

2.3.1. El espectro evolutivo

Considérese un proceso estocástico a tiempo continuo $\{X(t)\}$, tal que $E[X(t)] = 0$ y $E\left[X^2(t)\right] < \infty$ para todo t. Es decir que su media es constante y sus segundos momentos están bien definidos, aunque estos últimos pueden cambiar con el tiempo.

Por el momento se supondrá que acepta una representación de la forma

$$X(t) = \int_{-\pi}^{\pi} A(t;\omega) e^{i\omega t}\, dZ(\omega)$$

Con $\{Z(\omega)\}$ una familia de procesos ortogonales[1] tales que

- $E\left[|dZ(\omega)|^2\right] = d\omega$
- Para cada t el máximo de $A(t;\cdot)$ se encuentra en 0

Esta representación es análoga a la representación de Cramér para un proceso estacionario, salvo que se permite que la función A cambie con el tiempo. Siguiendo

[1] De nuevo, esto implica que $\mathrm{Cov}\left(dZ(\omega_1), dZ(\omega_2)\right)) = \delta(\omega_1, \omega_1)d\omega$, una condición más débil que la independencia

la analogía, se define el **espectro evolutivo** de $\{X(t)\}$, con respecto a la la familia $\mathcal{F} = \{e^{i\omega t}A(t;\omega)\}$ como

$$dF(\omega;t) = |A(t;\omega)|^2 d\omega$$

Ahora bien, si se supone que $\{X(t)\}$ es estocásticametne diferenciable, entonces se puede definir una **función de densidad espectral**

$$f(t;\omega) = |A(t;\omega)|^2$$

Cabe destaca que si la función $A(t;\omega)$ fuera constante con respecto a t, se obtendría un proceso estacionario de orden dos tal cual fue descrito en la sección anterior.

2.3.2. El estimador de doble ventana

Estimador de doble ventana (Priestley, 1965 & 1966) Sea una función $g(u)$ tal que

$$2\pi \int_{-\infty}^{\infty} |g(u)|^2 du = \int_{-\infty}^{\infty} |\Gamma(\omega)|^2 d\omega = 1$$

donde se define la **función de respuesta ante frecuencia** como

$$\Gamma(u) = \int_{-\infty}^{\infty} g(u) e^{iu\omega} du$$

Posteriormente se define

$$U(t,\omega) = \int_{t-T}^{t} g(u) X_{t-u} e^{i\omega(t-u)} du$$

Sea una función $w_{T'}(t)$ tal que

- $w_{T'}(t) \geq 0$ para cualesquiera t, T'
- $w_{T'}(t) \to 0$ cuando $|t| \to \infty$, para todo T'
- $\int_{-\infty}^{\infty} w_{T'}(t) dt = 1$ para todo T'

- $\int_{-\infty}^{\infty} (w_{T'}(t))^2 \, dt < \infty$ para todo T'

Ahora, si se define $W_{T'}(\lambda) = \int_{-\infty}^{\infty} e^{-i\lambda t} w_{T'}(t) dt$

- $\lim_{T' \to \infty} \left[T' \int_{t-T}^{t} |W_{T'}(\lambda)|^2 d\lambda \right] = C$

Se define el estimador para f_t, con $0 \leq t \leq T$

$$\widehat{f}_t(\omega) = \int_{t-T}^{t} w_{T'}(u) |U(t-u, \omega)|^2 du$$

Se define $Y_{i,j} = \log\left(\widehat{f_{t_i}}(\omega_j)\right)$, con las siguientes propiedades

$$E\left[Y_{i,j}\right] \sim \log\left(f_{t_i}(\omega_j)\right) \qquad \text{Var}\left(Y\left(t, \omega\right)\right) \sim \sigma^2$$

Luego, puede escribirse $Y_{i,j} = \log\left(f_{t_i}(\omega_j)\right) + \varepsilon_{i,j}$, con $\varepsilon_{i,j}$ va iid

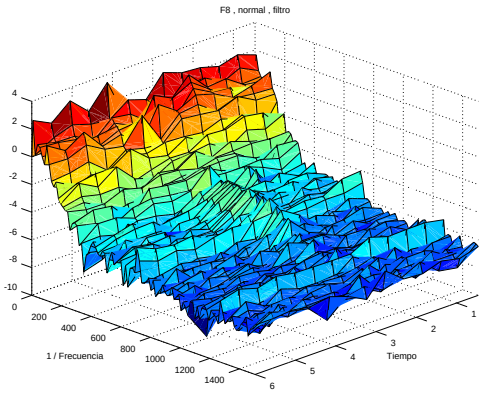
Usando un test ANOVA –de varianza conocida– se puede saber si ε

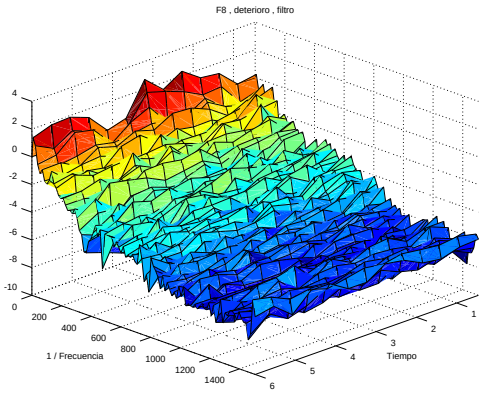
- Tiene marginales
- Constante sobre el tiempo
- Constante sobre las frecuencias

Priestley–Subba Rao stationarity Test for datos

Samples used	:	3072
Samples available	:	3069
Sampling interval	:	1
SDF estimator	:	Multitaper
Number of (sine) tapers	:	5
Centered	:	TRUE
Recentered	:	FALSE
Number of blocks	:	11

Block size	:	279
Number of blocks	:	11
p−value for T	:	0.4130131
p−value for I+R	:	0.1787949
p−value for T+I+R	:	0.1801353





T	:	0
I+R	:	5.787895e−09
T+I+R	:	0

T	:	0.00332259
I+R	:	0.03502537
T+I+R	:	0.01598073

Capítulo 3

"Resultados"

Visually, Rapid Eye Movement (REM) sleep is characterized by REMs, muscle atonia and desynchronized EEG activity. When quantitative analyses of the signals are carried out, usually, non-linearity and non-stationarity are assumed without an adequate analysis, especially in Old Adults (OA). Among the "weak" stationarity tests, the Priestley-Subba Rao (PSR) test calculates a "local" spectra that is "valid" only for punctual moments in time. A series of "smoothed" frequency filters give information of the time the local spectra is calculated. In here, weak REM sleep stationarity by the PSR test was compared to that from Wakefulness (W) and Non-REM (NREM) sleep. Methods: 8 Old Adults (OA) (age: 67.6 $\pm$ 5.7; education: 8.8 $\pm$ 2.6) without depression neither anxiety and with intact daily living activities were selected. Also, evaluations with the Mini-Mental State Examination (MMSE, 28.1 $\pm$ 1.8) and a one night polysomnography were performed. 30 second epochs were classified according to the AASM and every epoch of W, NREM and REM sleep was subjected to PSR tests. Percentages of stationary epochs were obtained with respect to the total number of epochs of each stage and Student t-tests were used to compare them. Results: The PSR effectively showed different proportions of stationarity according to the classification of stages in each subject. In Figure 1, in one OA, epochs with stationarity are shown in black and the classification of REM sleep is shown in green. Clearly, a lower proportion of stationarity was found in REM sleep vs the other stages. These differences reached significance in F7, Fp2, LOG and ROG ($p <$

0.05, Figure 2). Conclusions: In OA, REM sleep showed lower proportions of epochs with stationarity vs. W and NREM sleep at anterior areas, a result that could be explained by the tonic and phasic REM sleep. When stationarity measurements are planned, it is recommended to differentiate anterior from lateral and posterior areas.

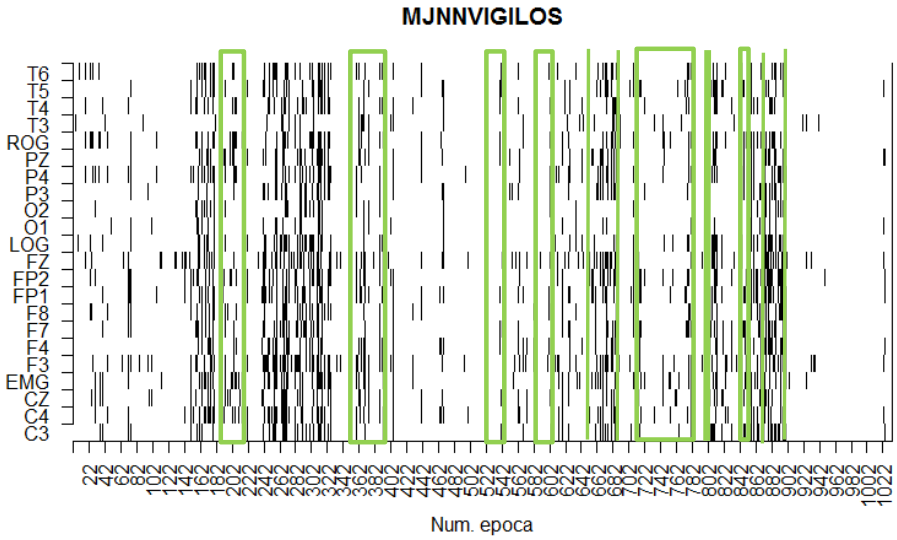
3.1. Resultados del test PSR

(Por ahora está copiado y pegado un reporte preeliminar sobre los resultados para tenerlo en cuenta y no olvidarlo; más adelante escribiré una explicaciópn adecuada.

Desde el punto de vista formal, se sigue directamente de la descripción del test PSR, y sólo hace falta indicar cómo se acomodaron los datos. Desde el punto de vista fisiológico es más interesante y extensa la parte que falta.)

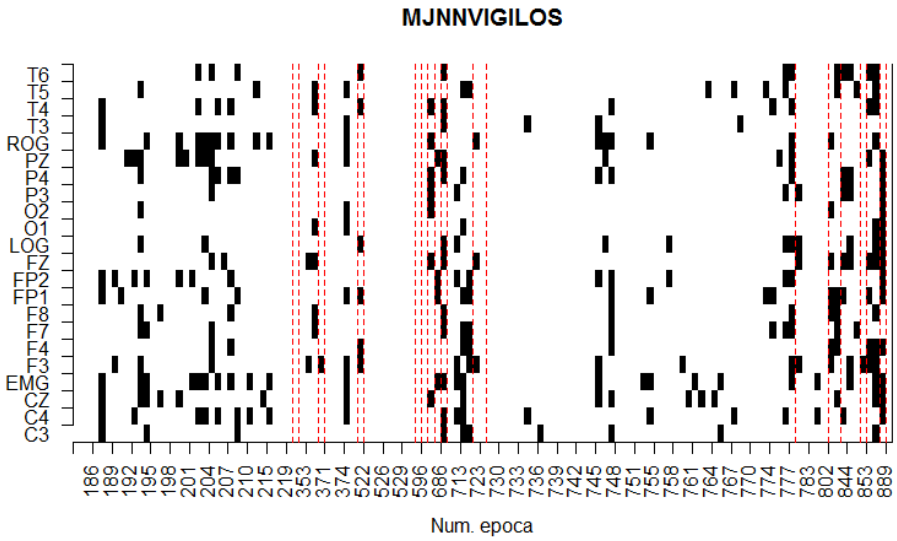
Se muestran los resultados del test PSR de estacionariedad en el sujeto MJNN para las 1032 épocas de sueño en los 22 canales. En el eje horizontal se muestra el número de época, en el eje vertical se muestra al nombre del canal, de modo que una fila tiene los resultados para un canal durante las diferentes épocas y una columna son los resultados para todos los canales durante una época dada. En verde se han encerrado las épocas MOR.

Se consideró con un p-valor menor a 0.1 el rechazo de hipótesis nula: el registro en es no-estacionario (blanco), mientras que el no-rechazo se consideró estacionario (negro).

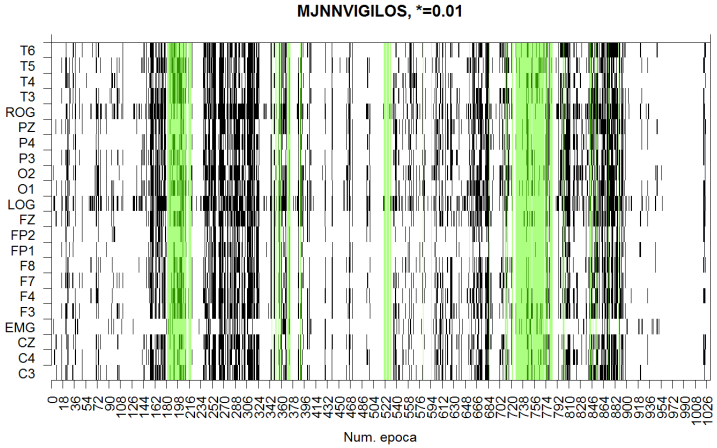


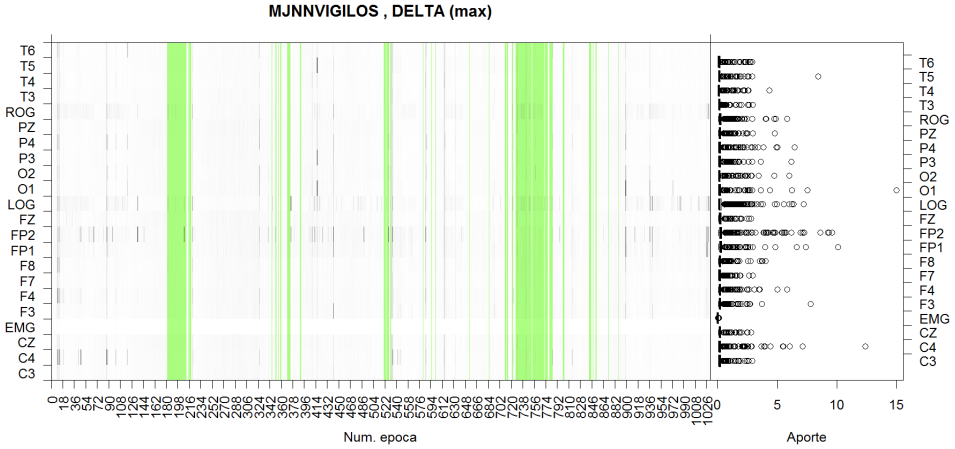
En este gráfico sólo se ilustran épocas MOR. Las líneas punteadas separan bloques continuos

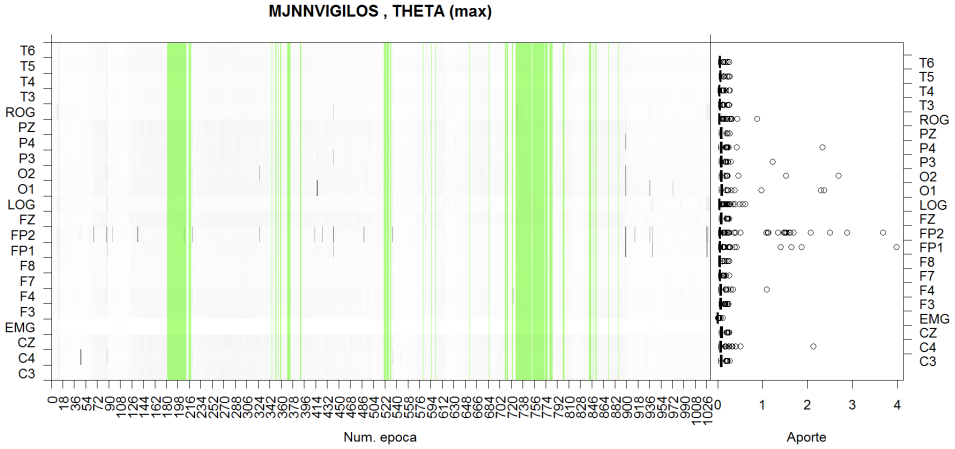
Total de épocas: 1032 , Épocas MOR: 127

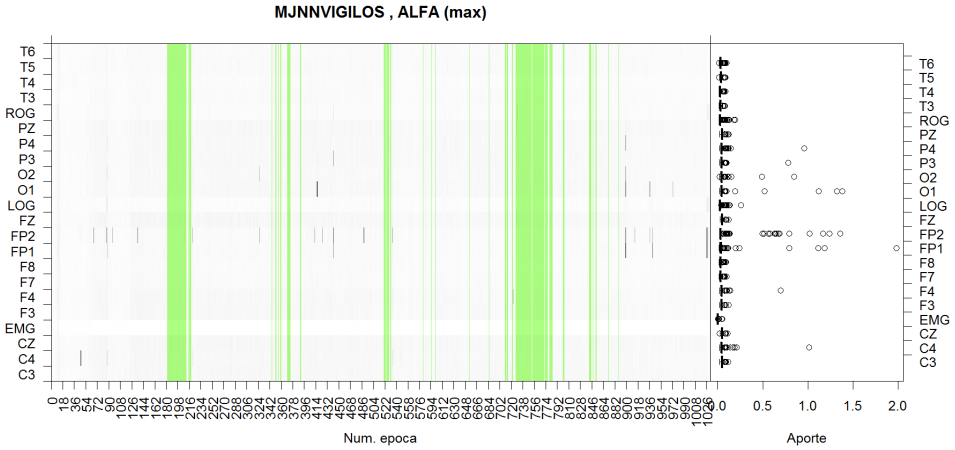


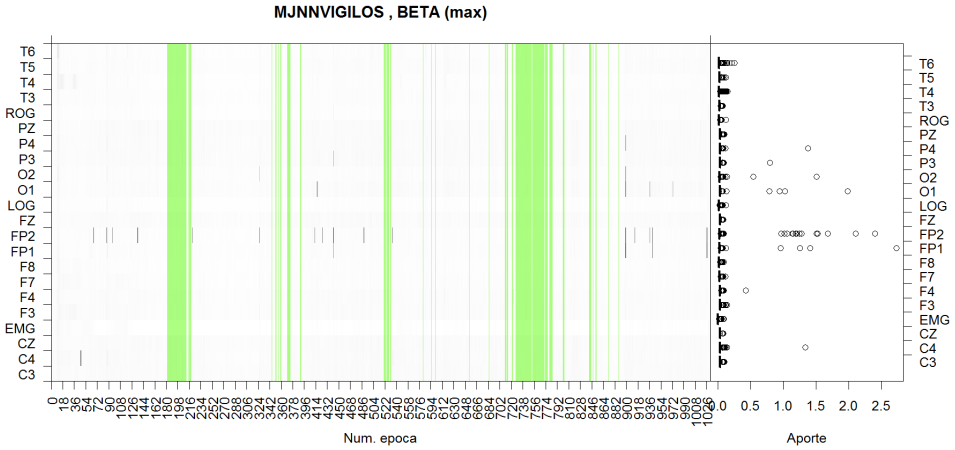
Se realizó un análisis de Fourier a cada época, luego se tomó el máximo de cada banda de frecuencias (delta, theta, alfa, beta). Se graficaron los resultados, escalados, con la misma topología anterior

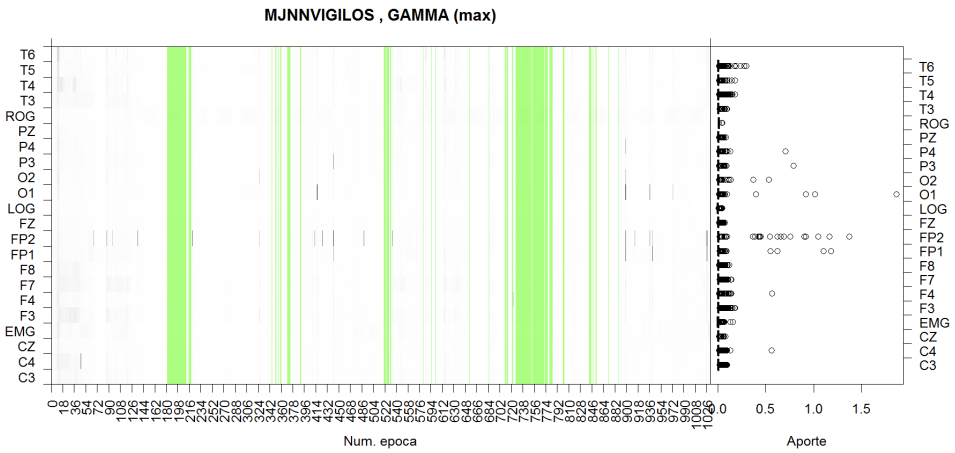


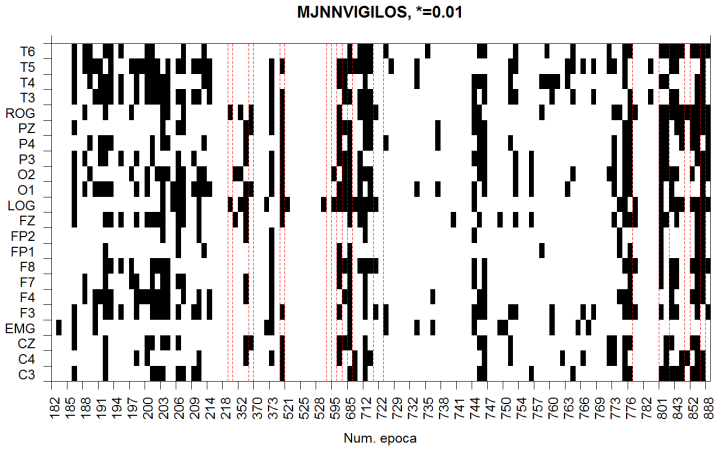


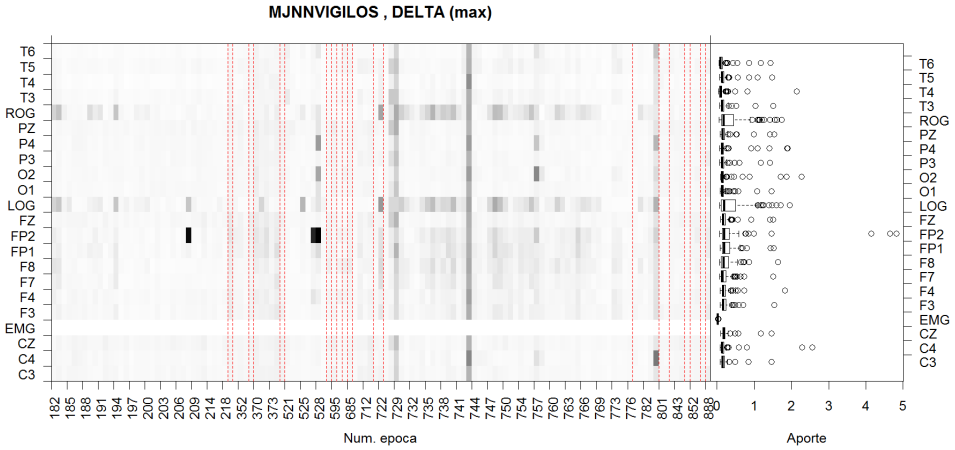


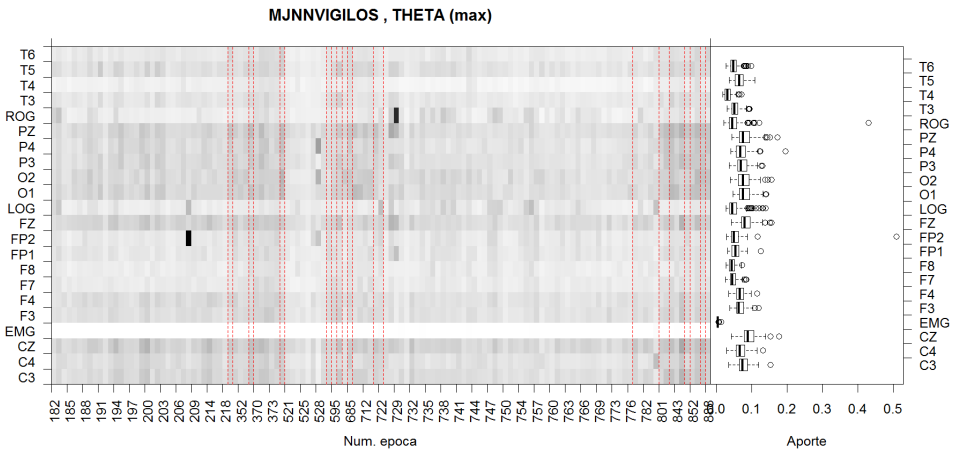

MJNNVIGILOS , ALFA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

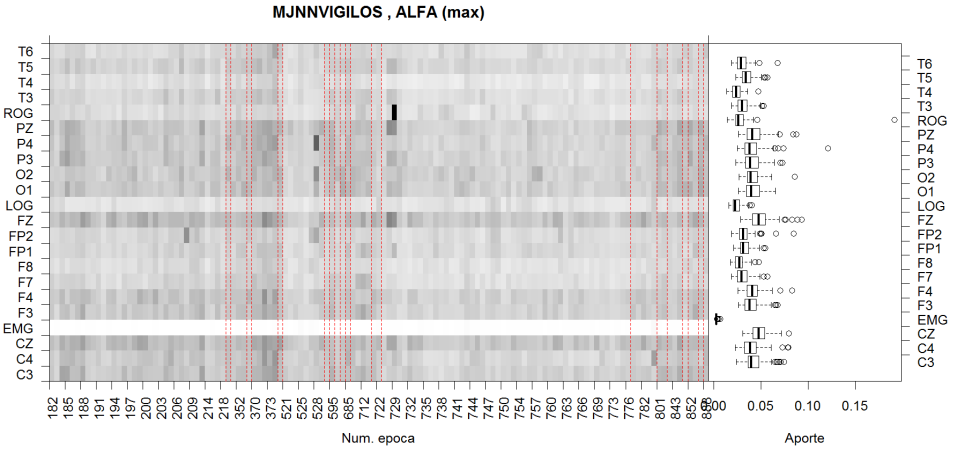

MJNNVIGILOS , BETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

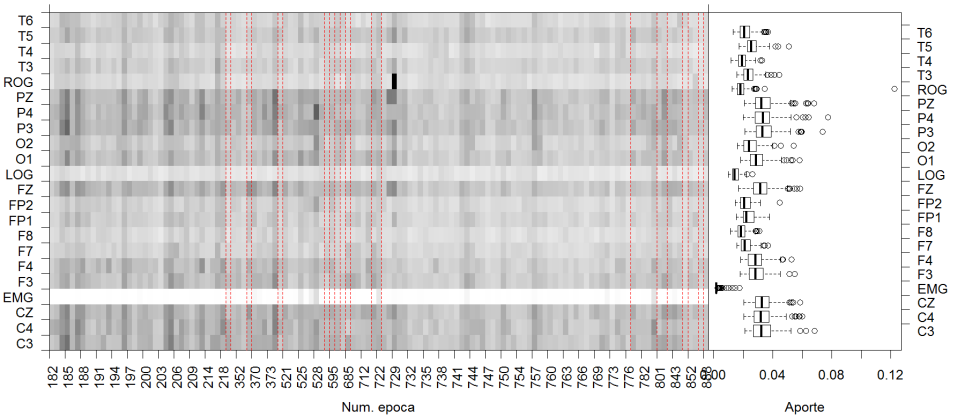

MJNNVIGILOS , GAMMA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

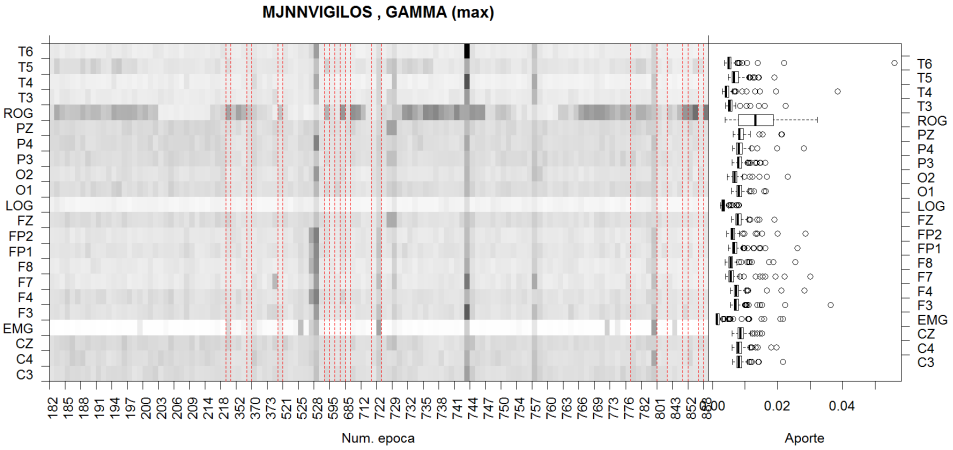

MJNNVIGILOS, *=0.01
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
182 185 188 191 194 197 200 203 206 209 214 218 352 370 373 521 525 528 595 685 712 722 729 732 735 738 741 744 747 750 754 757 760 763 766 769 773 776 782 801 843 852 888
Num. epoca

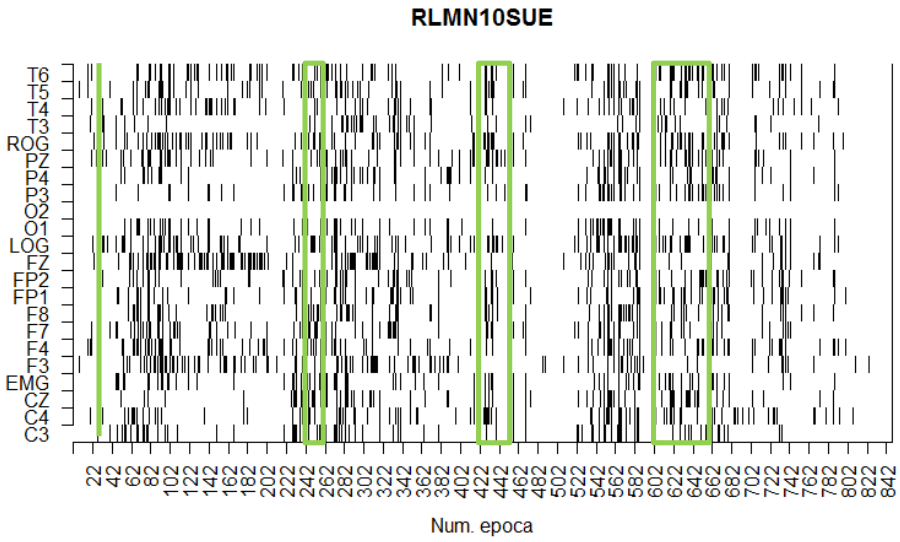

MJNNVIGILOS , DELTA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
182 185 188 191 194 197 200 203 206 209 214 218 352 370 373 521 525 528 595 685 712 722 729 732 735 738 741 744 747 750 754 757 760 763 766 769 773 776 782 801 843 852 888
Num. epoca
0 1 2 3 4 5
Aporte


MJNNVIGILOS , THETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
182 185 188 191 194 197 200 203 206 209 214 218 352 370 373 521 525 528 595 685 712 722 729 732 735 738 741 744 747 750 754 757 760 763 766 769 773 776 782 801 843 852 888
Num. epoca
0.0 0.1 0.2 0.3 0.4 0.5
Aporte

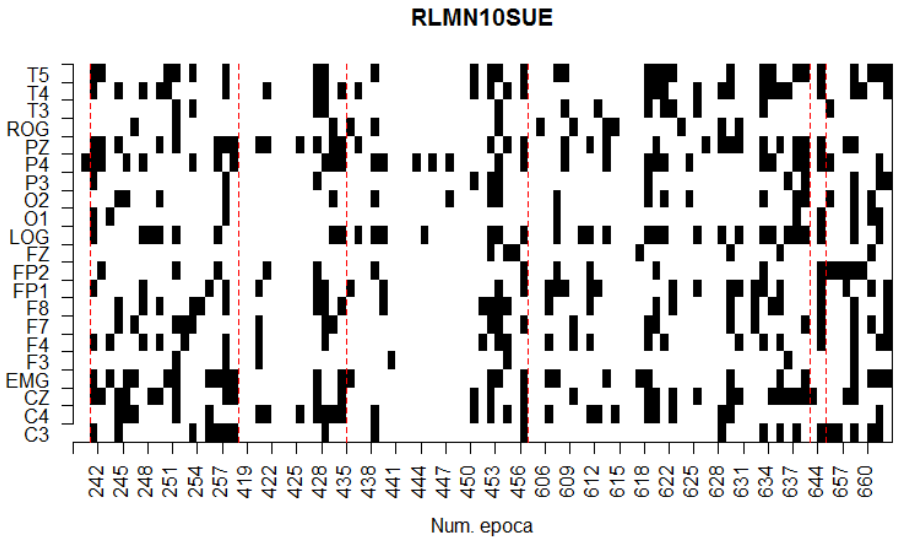

MJNNVIGILOS , ALFA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte
0.05
0.10
0.15


MJNNVIGILOS , BETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte
0.04
0.08
0.12

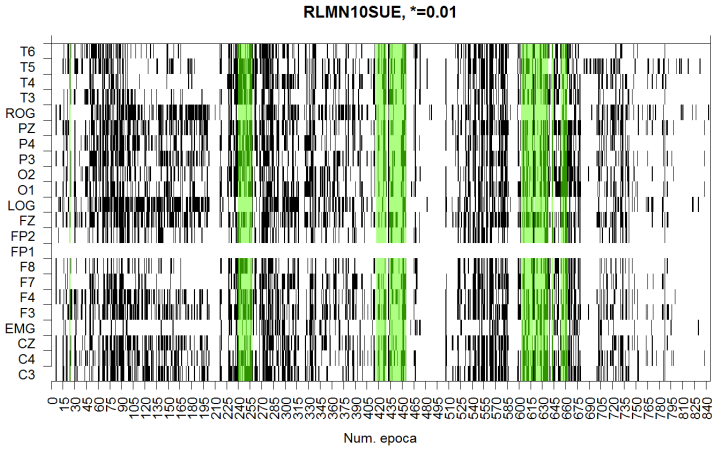

MJNNVIGILOS , GAMMA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte
0.02
0.04

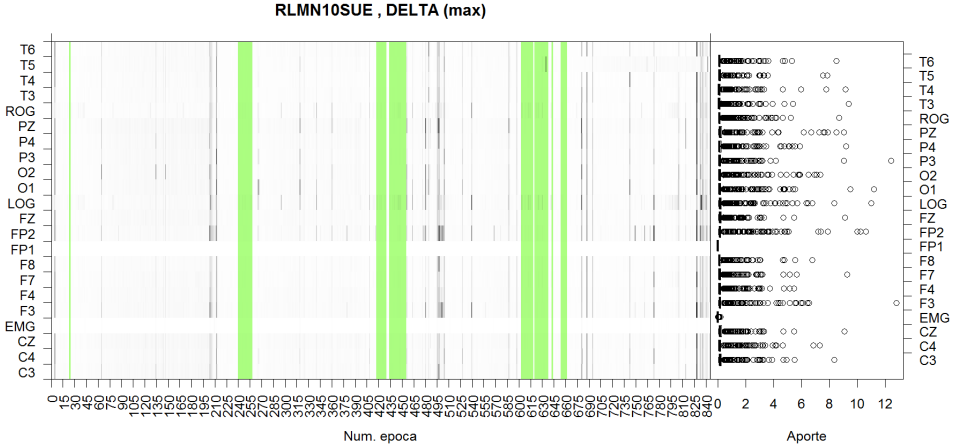


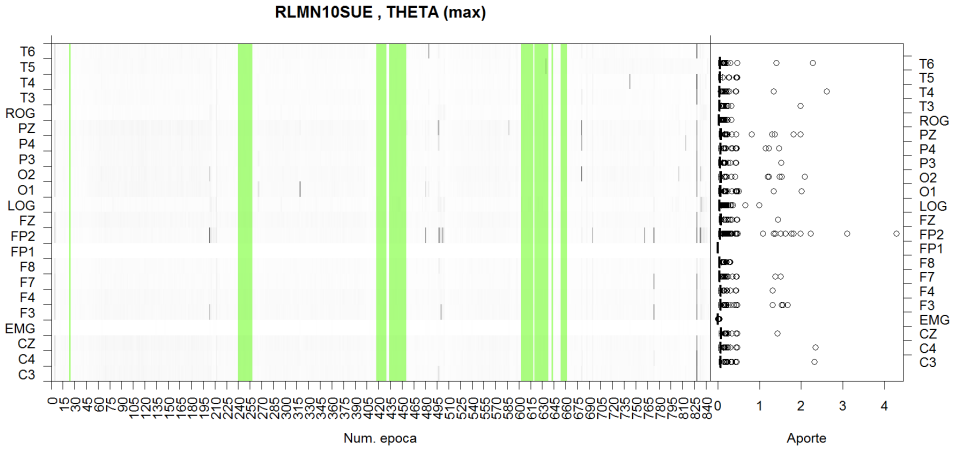
Total de épocas: 846 , Épocas MOR: 99

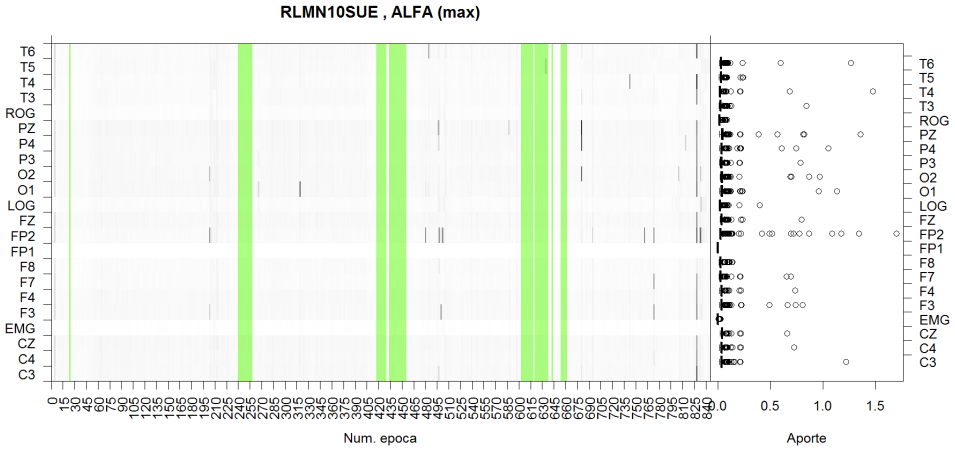


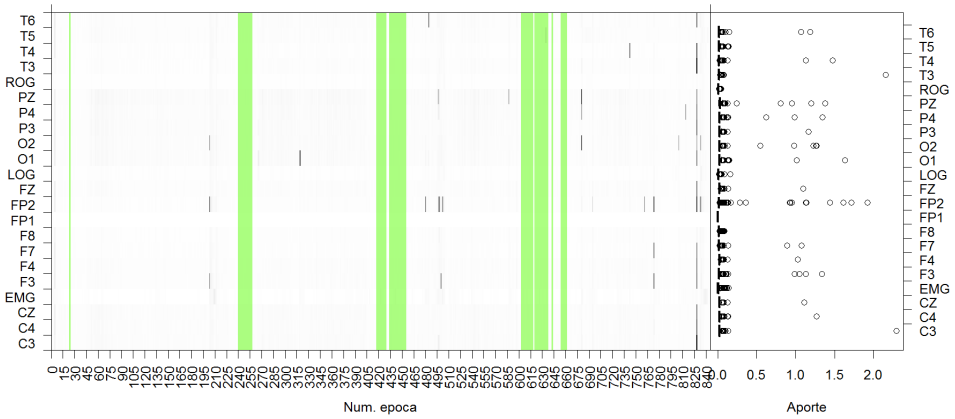
NOTA: ha habido un error al cargar los datos del canal 02

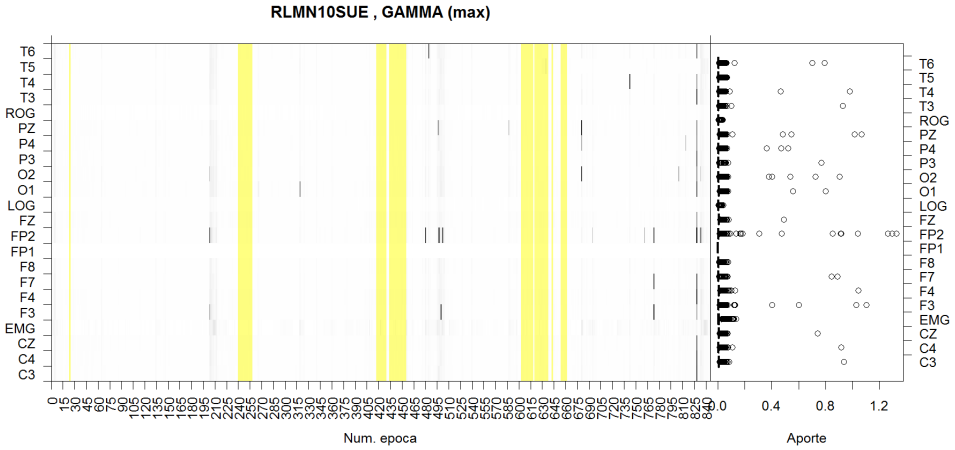

RLMN10SUE, *=0.01
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca

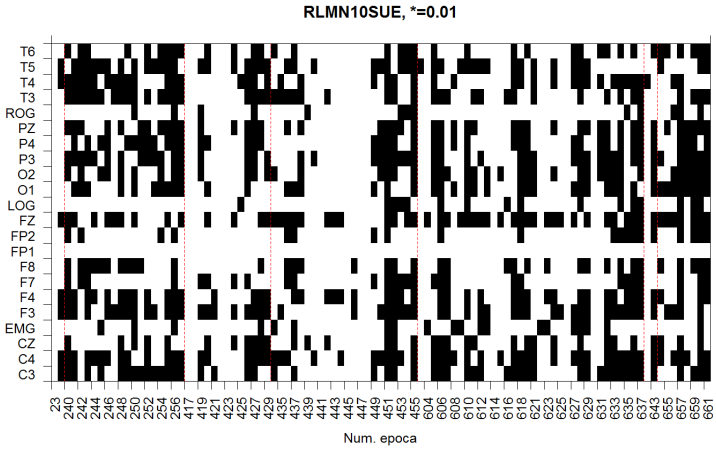

RLMN10SUE , DELTA (max)
Num. epoca
Aporte

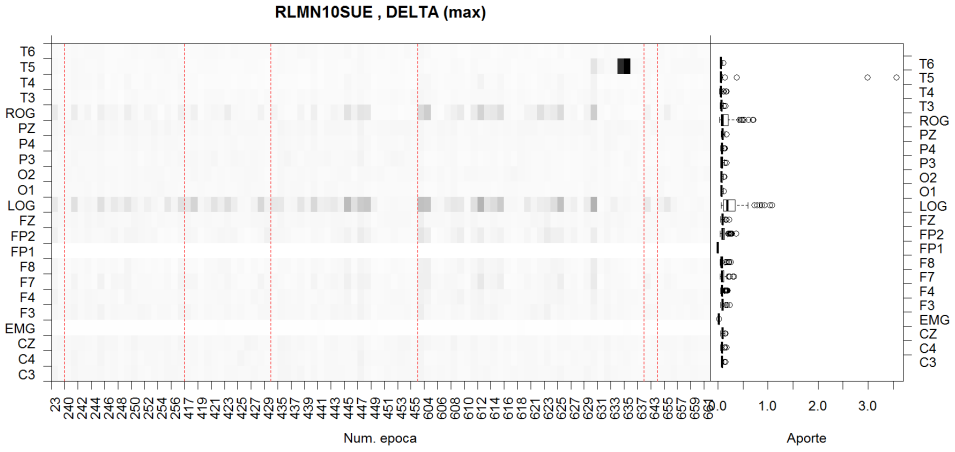

RLMN10SUE , THETA (max)
Num. epoca
Aporte

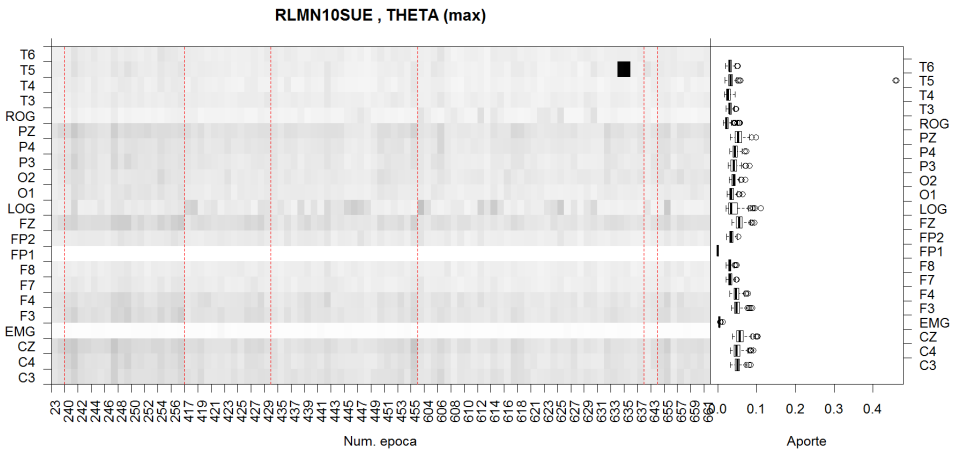

RLMN10SUE , ALFA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

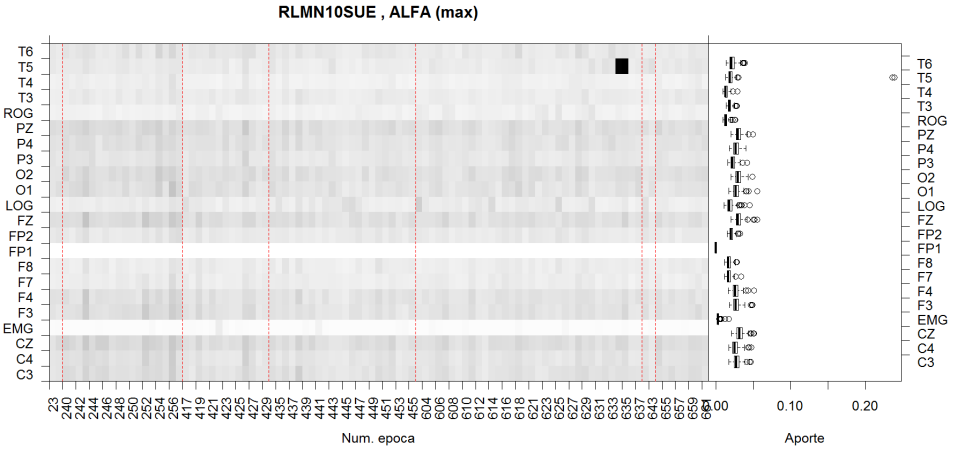

RLMN10SUE , BETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

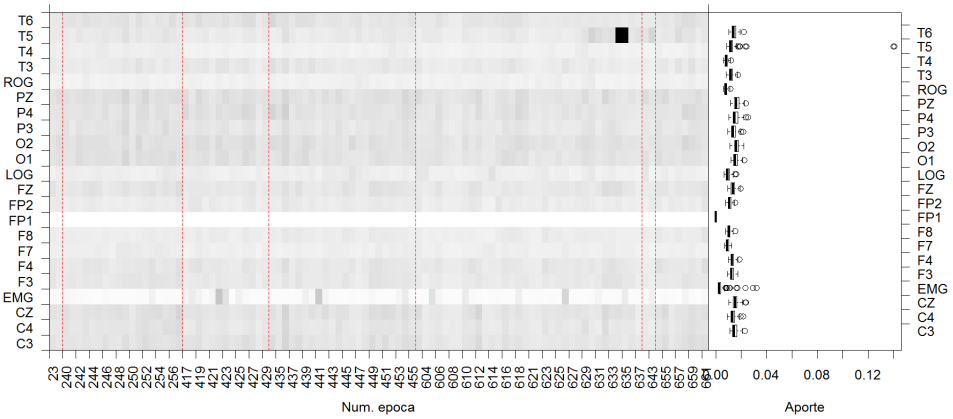

RLMN10SUE , GAMMA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte

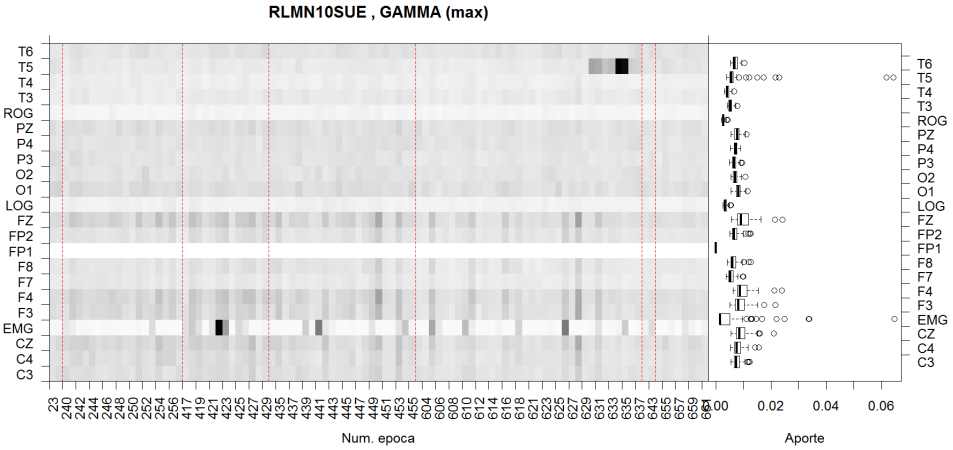

RLMN10SUE, *=0.01
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca


RLMN10SUE , DELTA (max)
Num. epoca
Aporte


RLMN10SUE , THETA (max)
Num. epoca
Aporte


RLMN10SUE , ALFA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
0.00
0.10
0.20
Num. epoca
Aporte


RLMN10SUE , BETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
0.00
0.04
0.08
0.12
Num. epoca
Aporte


RLMN10SUE , GAMMA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
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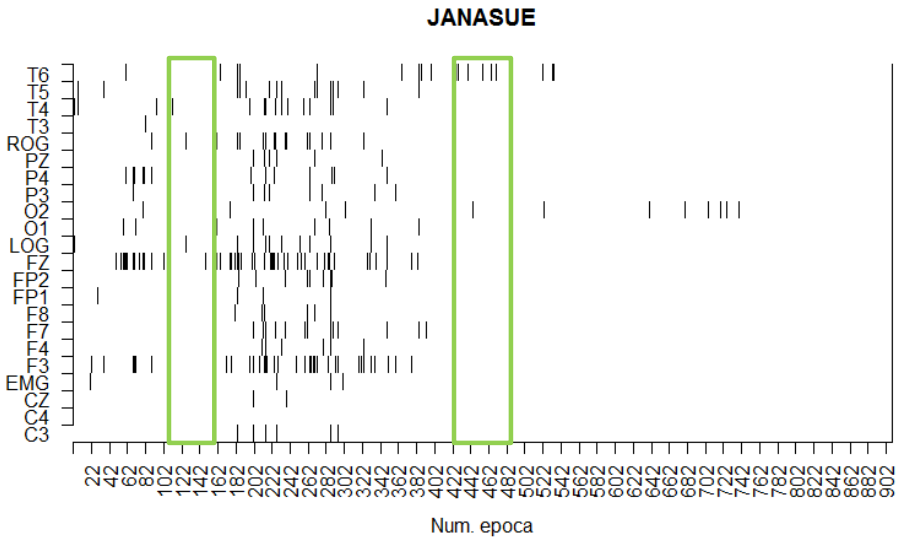
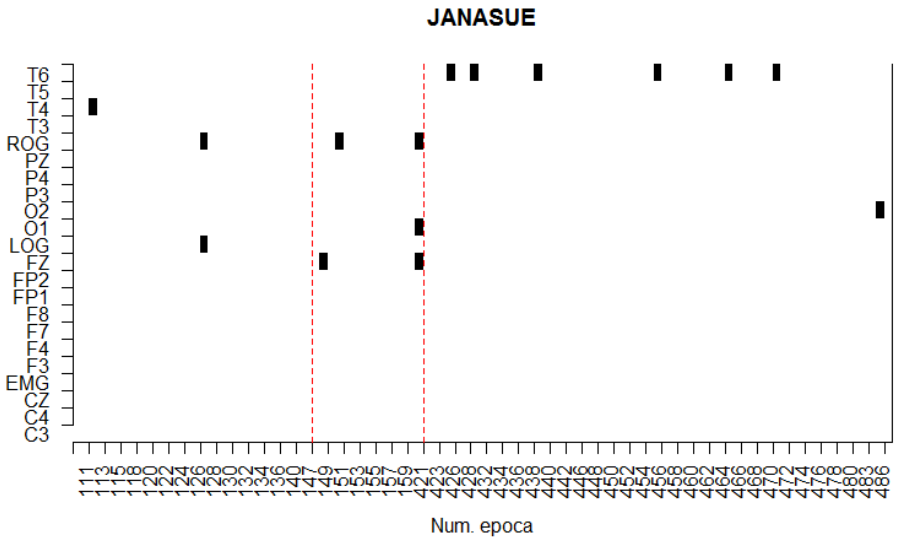
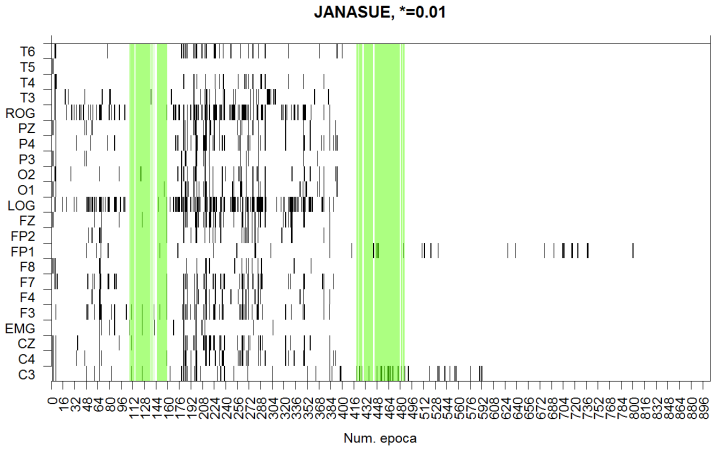
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
0.00
0.02
0.04
0.06
Num. epoca
Aporte



Total épocas: 907 , Épocas MOR: 103




JANASUE, *=0.01
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T5
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T3
ROG
PZ
P4
P3
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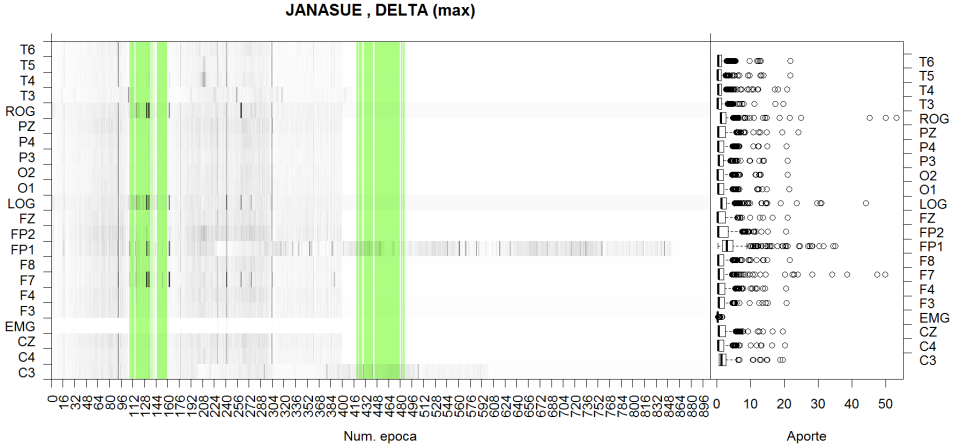
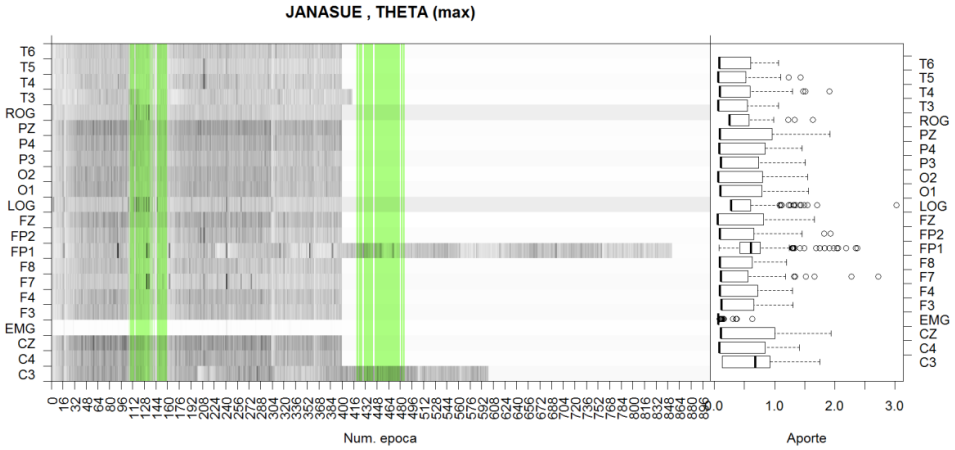
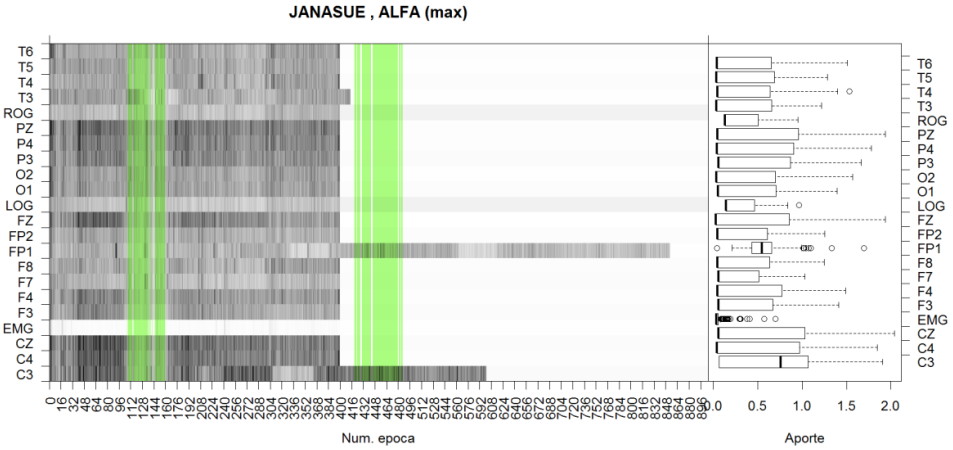
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca


JANASUE , DELTA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte


JANASUE , THETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte


JANASUE , ALFA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
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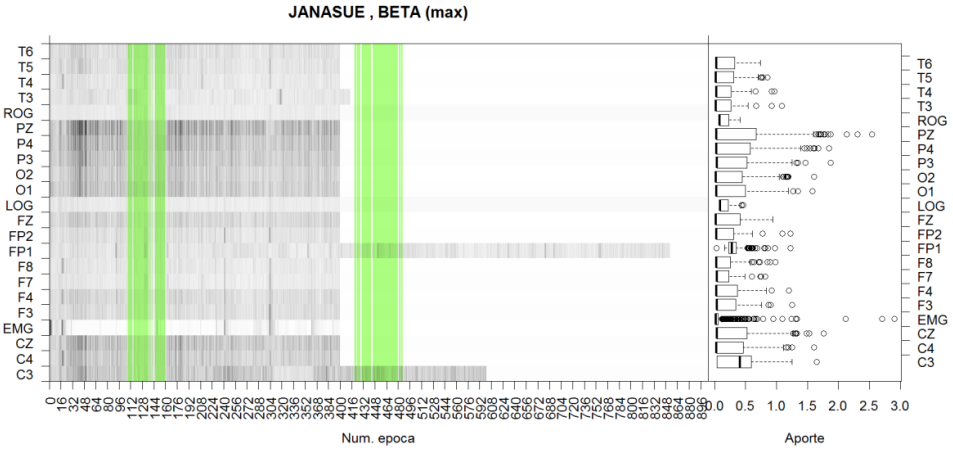
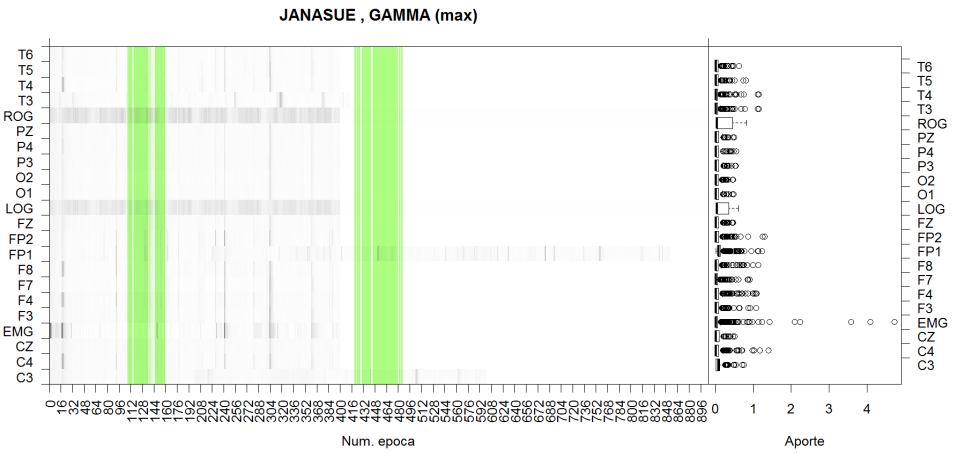
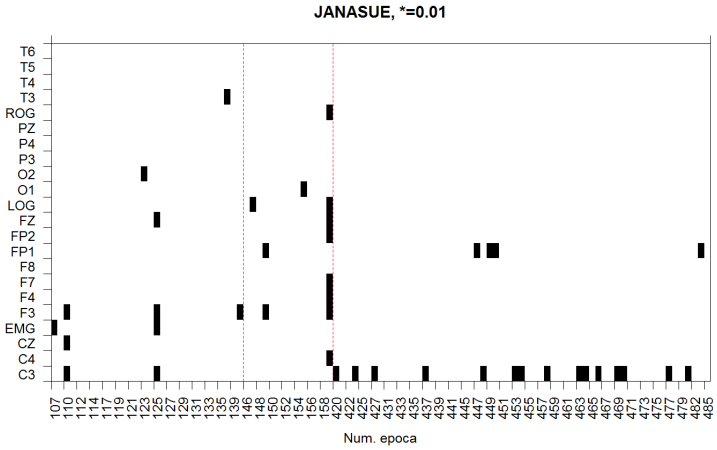
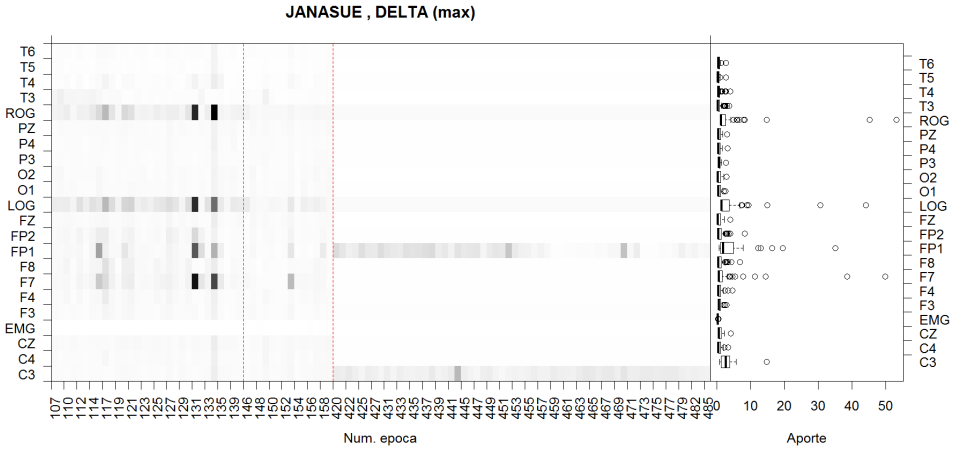
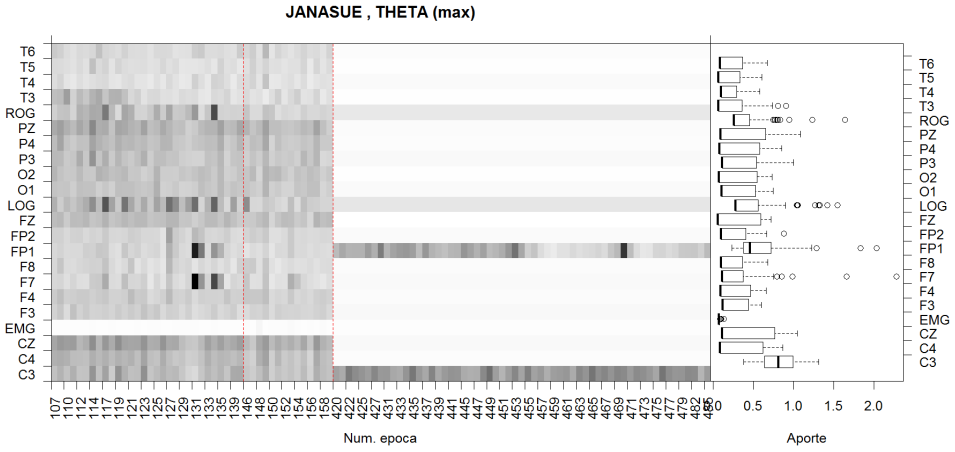
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte


JANASUE , BETA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte


JANASUE , GAMMA (max)
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca
Aporte


JANASUE, *=0.01
T6
T5
T4
T3
ROG
PZ
P4
P3
O2
O1
LOG
FZ
FP2
FP1
F8
F7
F4
F3
EMG
CZ
C4
C3
Num. epoca


JANASUE , DELTA (max)
Num. epoca
Aporte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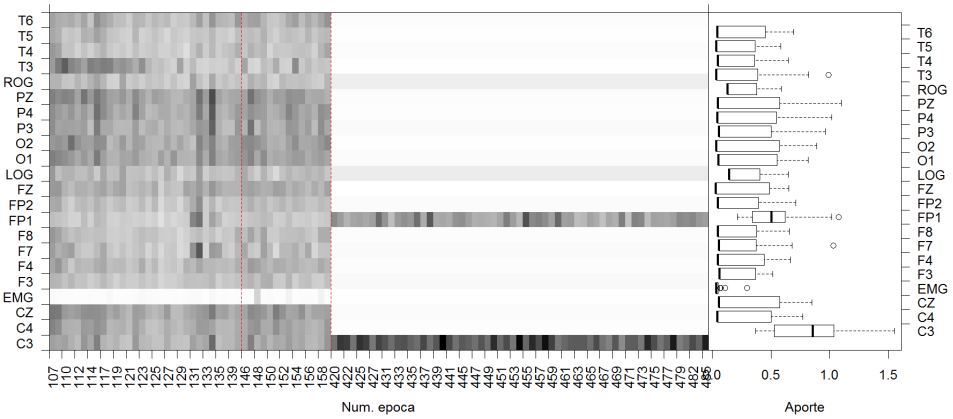

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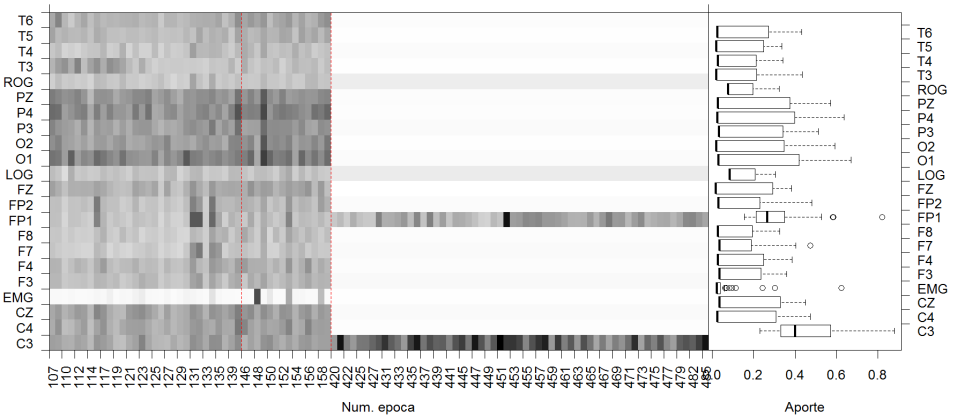

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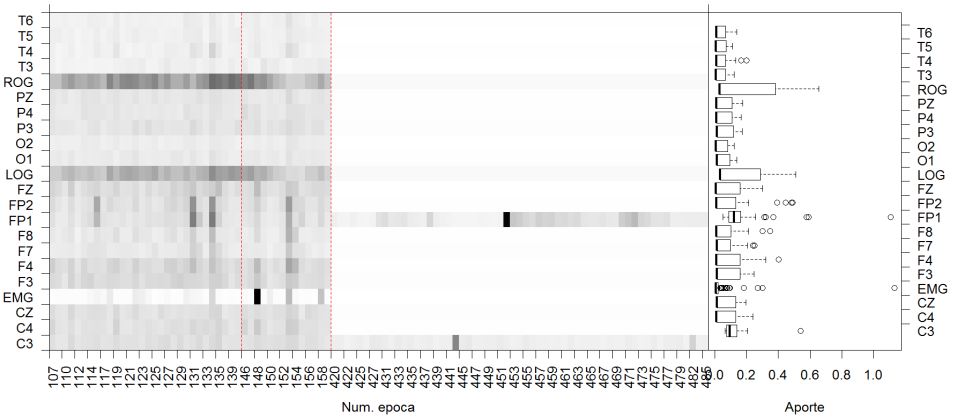

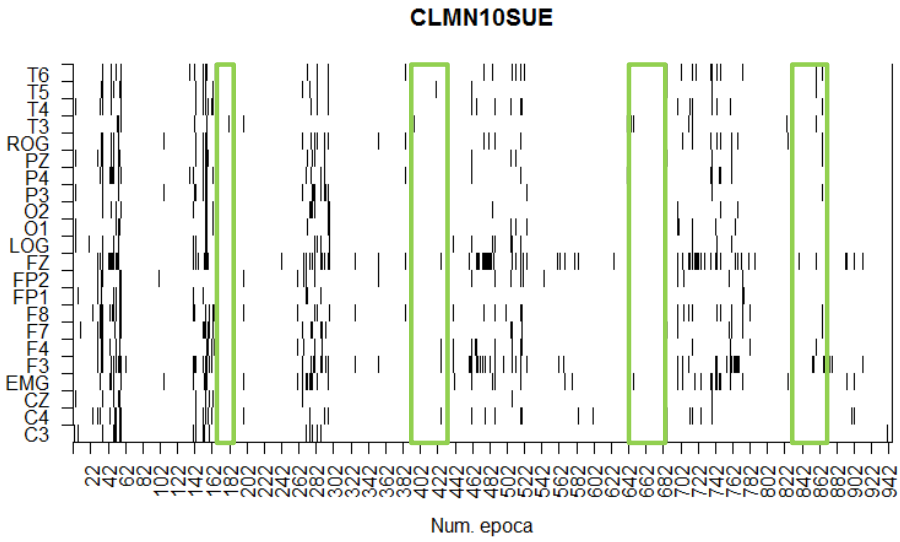

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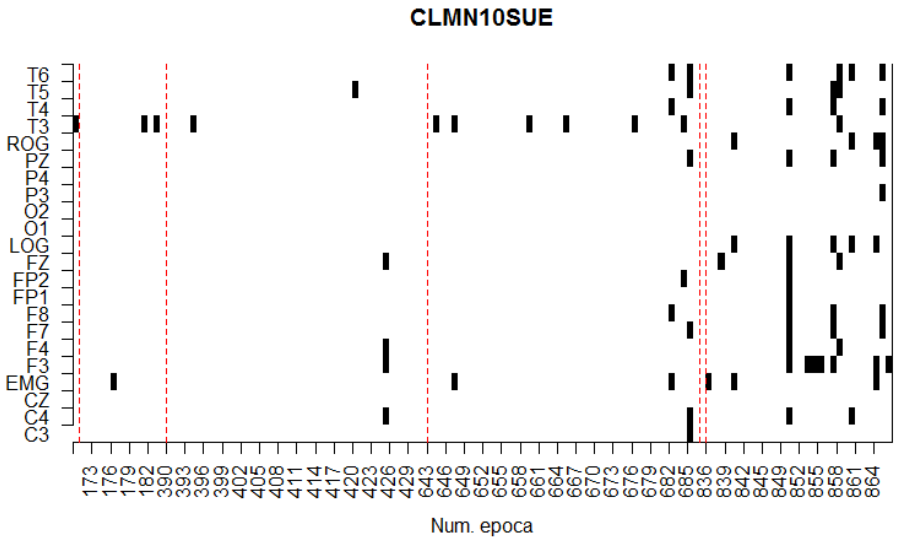

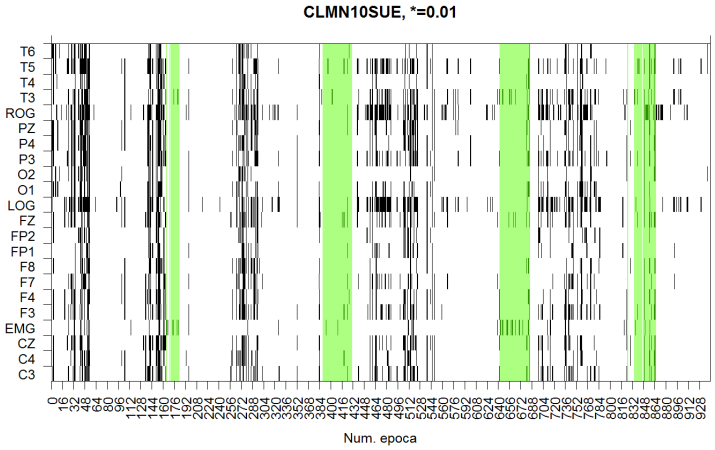
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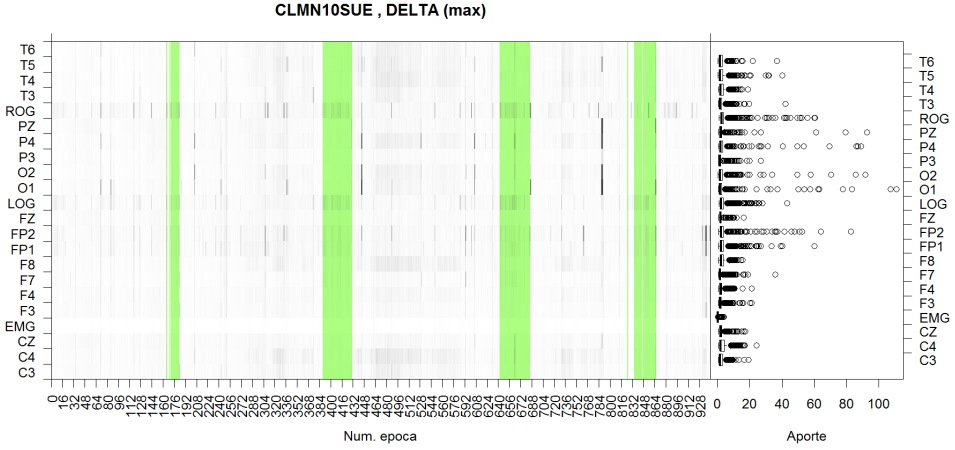
Num. epoca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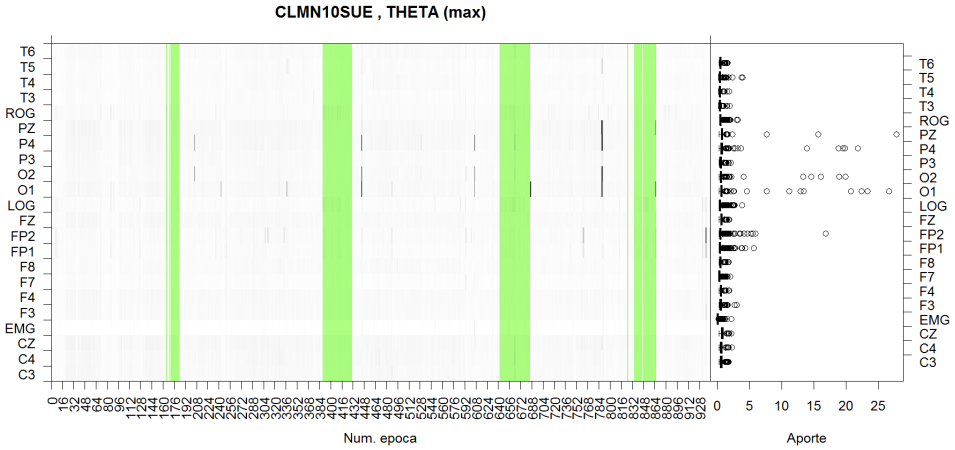
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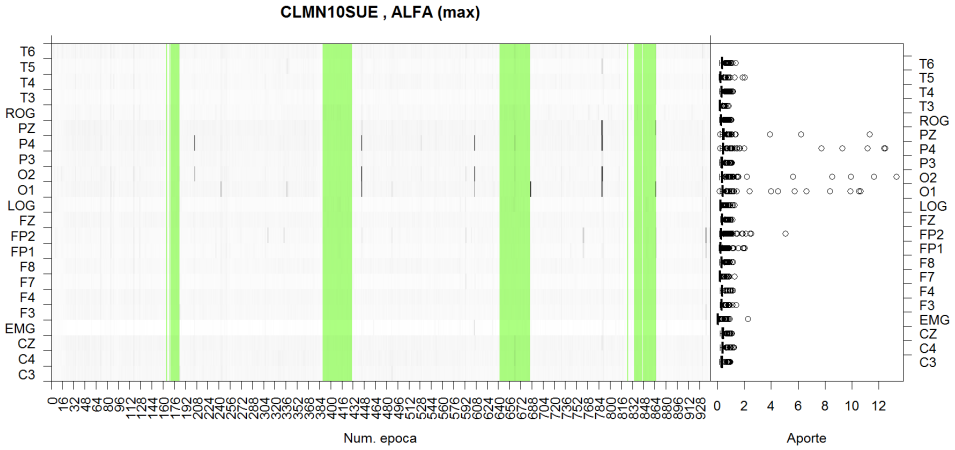
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Num. epoca
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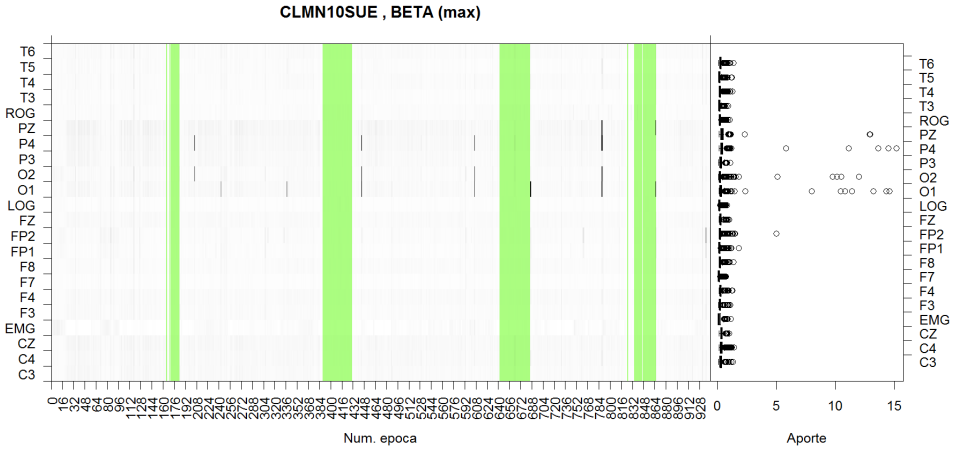
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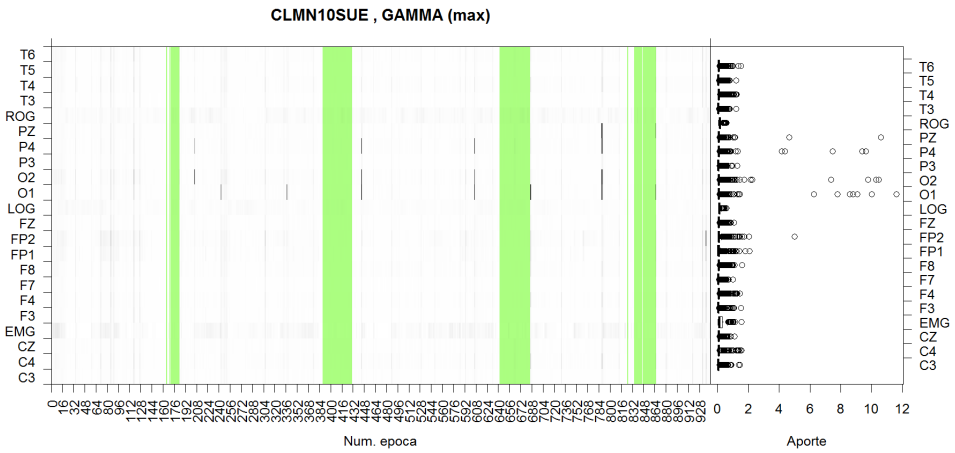
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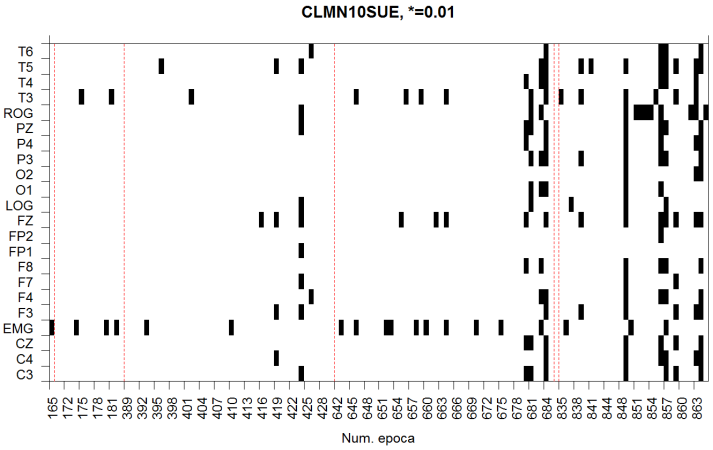
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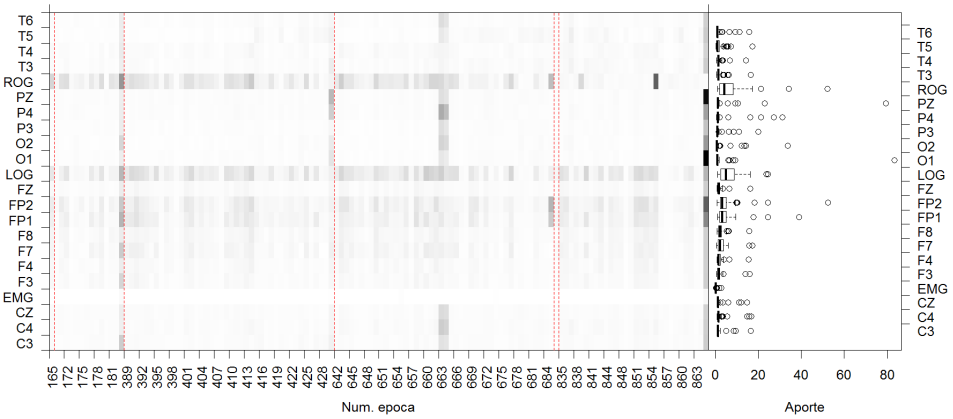
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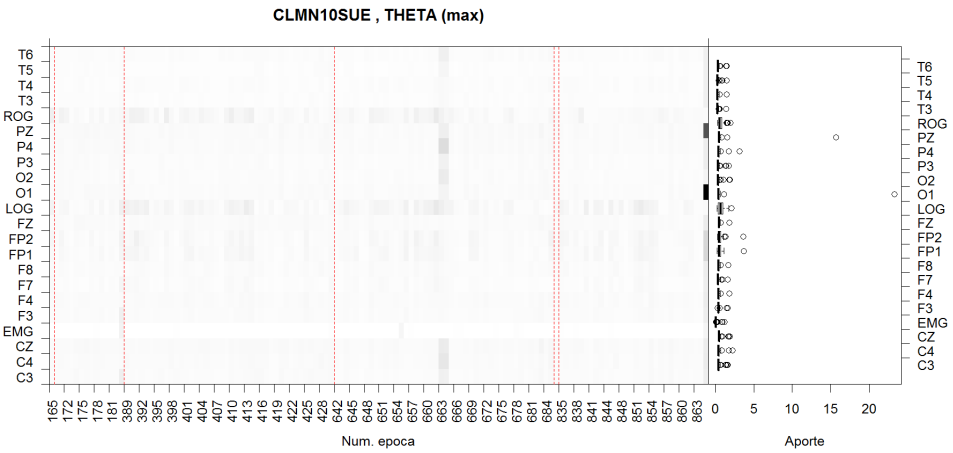
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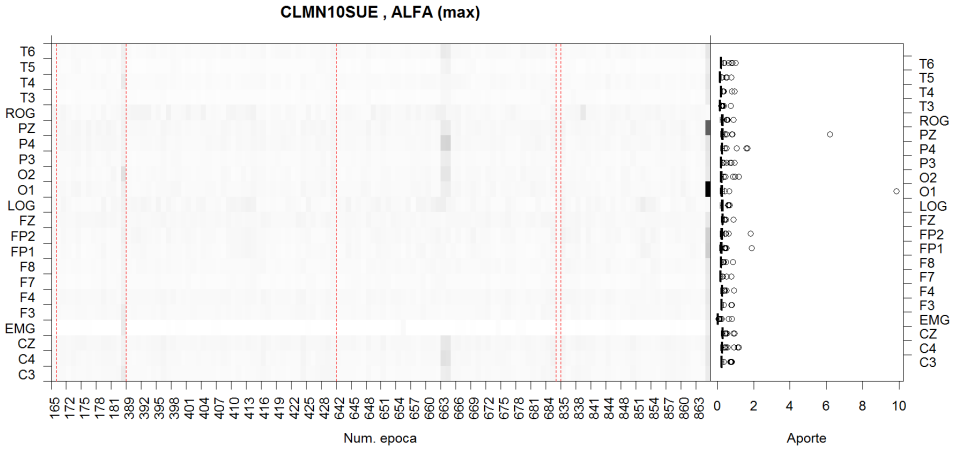
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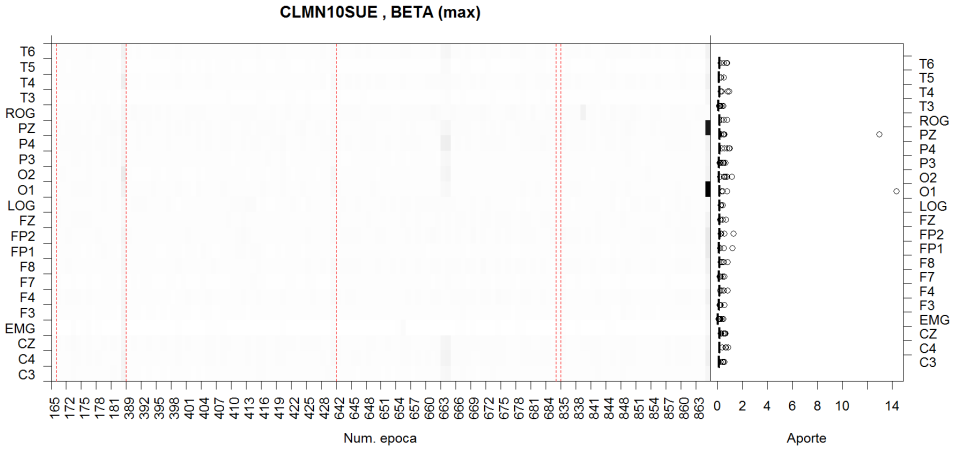
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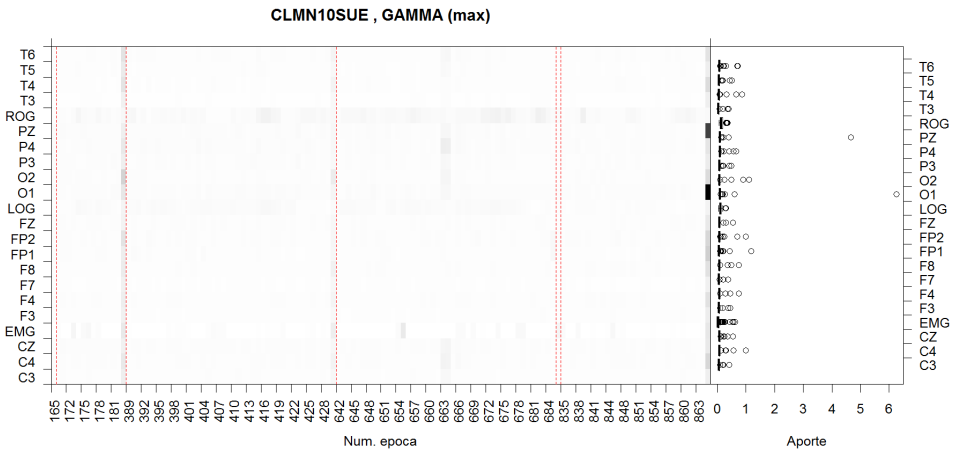
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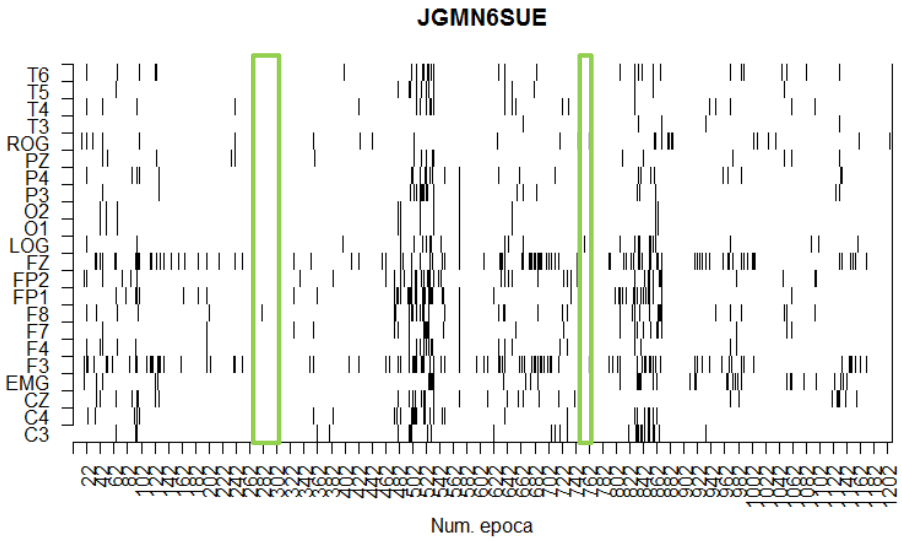

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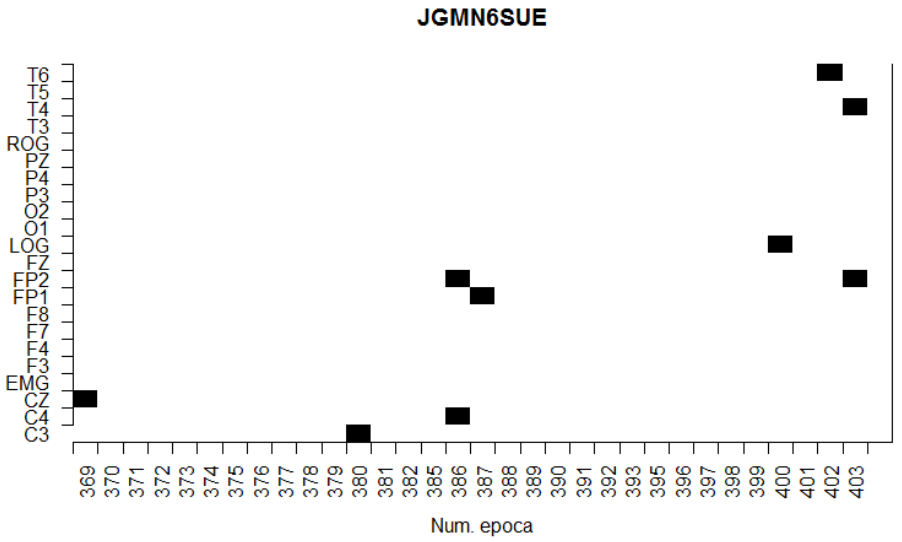

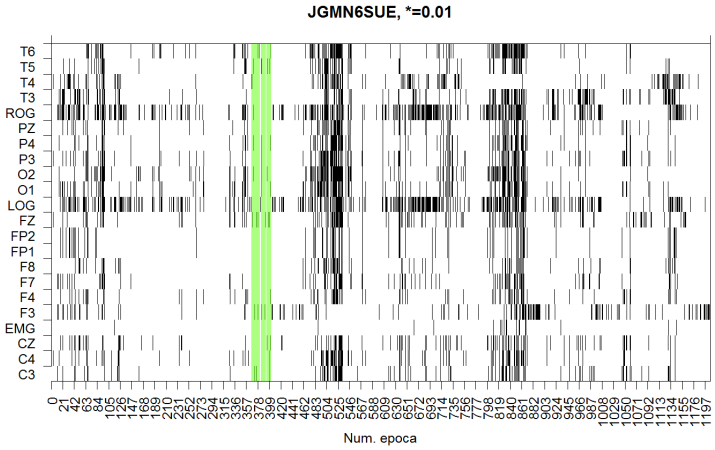
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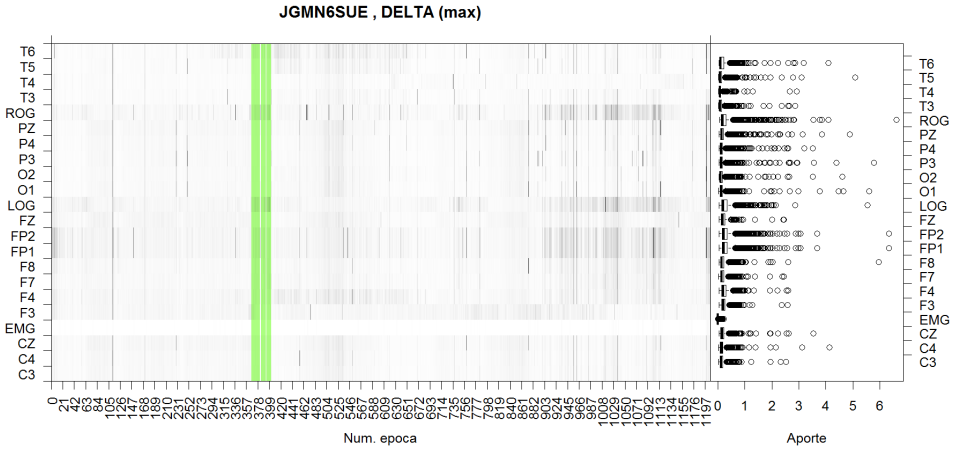
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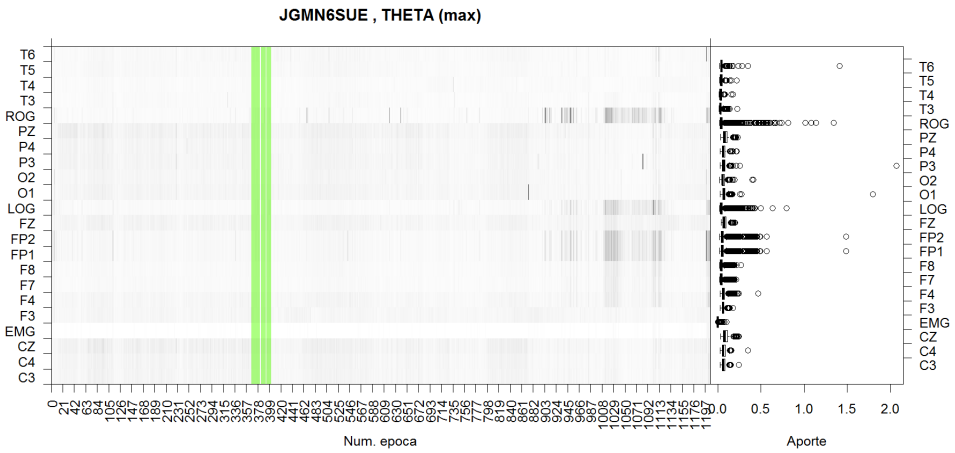
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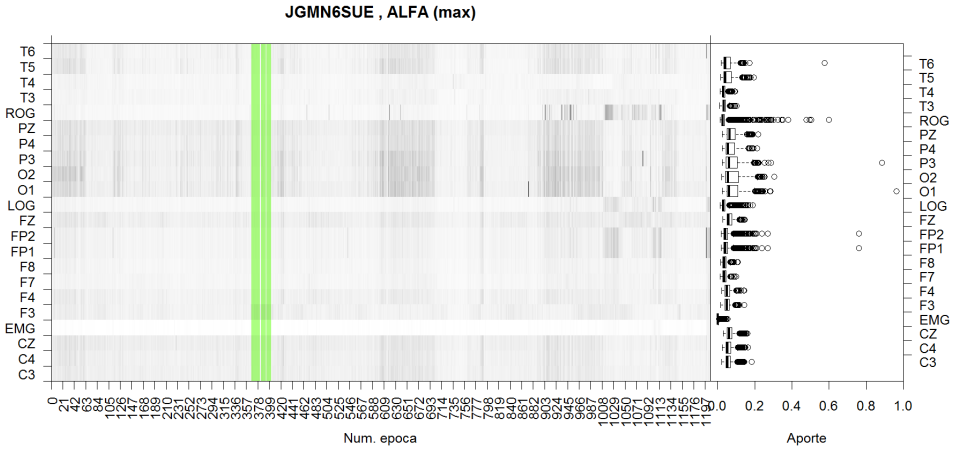
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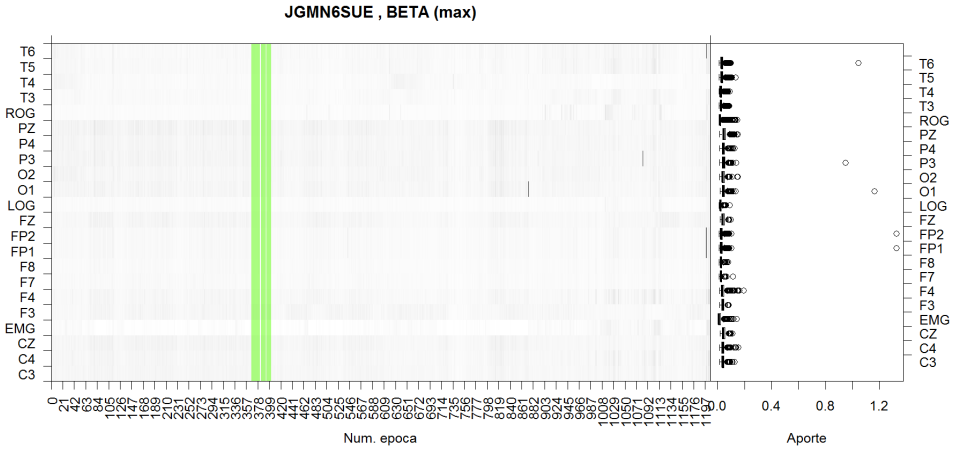
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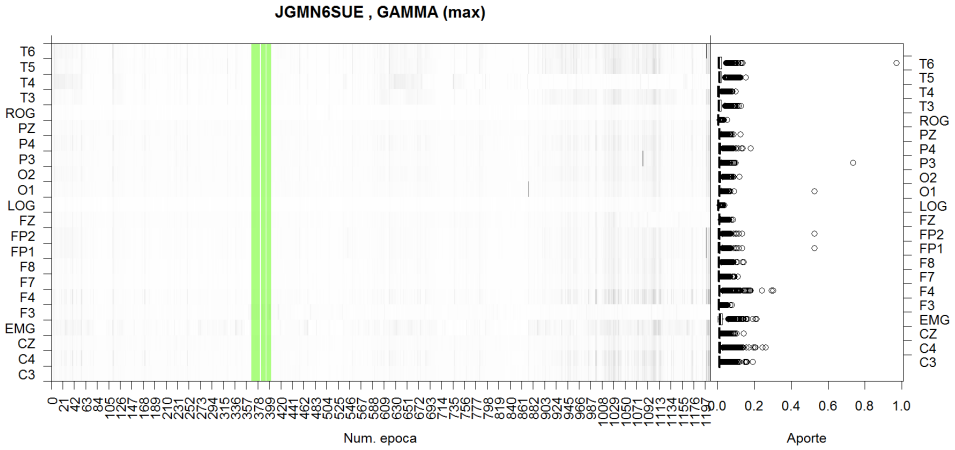
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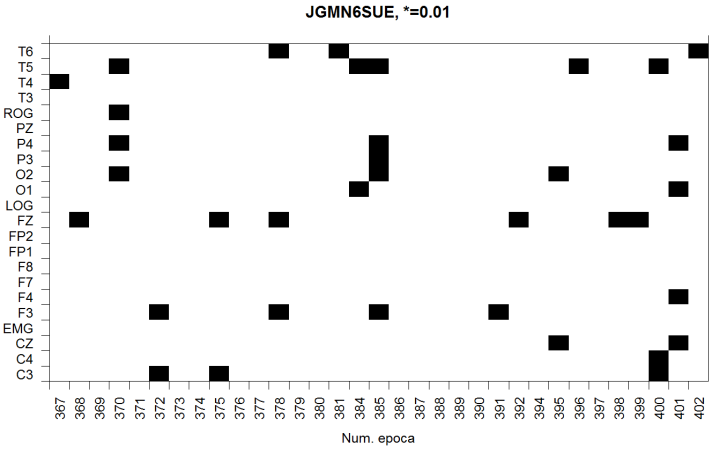
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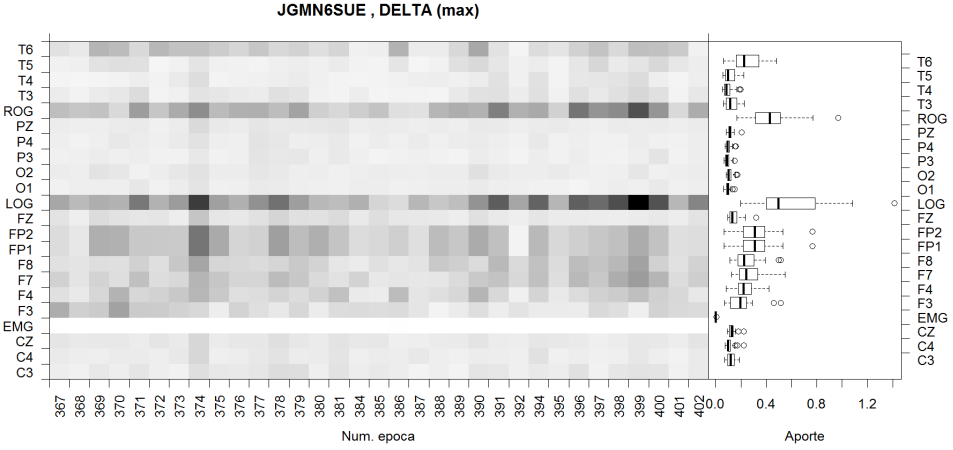
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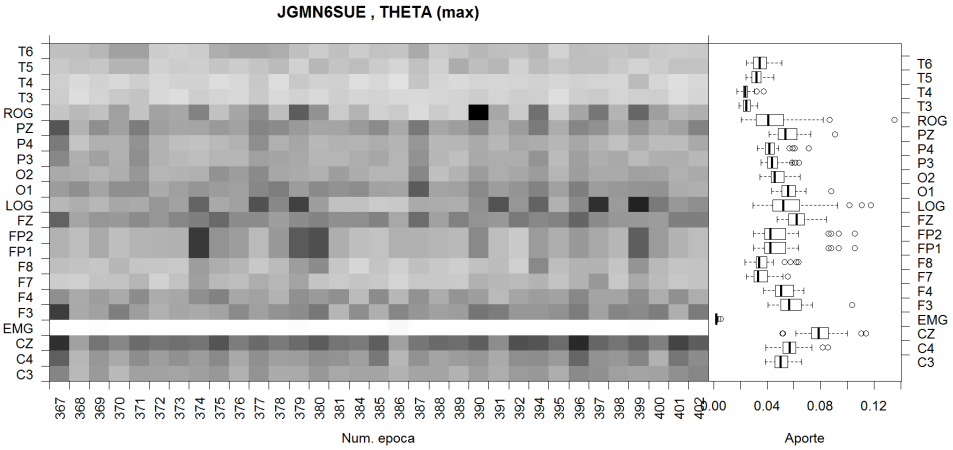
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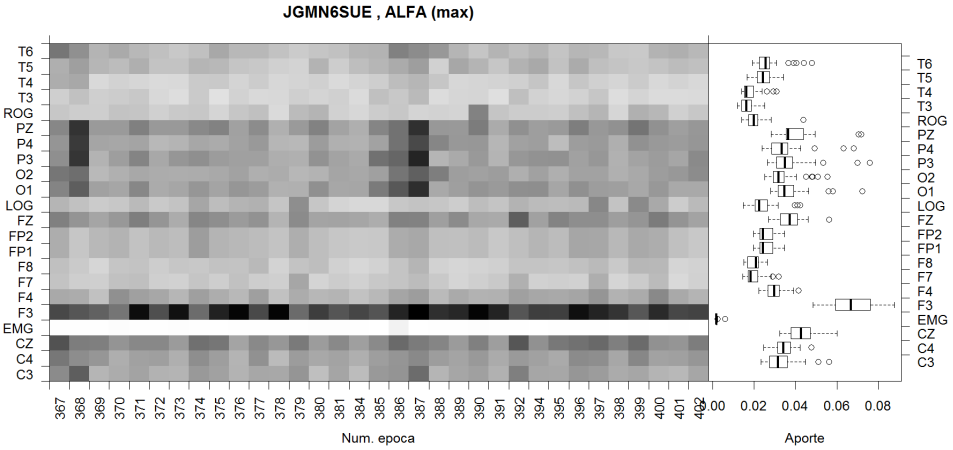
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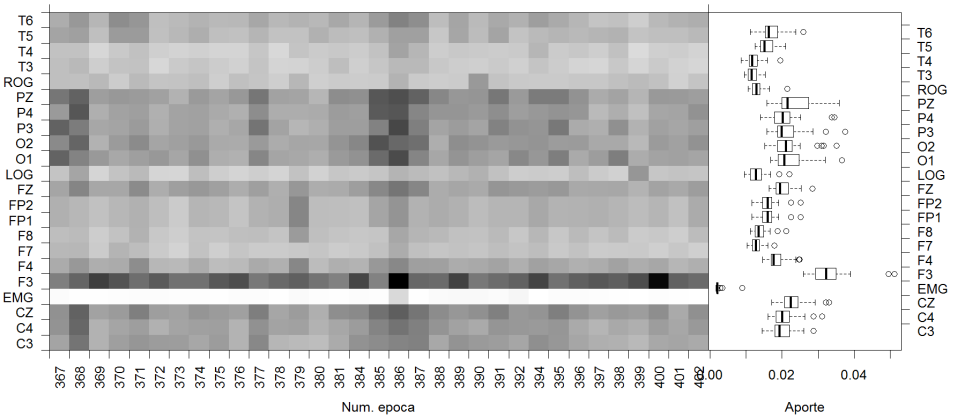
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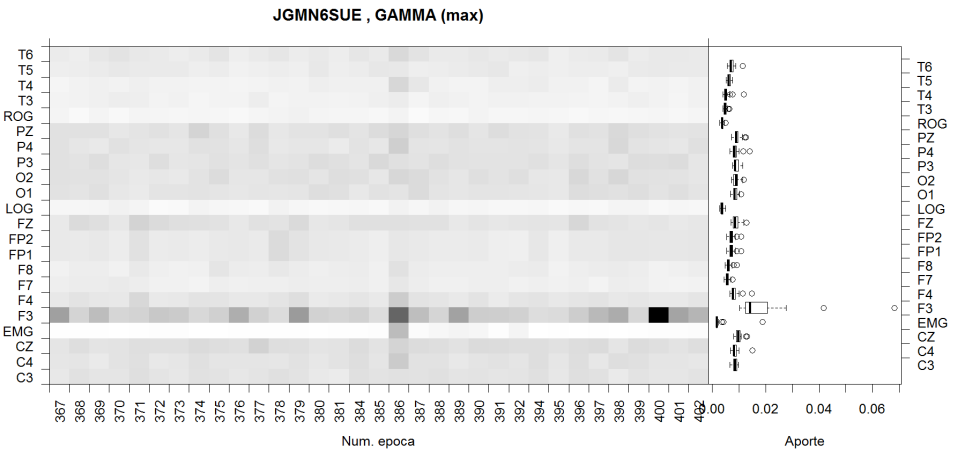
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Num. epoca
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Aporte

Capítulo 4

"Resultados"

Esta parte tiene material ya que se ha discutido plenamente el trabajo; sin embargo, por esto mismo es difícil de redactar.

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