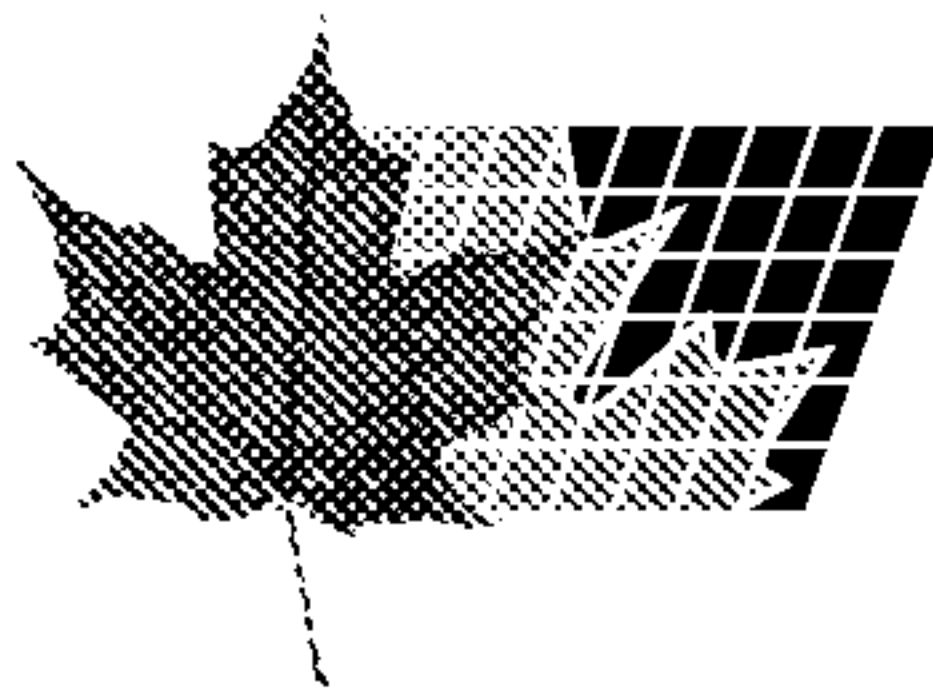




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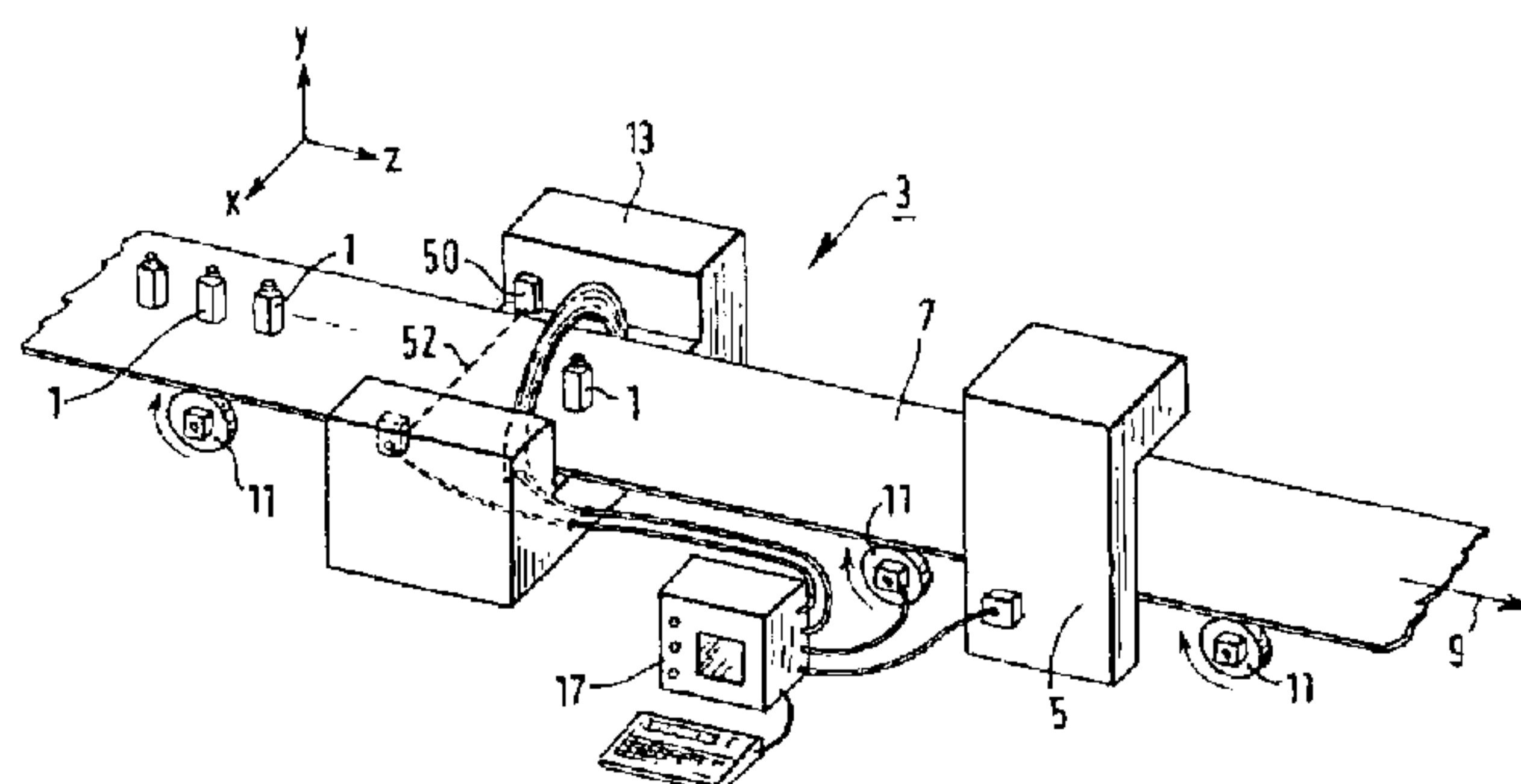
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(54) **APPAREIL ET PROCEDE DE VERIFICATION DU PESAGE**

(54) **CHECK WEIGHING APPARATUS AND METHOD**



(57) L'invention concerne un système formant balance de vérification qui permet de vérifier le poids d'échantillons (1) sur une ligne de production. Ce système comprend un aimant (13) afin de générer un champ magnétique statique sur une zone d'interrogation pour créer une magnétisation nette dans un échantillon (1) placé dans la zone d'interrogation. En outre, ce système comporte une bobine HF pour appliquer un champ magnétique alternatif sur ladite zone d'interrogation afin de provoquer une excitation de l'échantillon (1) dans cette zone d'interrogation, selon les principes de la résonance magnétique nucléaire. Ce système de vérification comprend également un capteur pour capter l'énergie émise lorsque l'échantillon retrouve un état d'équilibre après son excitation, lors du passage des échantillons dans la zone d'interrogation sur un transporteur à courroie (9) formant partie de la ligne de production. Le signal capté à partir de l'échantillon est ensuite comparé aux données de calibrage qui sont obtenues pour au moins un échantillon semblable de masse connue. Ces données de calibrage concernent la masse de l'échantillon semblable pour le signal correspondant émis par le capteur, pour constituer une indication de la masse de l'échantillon.

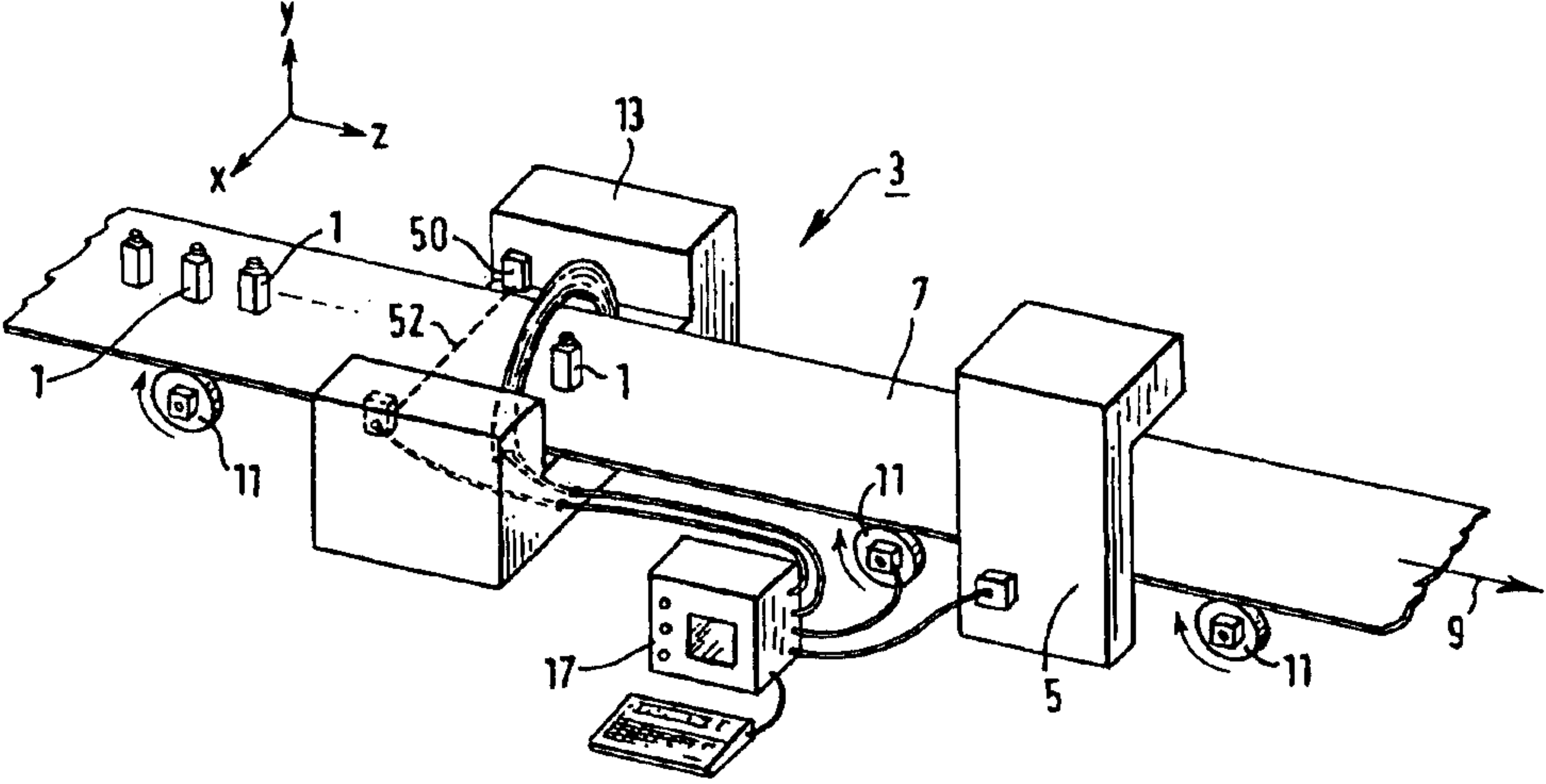
(57) A check weighing system is provided which can check weigh samples (1) on a production line. The check weighing system comprises a magnet (13) for creating a static magnetic field over an interrogation zone for creating a net magnetisation within a sample (1) located within the interrogation zone and an RF coil for applying an alternating magnetic field over the interrogation zone for causing excitation of the sample (1) within the interrogation zone according to the principles of NMR. The check weighing system also comprises a sensor for sensing the energy emitted as the sample relaxes back to an equilibrium state after excitation as the samples pass through the interrogation zone on a conveyor belt (9) forming part of the production line. The sensed signal from the sample (1) is then compared with calibration data which is obtained for at least one similar sample of known mass, which calibration data relates the mass of the similar sample to the corresponding signal output by the sensor, to provide the indication of the mass of the sample.



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(54) Title: CHECK WEIGHING APPARATUS AND METHOD  (57) Abstract A check weighing system is provided which can check weigh samples (1) on a production line. The check weighing system comprises a magnet (13) for creating a static magnetic field over an interrogation zone for creating a net magnetisation within a sample (1) located within the interrogation zone and an RF coil for applying an alternating magnetic field over the interrogation zone for causing excitation of the sample (1) within the interrogation zone according to the principles of NMR. The check weighing system also comprises a sensor for sensing the energy emitted as the sample relaxes back to an equilibrium state after excitation as the samples pass through the interrogation zone on a conveyor belt (9) forming part of the production line. The sensed signal from the sample (1) is then compared with calibration data which is obtained for at least one similar sample of known mass, which calibration data relates the mass of the similar sample to the corresponding signal output by the sensor, to provide the indication of the mass of the sample.		

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CHECK WEIGHING APPARATUS AND METHOD

The present invention relates to an apparatus and method for check weighing material contained in a container
5 which is passing along a production line. The invention particularly relates to the use of magnetic resonance techniques for such check weighing.

In today's industrial environment there is a continuous
10 need to improve efficiency, quality and yield. As a result, automated control and quality assurance (QA) systems for manufacturing lines are becoming increasingly important. One type of monitoring device commonly used on product filling lines is a check weighing device,
15 which is used to ensure that the required amount of product is put in each container.

As one example, check weighing is used by the pharmaceuticals industry for the monitoring and
20 regulation of the amount of a drug in a sealed glass vial during filling. The drug weight can be as small as a fraction of a gram, and is required to be weighed with an accuracy of a few per cent or better, in a vial weighing tens of grams at a rate of several weighings per
25 second. At present, to obtain the required accuracy, it is necessary to remove the vials from the production line and to weigh them on precision balances. This must be done both before and after filling in order to take into account the weight of the container. Inevitably this is
30 a time consuming process and 100% inspection cannot be achieved while maintaining throughput. As a result only a fraction of the product is ever tested. Therefore, if something does go wrong and the vials are not being filled with the correct amount of the drug, then a large
35 batch of product can be wasted before the problem is even

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noticed. Furthermore, since the vial must be weighed both before and after filling, the weighing must be performed in the aseptic environment between filling and sealing.

5

The present invention aims to provide an alternative technique for check weighing products on a production line.

10 According to one aspect, the present invention provides an apparatus for determining the mass of a sample comprising: means for generating a static magnetic field in a first direction through the sample; means for applying an alternating excitation magnetic field in a
15 second different direction through the sample; means for sensing energy emitted by the sample in response to the excitation magnetic field and for outputting a signal in dependence thereon; and means for comparing the signal output by said sensing means with stored calibration data
20 to provide an indication of the mass of the sample. This apparatus has the advantage that it can be used on-line in a product filling line. It is also advantageous because it can provide a contactless measure of the mass of the contents of a container independently of the
25 container mass if the container is made of a material which is not responsive to MR. It is therefore very useful for determining the mass of small quantities of sample such as samples weighing between 0.1 grams and 10 grams which may be contained in glass containers of 20
30 grams or more. It is also fast and accurate, it is easily integrated into the production line and it provides an indication of mass and not weight of the sample.

35 The above apparatus can be used in a number of different

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applications, such as for pharmaceuticals, cosmetics, perfumes, industrial chemicals, biological samples and food products. It is particularly useful to measure high valued products where 100% sampling can considerably
5 reduce wastage. It can be used to determine the mass of samples which are in solid form, in powder form, in liquid form and in gas form or any combination of these.

The present invention also provides a method of producing
10 sealed containers containing a predetermined amount of a sample, the method comprising the steps of: filling the container with the predetermined amount of sample; transporting each of the filled containers to a weighing station; weighing the sample within each of the
15 containers; sealing the sample within the container; and rejecting any containers which do not contain the predetermined amount of sample within a predetermined tolerance; characterised in that the weighing step comprises the steps of generating a static magnetic field
20 in a first direction through an interrogation zone for creating a net magnetisation within a sample located within the interrogation zone; applying a pulse of alternating magnetic field in a second different direction through the interrogation zone for temporarily
25 changing the net magnetisation of the sample located within the interrogation zone; sensing energy emitted by the sample as the net magnetisation of the sample returns to its original state and outputting a signal in dependence thereon; and comparing the signal output by
30 the sensing step with calibration data which relates the mass of at least one similar sample of known mass to the corresponding signal output by the sensing step, to provide said indication of the mass of the sample within each container.

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Exemplary embodiments of the invention will now be described with reference to the accompanying drawings in which:

- 5 Figure 1 is an overview of a production line with a magnetic resonance check weighing station for checking that each filled vial which passes through the weighing station has the required amount of product;
- 10 Figure 2 is a block diagram of excitation and processing electronics which form part of and control the check weighing station shown in Figure 1;
- 15 Figure 3 is a plot which illustrates how the net magnetisation of a sample varies with the time it is subjected to a static magnetic field which forms part of the check weighing station shown in Figure 1;
- 20 Figure 4 is a plot of a pulse of excitation current which is applied to an excitation coil which forms part of the check weighing station shown in Figure 1;
- 25 Figure 5 is a plot which shows the way in which the signal generated by a sample decays after the pulse of excitation current shown in Figure 4 ends;
- Figure 6 is a plot illustrating the time required between sample measurements of the same sample;
- 30 Figure 7a diagrammatically illustrates the form of a check weighing station according to an alternative embodiment in which a magnetic field gradient is applied over an interrogation zone;
- 35 Figure 7b illustrates the form of a narrow bandwidth

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pulse which is applied to the RF coil shown in Figure 7a for interrogating a selected region of the interrogation zone;

5 Figure 7c illustrates the narrow bandwidth of the pulse shown in Figure 7b;

Figure 8 diagrammatically illustrates the form of a check weighing station according to another embodiment of the
10 present invention;

Figure 9 illustrates the form of yet a further check weighing station embodying the present invention;

15 Figure 10 illustrates the form of another check weighing station embodying the present invention;

Figure 11 is a plot of the signal strengths generated by a sample under test and a seal used to close the vial in
20 which the sample is contained; and

Figure 12 is a plot of the signal strength generated by the sample under test and the seal of the vial in which the sample is contained after an inversion excitation
25 pulse is applied to the vial.

Figure 1 shows part of a production line which fills glass vials 1 with a drug sample. In particular, Figure 1 shows the weighing station 3 which is provided "in-
30 line" for weighing each of the filled vials which pass therethrough. Figure 1 also shows a reject station 5 which removes those vials from the line which do not have a sufficient amount of the drug to meet regulatory requirements. As shown, the vials 1 are transported to
35 the weighing station 3 from a filling and sealing station

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(not shown) by a conveyor belt 7 which, as represented by the arrow 9, moves in the z direction through the action of the rotating conveyor wheels 9.

5 As mentioned above, the present invention uses magnetic resonance (MR) techniques to determine the mass of the drug sample within each of the glass vials 1. As those skilled in the art of MR will appreciate, glass vials are used as the container in this embodiment, because they
10 do not give off an MR signal which might interfere with the measurement process. In this embodiment, the weighing station 3 comprises a permanent magnet 13, an RF coil 15 and a computer control system 17. The magnet 13 is used to create a homogeneous DC or static magnetic
15 field in the x direction across the conveyor belt 7. The sample in the glass vial contains nuclei which each possess a magnetic moment, e.g. ^1H nuclei (protons). This magnetic moment is a result of the spin of the nuclei. The magnetic moment acts like a small bar magnet and its
20 strength is dependent on the type of nuclei. Before the sample is placed in the static magnetic field, the individual nuclear magnetic moments are randomly orientated. When they enter the static magnetic field, they tend to align with the static field, along the X-
25 direction in this case. The magnetic moments can align themselves either parallel or anti-parallel to the static field. Alignment parallel to the static field is the lower energy state and thus more of the magnetic moments adopt this orientation. This results in the sample
30 having a resultant net macroscopic magnetisation parallel to the static field.

As mentioned above, the nuclei possess spin and, as a result of this, they rotate or precess around the static
35 magnetic field. The frequency of this precession is

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known as the Larmor frequency and is dependent on the strength of the static magnetic field. In particular, it can be defined as follows:

$$\text{frequency} = \gamma \cdot B \quad (1)$$

5

where γ is the gyromagnetic ratio of the sample and B is the magnetic field strength of the static magnetic field generated by the magnet 13. The gyromagnetic ratio (γ) is related to the strength of the magnetic moment for the nucleus in question. For example, the gyrometric ratio
10 for protons is 42.57 MHz/Tesla.

In the majority of magnetic resonance systems, the static magnetic field strength is such that the Larmor frequency
15 of the sample is in the radio frequency range of the electromagnetic spectrum. As those skilled in the art of magnetic resonance will appreciate, applying an AC magnetic field to the sample at the sample's Larmor frequency and orientated orthogonal to the static
20 magnetic field, will cause the sample's net magnetisation to rotate about the AC magnetic field's axis, away from the direction of the static field. In this embodiment, this magnetic field is generated by applying a corresponding AC current to the RF coil 15. The angle
25 of rotation of the net magnetisation can be varied by varying the amount of energy delivered to the RF coil 15. In this embodiment, an excitation field which causes a 90° rotation is used to excite the sample. After the 90° pulse has been applied to the sample, the sample is left
30 in a high-energy, non-equilibrium state, from which it will relax back to its equilibrium state. As it relaxes, electromagnetic energy at the Larmor frequency is emitted, the magnetic component of which induces current

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in the RF coil 15, the peak amplitude of which varies with, among other things, the number of magnetic moments in the sample and hence the number of molecules in the sample. The received signal is then passed to the
5 computer control system 17 which compares the peak amplitude of the signal received from the unknown sample with the peak amplitude of a signal received from a sample with a known mass (or weight), to determine the mass (or weight) of the sample being tested.

10

The operation of this embodiment will now be described in more detail with reference to Figures 2 to 5. Figure 2 is a block diagram of the principal components of the computer control system 17 used in this embodiment. As
15 shown, the control system comprises a connection terminal 21 for connecting the control system to the RF coil 15. As shown, the connection terminal 21 is connectable, through switch 23, to a signal generator 25 and a power amplifier 27 which are operable to generate and amplify
20 respectively the excitation signal which is applied to the RF coil 15. The connection terminal 21 is also connectable, through the switch 23, to a receiving amplifier 31 which amplifies the signal received from the sample under test. This amplified signal is then
25 filtered by the filter 33 to remove noise components and then passed to the mixer 35 where the received signal is down converted to an intermediate frequency (IF) by multiplying it with an appropriate mixing signal generated by the signal generator 25. The IF signal
30 output by the mixer 35 is then filtered by the filter 37 to remove the unwanted components generated by the mixer 35. The filtered IF signal is then converted into a corresponding digital signal by the A/D converter 39 and then passed to the microprocessor 41.

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As shown by the dashed control lines 43 and 45, the microprocessor 41 controls the operation of the signal generator 25 and the switch 23. In particular, the microprocessor 41 operates to ensure that the signal generator 25 generates the excitation signal when the filled vial 1 is at the desired location within the check weighing station 3. The microprocessor 41 knows when the vial 1 is at the correct location from a signal received from the position sensor electronics 47 which is connected, through connection terminal 49, to an optical position sensor 50 mounted in the check weighing station 3. In particular, referring to Figure 1, when the glass vial 1 passes by the optical position sensor 50, a light beam 52 is broken. This is detected by the position sensor electronics 47 which in turn signals the microprocessor 41. Based on this information and the speed of the conveyor belt 7 (provided by the conveyor controller 51), the microprocessor determines the appropriate timing for the application of the burst of excitation current and signals the signal generator 25 accordingly.

As those skilled in the art of magnetic resonance will appreciate, it takes a finite period of time after the sample enters the static field generated by the magnet 13 for the net magnetisation of the sample to develop along the X-direction. If the excitation signal is applied to the RF coil 15 before the magnetisation has fully developed, then the strength of the signal generated by the sample will not be at its maximum. Figure 3 illustrates the way in which the net magnetisation and thus the strength of the resultant signal produced by the sample varies with time in the static magnetic field. As shown, the plot has the general form of:

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$$K_1 (1 - e^{-t/T_1}) \quad (2)$$

where K_1 is a constant and T_1 is referred to as the longitudinal relaxation time and depends upon the sample being tested and the strength of the static magnetic field. Therefore, given the strength of the static magnetic field and the type of drug sample which is being tested, the relaxation time, T_1 , can be determined. This information, combined with the speed of the conveyor belt 7, determines the minimum length of the magnet 13 in the Z-direction which is required to ensure that as large a signal as possible is generated by the sample under test.

Figure 4 shows the 90° pulse of AC excitation current which is applied to the RF coil 15 by the signal generator 25 and the power amplifier 27. In this embodiment, the pulse of excitation current has a duration (t_p) of 30 microseconds and its frequency is equal to the Larmor frequency of the sample under test in the static magnetic field. In this embodiment, a capacitor (not shown) is connected across the ends of the RF coil 15 so that it is tuned to the Larmor frequency of the sample. The tuning of the RF coil 15 in this way makes the system less susceptible to electromagnetic interference or to other MR signals from nuclei with different gyromagnetic ratios. The excitation current flowing through the RF coil 15 generates a corresponding magnetic field in the Z-direction. As mentioned above, this excitation magnetic field causes the net magnetisation of the sample in the vial 1 to rotate or precess about the Z-axis at the Larmor frequency. When the excitation current is removed from the RF coil 15, the nuclei in the sample begin to relax back to their equilibrium positions, emitting RF energy at the Larmor

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frequency as they do so. This induces a signal in the RF coil 15 which is seen to decay exponentially and can be described as:

$$K_2 e^{-t/T_2} \quad (3)$$

5

where K_2 is a constant and T_2 is referred to as the transverse relaxation time and depends upon the sample being tested and not on the static field strength. Figure 5 shows the form of the signal induced in the RF coil 15 by the sample as it relaxes back to equilibrium. As shown, the peak amplitude of the induced signal is at its maximum shortly after the excitation current stops, after which point the signal exponentially decays to zero.

15

As mentioned above, the peak amplitude of the signal induced in the RF coil 15 by the sample is directly proportional to the number of magnetic moments in the sample. Consequently, in this embodiment, the microprocessor 41 monitors the peak signal level which it receives from the A/D converter 39 after the excitation signal has been removed from the RF coil 15. The microprocessor 41 then compares this peak signal level with calibration data obtained by testing a similar sample or samples of known mass, to provide an indication of the mass of the sample currently being tested. In this embodiment, this calibration data is obtained from a number of similar samples of different known masses during a calibration routine before the production batch is begun and is stored in memory 53. In this embodiment, the calibration data is a function which relates the peak amplitude of the MR signal received from the sample under test to the mass of the sample.

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In this embodiment, if the microprocessor 41 determines that the mass of the current sample being analysed is not of the required mass within a given tolerance, it outputs a control signal on control line 55 to the reject controller 57. The reject controller then outputs a signal to output terminal 59 which is connected to the reject station 5, for causing the reject station to remove the current vial 1 being tested from the conveyor belt 7 when it arrives at the reject station 5.

10

As shown in Figure 2, the computer control system 17 also comprises a user interface 61 for allowing the user to programme into the control system 17 what the correct mass of each sample should be for a given batch of product.

15

A general description of a check weighing device embodying the present invention has been given above. The apparatus can be used to determine the mass of most samples provided they contain an MR responsive element in a known amount relative to the other elements in the sample. Since the hydrogen nucleus, or proton, is the element which gives the largest MR signal, due to it possessing the strongest magnetic moment, it is the one most often used. Other isotopes which have nuclear spin and will therefore provide an MR signal include: certain isotopes of nitrogen, phosphorus, sodium, potassium, fluorine and carbon and oxygen. If the check weighing station 3 described above is to be able to determine the mass of various samples using the MR signals from different MR responsive elements, then the computer control system 17 must store calibration data for each of the different samples. It must also be able to generate and receive signals at the different Larmor frequencies needed to be able to excite the different MR

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responsive elements.

To illustrate the operation of the present invention further, an example will now be described.

5

EXAMPLE

In this example, 35 millilitre capacity glass vials 1 were used each containing five millilitres of water doped with copper sulphate (to reduce the water's T_1 relaxation time to 100 ms). The mass of the water was determined by measuring the MR signal from the hydrogen nuclei contained in the glass vial and comparing this with the stored calibration data. The static magnet used, generated a magnetic field in the X-direction of 0.15 Tesla. The Larmor frequency of hydrogen in such a DC field is 6.38MHz. This is calculated by multiplying the DC magnetic field strength by the gyromagnetic ratio for hydrogen (which is 42.57 MHz/Tesla). The gyromagnetic ratio for other MR responsive elements can be found in CRC Handbook of Chemistry & Physics, published by CRC Press Inc. The computer control system 17 then applied 6-7 amps of excitation AC current having a frequency of 6.4 MHz to the RF coil 15 for 30 μ s. The resonance of the hydrogen atoms in the water, caused by the excitation magnetic field initially induced a few milli-volts of signal in the RF coil 15. This peak signal level was then compared with the stored calibration data (obtained by taking similar MR measurements from a number of containers having different known amounts of water) to determine the mass of water in each glass vial. The results of the technique were then compared with weighings obtained using balance scales. This comparison revealed that the MR check weighing technique provides an indication of the amount of water with an accuracy of $\pm 2\%$.

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In this embodiment, the microprocessor requires approximately 100 microseconds to excite and to take a reading of the peak MR signal which is received. This is then processed to determine the mass of water in the vial in real time. The theoretical limit on throughput (i.e. the number of vials which can be weighed per second) is therefore approximately 10000 vials per second, which is well within the 300 vials per minute typically required by current product lines.

10

As those skilled in the art will appreciate, the above technique for check weighing provides a number of significant advantages over the prior art check weighing systems. These include:

15

- i) the technique involves a single step weighing process which can be carried out on-line - previously two weight measurements had to be obtained one before and one after filling, in order to take into account the weight of the vial;
- ii) the sample can be weighed in its final packaging after it has been sealed and can therefore be weighed outside the aseptic filling area;
- iii) the technique provides a contactless measure of the mass of the sample independently of the vial mass;
- iv) the measurement does not affect the composition or quality of the sample and compositional information can also be obtained from the MR signal if required;
- v) the technique allows for fast measurement of the sample's mass so that 100% sampling of the products can be made even at normal production throughputs;
- vi) since the technique provides a measure of the

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- sample's mass independently of the vial mass, the technique can provide an accurate determination of the mass of samples which are small relative to the vial (e.g. 200 mg sample in 10 g vials);
- 5 vii) the technique generally requires relatively low levels of static or DC magnetic field (less than 0.5 Tesla) since, in most cases, a bulk measurement over the entire sample volume is performed, thereby reducing the magnet cost and
- 10 also making it possible to use permanent or electro-magnets and not superconducting magnets;
- viii) the technique allows a wide variety of sample sizes to be accurately weighed by the same system either using vials of the same size or using
- 15 different vial sizes with different sized RF coils; and
- ix) the technique allows the sample to continuously move through the weighing station without stopping since the measurement can be performed in a short
- 20 time relative to the throughput.

MODIFICATIONS AND ALTERNATIVE EMBODIMENTS

In the above embodiment, a single measurement of the sample's mass was determined for each vial. The accuracy

25 of the measurement is limited only by the random noise in the system. This can be improved by taking an average of repeated measurements. However, the rate at which measurements can be made on the same sample is determined by the T_1 relaxation time discussed above. In

30 particular, after the excitation signal has been removed, it takes approximately $3T_1$ for the protons to return to their original aligned state in the static magnetic field, at which point a further burst of excitation current can be applied. This is illustrated in Figure

35 6. In the example discussed above, the T_1 relaxation

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time for the water is approximately 100 milliseconds and therefore, if four measurements are taken on each sample, then the throughput can be approximately two weighings per second. Separate measurements could be obtained
5 either by using a number of different RF coils spatially separated along the Z-direction. Alternatively, the conveyor belt could be stopped each time a vial reaches the interrogation area and multiple measurements made. Multiple measurements of the same sample may also be
10 possible if the interrogation zone of the magnet and RF coil is large enough to allow multiple measurements to be taken considering the speed of the conveyor belt. In such an embodiment, the accuracy of the system will depend upon the homogeneity of the RF coil and the
15 magnetic field within the interrogation zone as well as on the system signal to noise and the RF coil's fill factor. If the field patterns of the magnet and RF coil are known in advance, then this knowledge can be used to make corrections on the different measurement signals.
20 Additionally, additional X, Y and Z coils (known in the art as shims) may also be provided to improve the homogeneity of the static magnetic field.

In the first embodiment, a single vial was located within
25 the RF coil's interrogation zone at any one time. Figure 7a diagrammatically illustrates the components of a check weighing station 3 which allows multiple vials to be located within the RF coil's interrogation zone at the same time and which allows a mass measurement to be made
30 of the sample within each vial individually. To achieve this, in this embodiment, in addition to the static magnet 13 and the RF coil 15, a separate pair of coils 71 and 73 are located either side of the conveyor belt 7, which operate to provide a magnetic field gradient
35 across the conveyor belt 7. As a result of this

gradient, the static magnetic field experienced by each of the glass vials will be different and hence the Larmor frequency of the sample in each of the three vials in the interrogation zone will be different. Consequently, each

5 vial can be interrogated separately by applying three different narrow band RF pulses at the appropriate Larmor frequency. Figure 7b illustrates the form of a narrow band pulse which can be used to interrogate one of the three samples in the RF coil's interrogation zone and

10 Figure 7c shows the frequency content of the pulse. As shown, the pulse has a sinc function envelope and has a time duration (t_p) of approximately 4 milliseconds. It therefore has a bandwidth (Δf) of approximately 1 KHz and is centred at the appropriate Larmor frequency f_0 .

15 Alternatively, a broad band RF pulse could be applied over the interrogation zone and the resulting MR signals from the samples can be resolved by taking the Fourier transform of the received signal after the excitation pulse has ended, as is standard practice in MR imaging.

20

In the example described above with reference to Figure 7, the gradient coils were arranged to apply a gradient in the same direction as the static magnetic field which is generated by the magnet 13. As is well known in the

25 art of magnetic resonance imaging, gradient coils can be arranged to provide magnetic field gradients in one or more of the X, Y or Z axes so that the entire volume of the interrogation zone can be spatially resolved. Figure 8 illustrates an embodiment where the two gradient coils

30 71 and 73 are provided at opposite ends of the RF coil's interrogation zone. As shown, in this embodiment, the RF coil 15 comprises three separate portions 15a, 15b and 15c. As those skilled in the art will appreciate, by applying a magnetic field gradient along the length of

35 the conveyor belt 7 through the interrogation zone, each

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of the samples can be interrogated separately or simultaneously in the same way as in the embodiment described with reference to Figure 7.

5 In the embodiments described with reference to Figures 7 and 8, a plurality of samples were located within the interrogation zone and either interrogated separately or simultaneously. In these embodiments, since each of these samples will experience a slightly different
10 magnetic field and will be in a different position relative to the RF coil, separate calibration data can be used for each of the sensing positions in order to try to reduce errors caused by inhomogeneities in the static magnetic field or in the RF coil.

15 In the above embodiments, the RF coil generated a magnetic field in the Z-direction along the direction of movement of the conveyor belt 7. As those skilled in the art will appreciate, this is not essential. The RF coil
20 can be located at any angle relative to the DC magnetic field, provided the field which it generates is relatively homogenous over the sample being tested and provided it comprises a component which is orthogonal to the static magnetic field. Figure 9 diagrammatically
25 illustrates an embodiment where three separate RF coils 15d, 15e and 15f are provided under the conveyor belt 7, each of which is operable to generate an AC magnetic field in the Y-direction, i.e. out of the paper. This embodiment allows the samples in three vials to be tested
30 simultaneously. It also allows the system to interrogate the sample in each vial three times, once by each of the RF coils.

In the above embodiments, a permanent magnet was used to
35 generate the required static magnetic field. As those

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skilled in the art will appreciate, electromagnets, current carrying coils or superconducting magnets could be used in place of the permanent magnet to generate the necessary DC magnetic field. Additionally, in the above
5 embodiments, the DC magnetic field was applied across the conveyor belt in the X-direction. As those skilled in the art will appreciate, the DC magnetic field can be applied through the sample in any direction. For example, the north and south pole of the magnet may be
10 placed above and below the conveyor with the RF coil being, for example, in the same orientation as in the first embodiment. Figure 10 shows yet another embodiment in which a solenoid coil 75 is wound along a length of the conveyor belt 7 for generating the static magnetic
15 field along the length of the conveyor belt 7, i.e. in the Z-direction. In this embodiment, the RF coil 15 is provided at one side of the conveyor 7 and a separate detector coil 77 is provided at the opposite side of the conveyor 7.

20

As those skilled in the art of MR will appreciate, there are many other configurations which will allow a measurement of the mass of the sample to be obtained.

25 In the above embodiments, the check weighing was performed after the vial had been filled and sealed. However, in some applications, the material which is used to seal the vial will generate an MR signal. For example, if a plastic or rubber top is used to seal the
30 vial, then the hydrogen atoms contained in the plastic seal will also generate an MR signal which could interfere with the measurement results. There are various ways that this problem can be solved. Firstly, the check weighing station could be provided before the
35 sealing station. However, such an embodiment is not

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preferred, since the check weighing station would then also have to be located within the aseptic environment of the filling station. Alternatively, this problem can be alleviated by using receive coils which are located
5 underneath the conveyor 7, such as those shown in Figure 9, because these coils are more sensitive to the MR signal generated by the sample than they are to the MR signal generated by the seal (because the sample is closer to the RF coil than the seal). Alternatively
10 still, a magnetic field gradient may be applied along the length of the bottle and a narrow bandwidth RF pulse applied as in Figure 7b, so that only the part of the bottle containing the sample is interrogated.

15 If the T_2 relaxation time for the seal is smaller than the T_2 relaxation time for the sample under test, then this problem can also be overcome, as illustrated in Figure 11, by waiting a fixed period (t_m) before measuring the peak signal amplitude of the received MR
20 signal. This is because the MR signal 81 from the seal will die off more quickly than the MR signal 83 from the sample. In a similar manner, if the T_1 relaxation time of the sample is different from the T_1 relaxation time of the seal, then this problem can also be overcome by
25 firstly applying a 180° (inversion) RF pulse to the vial under test to invert the net magnetisation of the sample and the seal and then waiting until the nuclei of the seal are in such a state that when a further 90° RF interrogation pulse is applied, no signal is generated
30 by the seal. This is illustrated in Figure 12, which shows the signal strength 85 which can be obtained from the sample and the signal strength 87 which can be obtained from the seal after the application of the 180° pulse. As shown, because the two materials have
35 different T_1 relaxation times, if a 90° interrogation

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pulse is applied at time t_s , then no signal will be generated by the seal but a signal will be generated by the sample.

- 5 In the above embodiments, a vial which does not generate an MR signal was used. As those skilled in the art will appreciate, vials which do generate an MR signal may also be used and the above techniques which were employed to separate the signals from the seal and the sample could
10 be used to separate the signals from the sample and the vial.

In the first embodiment, a heterodyne type receiver circuit was used to receive and process the MR signal
15 generated by the sample. As those skilled in the art will appreciate, various other types of receiver circuits, such as simple envelope detector circuits or synchronous detectors can be used. However, the heterodyne type receiver is preferred, because the
20 microprocessor can also process the received signal to extract phase information which can be used, for example, to spatially resolve the sample in a given dimension.

In the first embodiment, the processing circuitry
25 determined the peak signal which was received after the excitation signal has been removed from the RF coil. As those skilled in the art will appreciate, other processing techniques can be used to output a signal which varies in dependence upon the size of the sample's
30 net magnetisation and thus the number of magnetic moments contained therein, provided the signals from the calibration samples are processed in a similar manner. For example, the microprocessor may be arranged to determine the average signal level of the received signal
35 over a predetermined period of time.

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In the above embodiment, the calibration data was stored as a function which relates the peak amplitude of the MR signal received from the sample under test to the mass or the weight of the sample. In an alternative
5 embodiment, the calibration data may be stored as a look-up table with the peak amplitude of the MR signal received from the current sample under test being used to address the look-up table and with interpolation being used to determine the sample's mass or weight if the MR
10 signal received from the current sample under test falls between values in the look-up table. Additionally, the calibration data may be generated using a plurality of signals of each of the different masses so that statistics can be determined which describe how the
15 signals generated by samples of the same mass vary. These statistics can then be used to provide a possible range of error for any given measurement for a sample of unknown weight which may be used in the decision as to whether or not the sample should be rejected from the
20 line.

As those skilled in the art will appreciate, selecting the strength of magnetic field of the DC magnet is dependent on the signal-to-noise ratio (SNR) required by
25 the processing electronics, since the signal-to-noise ratio increases as the static magnetic field increases and a high signal-to-noise ratio will give high repeatability. Therefore, if high accuracy is required on very small samples, then a higher static magnetic
30 field would be used than for moderate accuracy on larger samples. It is also possible to increase the signal-to-noise ratio by effectively reducing the noise level by using small RF coils in order to maximise the fill factor and thus the resultant signal level. However, there is
35 a trade-off in this case, since good RF homogeneity over

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the sample volume is required to minimise the effect of repositioning inaccuracies and this is best achieved using as large an RF coil as possible.

- 5 In the above embodiment, the weight of the sample was measured using MR techniques. As those skilled in the art will appreciate, in addition to weighing each of the samples, the signal received back from the samples can be used for other quality control purposes. In this
10 case, parameters other than the peak amplitude of the MR signal received from the sample will be used, such as the T_2 relaxation time.

- In the above embodiments nuclear magnetic resonance
15 techniques were used to determine the mass of a test sample. Other techniques, such as Electron Spin Resonance (ESR) also called Electron Paramagnetic Resonance and Nuclear Quadrupole Resonance (NQR) could be used. ESR is closely related to NMR but instead of
20 the sensed signal originating in the magnetic moment of the nucleus, the signal is generated by the interaction of the magnetic moment of the electron with the external field. Because of the lighter mass of the electron as compared to the nucleus, the electron magnetic moment is
25 much higher than the nuclear moment and therefore any ESR signal will be at a frequency several hundred times higher than the NMR signal in the same field. The above described relaxation times are also typically much shorter. Since only unpaired electrons will give rise
30 to an ESR signal, this technique can be used on materials containing transition metals with incomplete inner electron shells, conduction electrons in metals, imperfections in insulators etc.

- 35 NQR arises when a nucleus with a quadrupole moment

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interacts with a non-uniform electric field of low symmetry (below cubic). NQR signals therefore only arise in solid materials and are most easily observed in crystals which are not of cubic symmetry, such as chlorine and nitrogen. The frequencies of the signals which are characteristic of the chemical compound being inspected range from a few hundred KHz to many MHz and do not require the sample to be located in a static magnetic field.

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CLAIMS:

1. An apparatus for determining an indication of the mass of a sample comprising:

5 means for generating a static magnetic field in a first direction through an interrogation zone for creating a net magnetisation within a sample located within the interrogation zone;

10 means for applying a pulse of alternating magnetic field in a second different direction through the interrogation zone for temporarily changing the net magnetisation of the sample located within the interrogation zone;

15 means for sensing energy emitted by the sample as the net magnetisation of the sample returns to its original state and for outputting a signal in dependence thereon;

20 means for storing predetermined calibration data for at least one similar sample of known mass, which calibration data relates the mass of the at least one similar sample to the corresponding signal output by said sensing means; and

25 means for comparing the signal output by said sensing means with said calibration data to provide said indication of the mass of the sample.

2. An apparatus according to claim 1, wherein said means for generating a static magnetic field comprises first and second oppositely magnetised materials which, 30 in use, are located on opposite sides of the sample in the first direction.

3. An apparatus according to claim 1 or 2, wherein said means for generating a static magnetic field comprises 35 a magnet.

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4. An apparatus according to claim 1, wherein said means for generating a static magnetic field comprises at least one static loop coil and a static current generating means for applying a static current to the static loop coil.

5. An apparatus according to any preceding claim, wherein said means for applying an alternating magnetic field comprises an AC loop coil and AC current generating means for applying an AC current to the AC loop coil.

6. An apparatus according to any preceding claim, wherein said second direction is substantially orthogonal to the first direction.

7. An apparatus according to any preceding claim, wherein energy emitted by said sample comprises electromagnetic energy and wherein said sensing means comprises a sensing loop coil which is operable to receive the emitted electromagnetic energy and processing circuitry for processing the resulting signal induced in said sensing loop coil.

8. An apparatus according to claim 7, wherein said signal induced in said sensing loop coil oscillates at the Larmor frequency of the sample and wherein said processing circuitry comprises means for detecting a peak signal value of the signal induced in the sensing loop coil.

9. An apparatus according to claim 8, wherein said peak determining means comprises means for determining the average signal over a predetermined period.

10. An apparatus according to any of claims 7 to 9 when

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dependent upon claim 5, wherein said AC current generating means is operable to apply a burst of AC signal to said AC loop coil and wherein said processing circuitry is operable to process the signal induced in
5 said sensing loop coil after said burst of excitation current has ended.

11. An apparatus according to claim 10, wherein said sensing loop coil and said AC loop coil comprise the same
10 loop coil.

12. An apparatus according to any preceding claim, wherein said calibration data is obtained from a plurality of similar samples of different known mass and
15 their corresponding signals output by said sensing means.

13. An apparatus according to claim 12, wherein said calibration data is stored as a function relating the strength of the signal output by said sensing means to
20 the mass of the sample.

14. An apparatus according to claim 12, wherein said calibration data is stored as a look-up table generated from said plurality of similar samples and their
25 corresponding sensor signals and wherein said comparing means is operable to address said look-up table with the signal output by said sensing means and further comprises interpolation means for interpolating between the entries in the look-up table to provide said indication of the
30 mass of the sample.

15. An apparatus according to any preceding claim, wherein said indication of the mass of the sample is the weight of the sample.

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16. An apparatus according to any preceding claim,
wherein said storing means is operable to store
calibration data for samples of different constitution
and wherein said apparatus further comprises selection
5 means for selecting the calibration data corresponding
to the current sample under test.

17. An apparatus according to claim 16, wherein said
selection means comprises a user interface for allowing
10 a user to select the calibration data for the current
sample under test.

18. An apparatus according to any preceding claim,
wherein said sample comprises a number of chemical
15 components and wherein said means for applying an
alternating magnetic field is operable to cause the net
magnetisation of one of said chemical components to
change.

20 19. An apparatus according to any preceding claim,
wherein said sample is contained within a container which
does not generate a magnetic resonance signal.

20. An apparatus according to any of claims 1 to 18,
25 wherein said sample is sealed within a container, wherein
said seal and/or said container generate a magnetic
resonance signal, and wherein said apparatus further
comprises means for separating the magnetic resonance
signal from the sample from the magnetic resonance signal
30 from the seal and/or container.

21. An apparatus for determining an indication of the
mass of each one of a plurality of samples in a
production line, the apparatus comprising:
35 an apparatus according to any of claims 1 to 20 for

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determining an indication of the mass of a sample within an interrogation zone; and

transport means for transporting said plurality of samples through said interrogation zone.

5

22. An apparatus according to claim 21, wherein said transport means comprises a conveyor belt.

23. An apparatus according to claim 22, wherein said
10 means for generating a static magnetic field is operable to generate said static magnetic field in a direction which is transverse to the direction of movement of the conveyor belt and which is substantially homogeneous over a length of the conveyor belt so that each sample is
15 exposed to the static magnetic field for a predetermined period of time before it reaches the interrogation zone.

24. An apparatus according to any of claims 22 or 23, wherein said means for applying an alternating magnetic
20 field is operable to apply said field in the direction of movement of the conveyor belt.

25. An apparatus according to any of claims 21 to 24, wherein said transport means is operable to continuously
25 move said samples through said interrogation zone.

26. An apparatus according to any of claims 21 to 25, wherein said apparatus for determining an indication of the mass of each sample is operable to determine a
30 plurality of measurements of the mass of each sample.

27. An apparatus according to any of claims 21 to 26, wherein said transport means is arranged to transport a plurality of said samples through said interrogation zone
35 at the same time.

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28. An apparatus according to claim 27, wherein said apparatus further comprises means for applying a magnetic field gradient over said interrogation zone so that magnetic resonance signals from the different samples can
5 be obtained from a single sensing means.

29. An apparatus according to any one of claims 21 to 26, wherein said transport means is arranged to transport said samples one at a time through said interrogation
10 zone.

30. An apparatus according to any of claims 21 to 29, further comprising means for comparing the indication of mass output by said apparatus with a desired sample mass
15 and means for removing a sample from the production line if the mass of the sample is not within a given tolerance of the desired sample mass.

31. An apparatus for determining an indication of the mass of a plurality of samples in a production line, the
20 apparatus comprising:

means for generating a static magnetic field in a first direction through an interrogation zone for creating a net magnetisation within a sample located
25 within the interrogation zone;

means for applying an alternating magnetic field in a second different direction through the interrogation zone for causing the magnetisation of a sample within the interrogation zone to oscillate;

30 means for transporting said plurality of samples through said interrogation zone;

means for sensing the oscillation of the magnetisation of each of the samples as they pass through said interrogation zone and for outputting a respective
35 signal in dependence thereon;

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means for storing predetermined calibration data for at least one similar sample of known mass, which calibration data relates the mass of the at least one similar sample to the corresponding signal output by said sensing means; and

means for comparing the signals output by said sensing means with said calibration data to provide said indications of the mass of said plurality of samples.

32. A method of determining an indication of the mass of a sample comprising the steps of:

generating a static magnetic field in a first direction through an interrogation zone for creating a net magnetisation within a sample located within the interrogation zone;

applying a pulse of alternating magnetic field in a second different direction through the interrogation zone for temporarily changing the net magnetisation of the sample located within the interrogation zone;

sensing energy emitted by the sample as the net magnetisation of the sample returns to its original state and outputting a signal in dependence thereon; and

comparing the signal output by said sensing means with calibration data obtained from at least one similar sample of known mass, which calibration data relates the mass of the at least one similar sample to the corresponding signal output by said sensing step, to provide said indication of the mass of the sample.

33. A method of producing sealed containers containing a predetermined amount of a sample, the method comprising the steps of:

filling the container with the predetermined amount of sample;

sealing the sample within the container;

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transporting each of the filled containers to a weighing station;

weighing the sample within each of the containers;
and

5 rejecting any containers which do not contain the predetermined amount of sample within a predetermined tolerance;

characterised in that said weighing step comprises the steps of:

10 generating a static magnetic field in a first direction through an interrogation zone for creating a net magnetisation within a sample located within the interrogation zone;

15 applying a pulse of alternating magnetic field in a second different direction through the interrogation zone for temporarily changing the net magnetisation of the sample located within the interrogation zone;

20 sensing energy emitted by the sample as the net magnetisation of the sample returns to its original state and outputting a signal in dependence thereon; and

25 comparing the signal output by said sensing step with calibration data which relates the mass of at least one similar sample of known mass to the corresponding signal output by the sensing step, to provide said indication of the mass of the sample within each container.

34. A method according to claim 33, wherein said sealing step is performed after said weighing step.

30

35. An apparatus for determining an indication of the mass of a sample comprising:

35 means for generating a static magnetic field in a first direction through an interrogation zone for creating a net magnetisation in the first direction

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within a sample located within the interrogation zone;

means for applying a pulse of alternating magnetic field in a second different direction through the interrogation zone for temporarily changing the direction
5 of the net magnetisation of the sample located within the interrogation zone;

means for sensing energy emitted by the sample as the net magnetisation of the sample returns to its original direction and for outputting a signal in
10 dependence thereon;

means for storing predetermined calibration data for at least one similar sample of known mass, which calibration data relates the mass of the at least one similar sample to the corresponding signal output by said
15 sensing means; and

means for comparing the signal output by said sensing means for the current sample under test with the calibration data to provide said indication of the mass of the sample.

20

36. An apparatus for determining an indication of the mass of a sample comprising:

means for generating a static magnetic field in a first direction through an interrogation zone for
25 creating a net magnetisation in the first direction within a sample located within the interrogation zone;

means for applying an alternating electromagnetic excitation field whose magnetic component is orientated in a second different direction through the interrogation
30 zone for causing nuclei in the sample located within the interrogation zone to be excited and to thereby change the net magnetisation;

means for sensing emission of energy by the nuclei in the sample as the net magnetisation returns to its
35 original state and for outputting a signal in dependence

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thereon;

means for storing predetermined calibration data for at least one similar sample of known mass, which calibration data relates the mass of the at least one similar sample to the corresponding signal output by said sensing means; and

means for comparing the signal output by said sensing means for the current sample under test with the calibration data to provide said indication of the mass of the sample.

37. An apparatus for determining the mass of a sample comprising:

means for generating a static magnetic field in a first direction through the sample;

means for applying an alternating excitation magnetic field in a second different direction through the sample;

means for sensing energy emitted by the sample in response to the excitation magnetic field and for outputting a signal in dependence thereon; and

means for comparing the signal output by said sensing means with stored calibration data which relates the mass of at least one similar sample of known mass to the corresponding signal output by the sensing means, to provide an indication of the mass of the sample.

38. An apparatus for determining an indication of the mass of a sample comprising:

means for applying a pulse of alternating magnetic field through an interrogation zone for temporarily changing the net magnetisation of a sample located within the interrogation zone;

means for sensing energy emitted by the sample as the net magnetisation of the sample returns to its

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original state and for outputting a signal in dependence thereon;

means for storing predetermined calibration data for at least one similar sample of known mass, which
5 calibration data relates the mass of the at least one similar sample to the corresponding signal output by said sensing means; and

means for comparing the signal output by said sensing means with said calibration data to provide said
10 indication of the mass of the sample.

39. An apparatus for determining an indication of the mass of a sample comprising:

means for applying a pulse of alternating electro-
15 magnetic field through an interrogation zone for temporarily changing the net magnetisation of a sample located within the interrogation zone;

means for sensing energy emitted by the sample as the net magnetisation of the sample returns to its
20 original state and for outputting a signal in dependence thereon;

means for storing predetermined calibration data for at least one similar sample of known mass, which calibration data relates the mass of the at least one
25 similar sample to the corresponding signal output by said sensing means; and

means for comparing the signal output by said sensing means with said calibration data to provide said indication of the mass of the sample.

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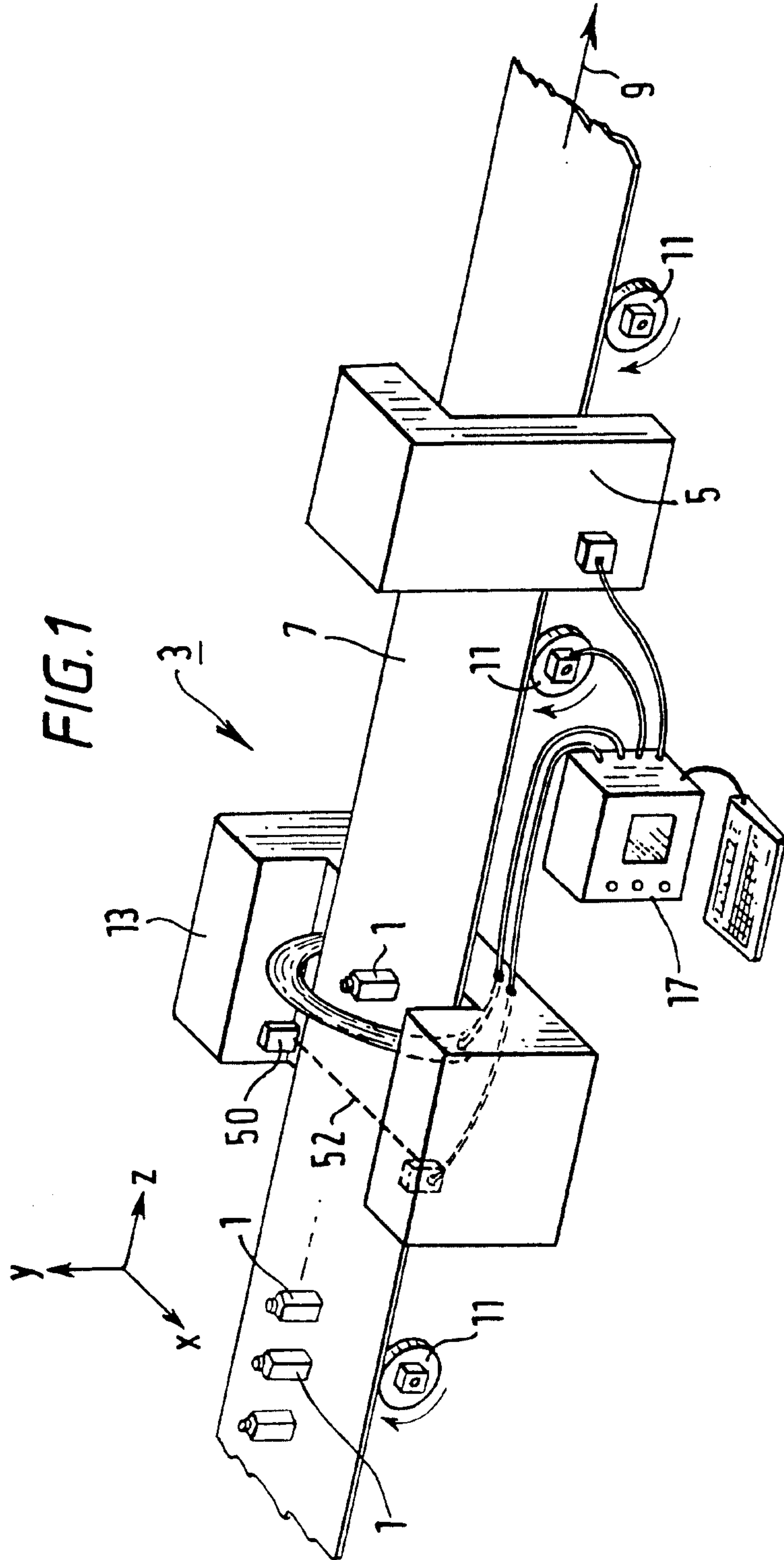
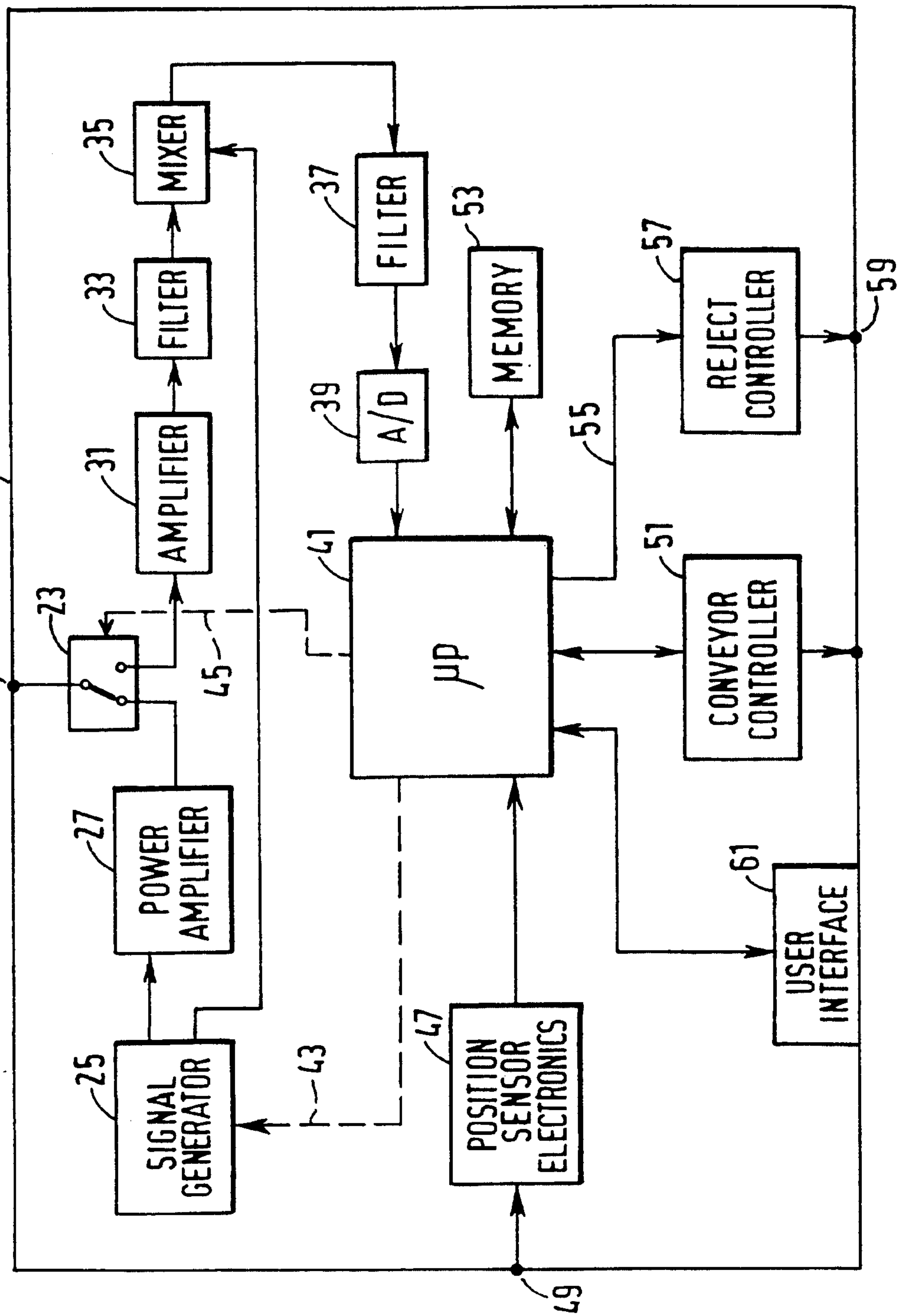


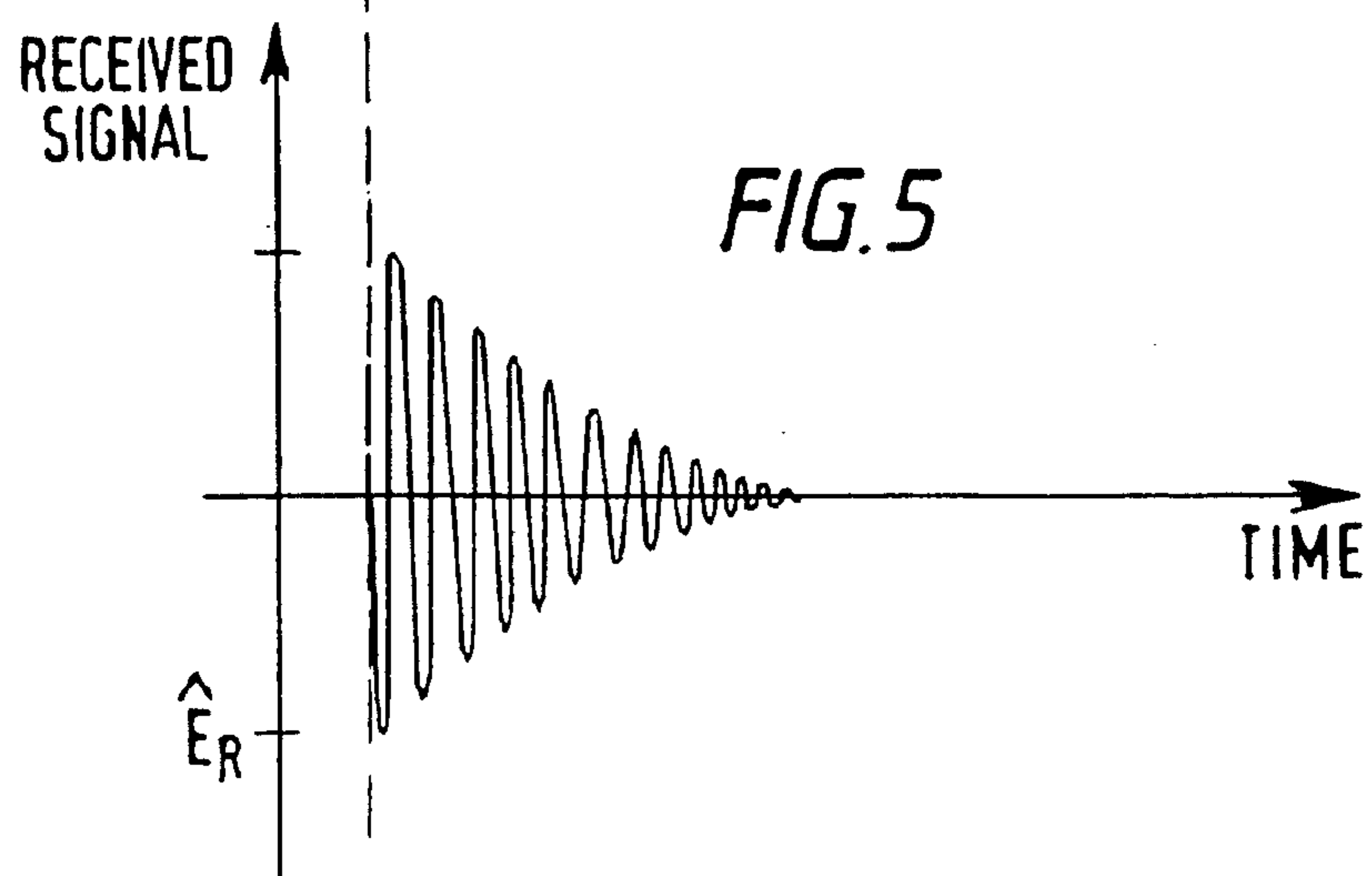
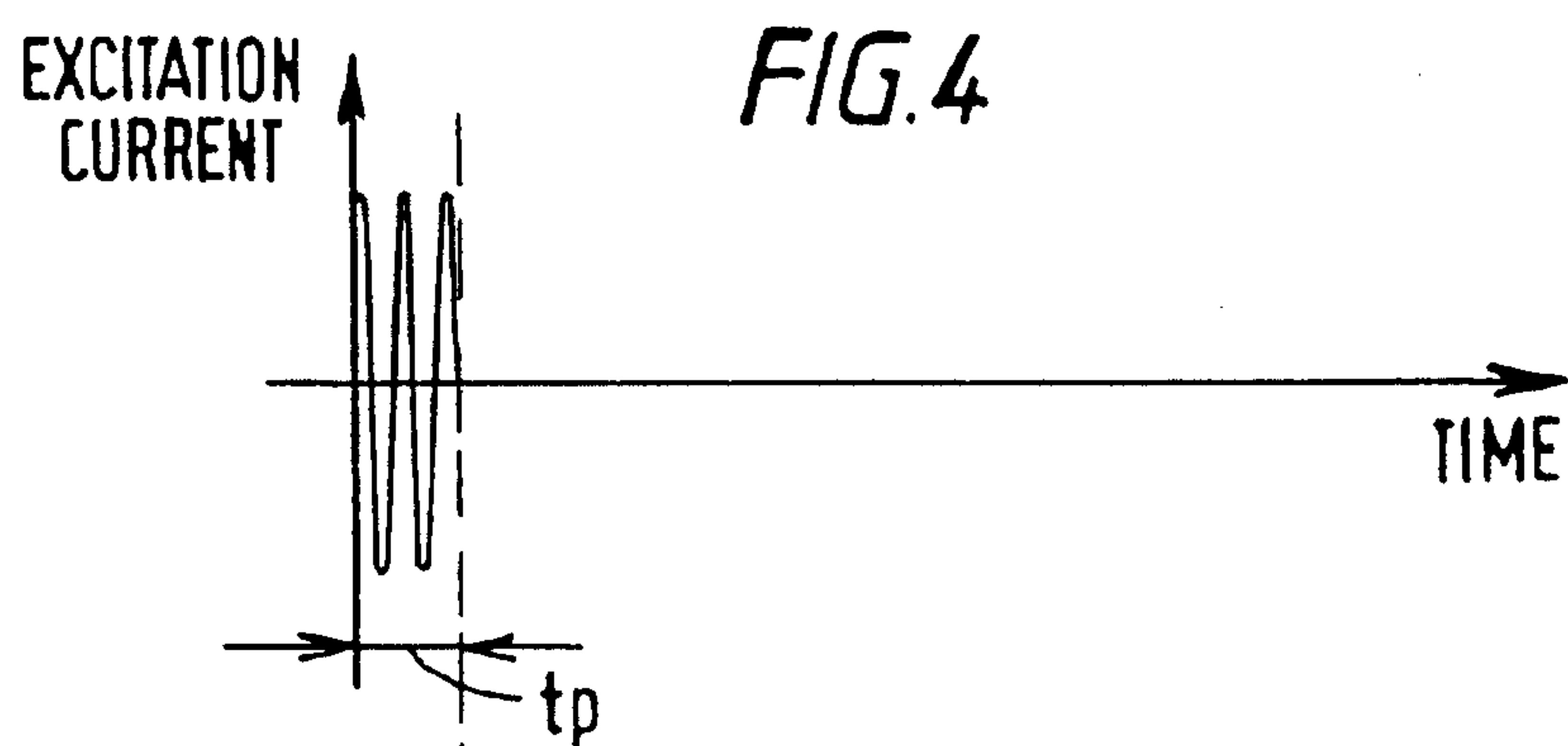
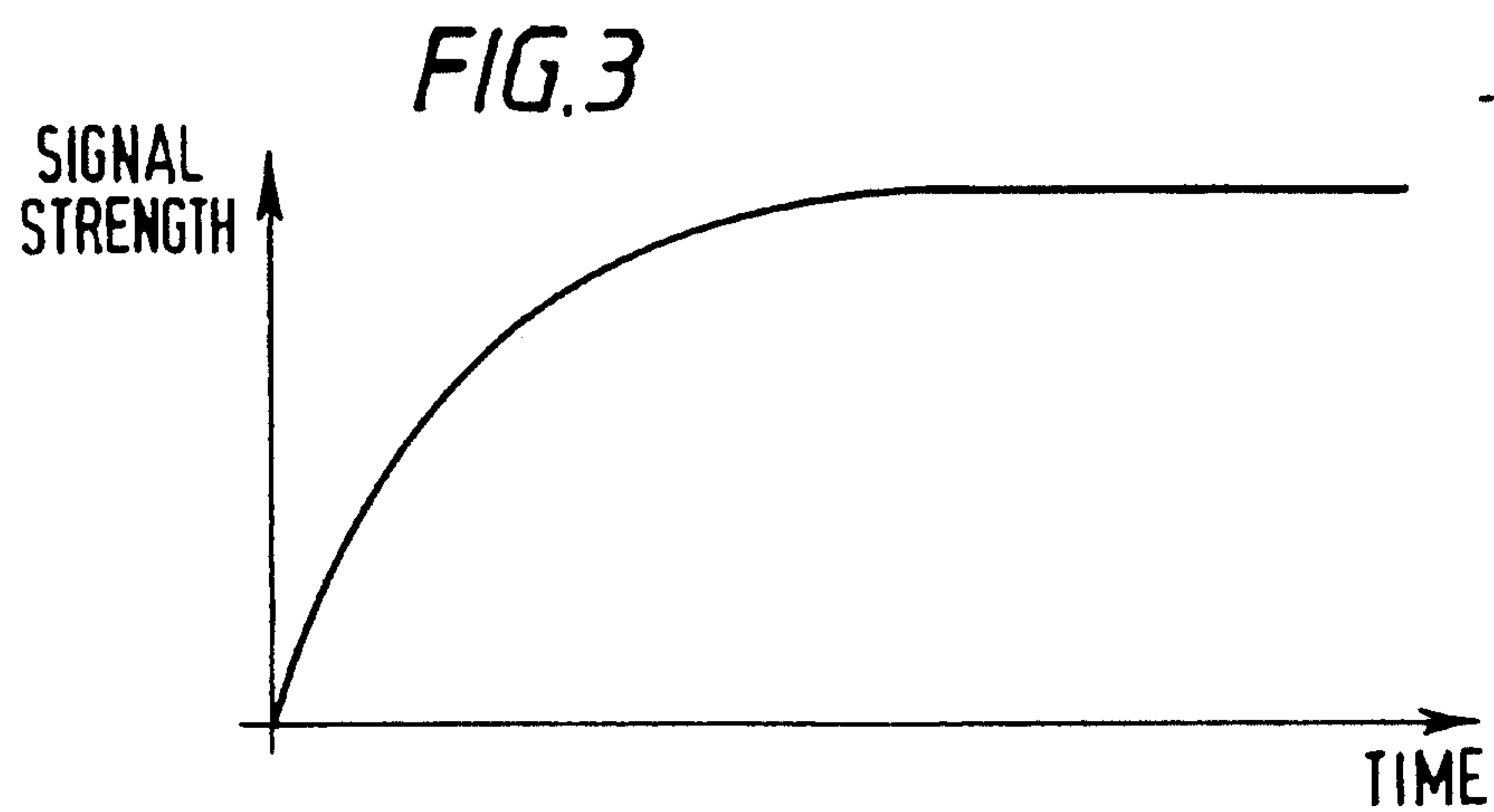
FIG. 2

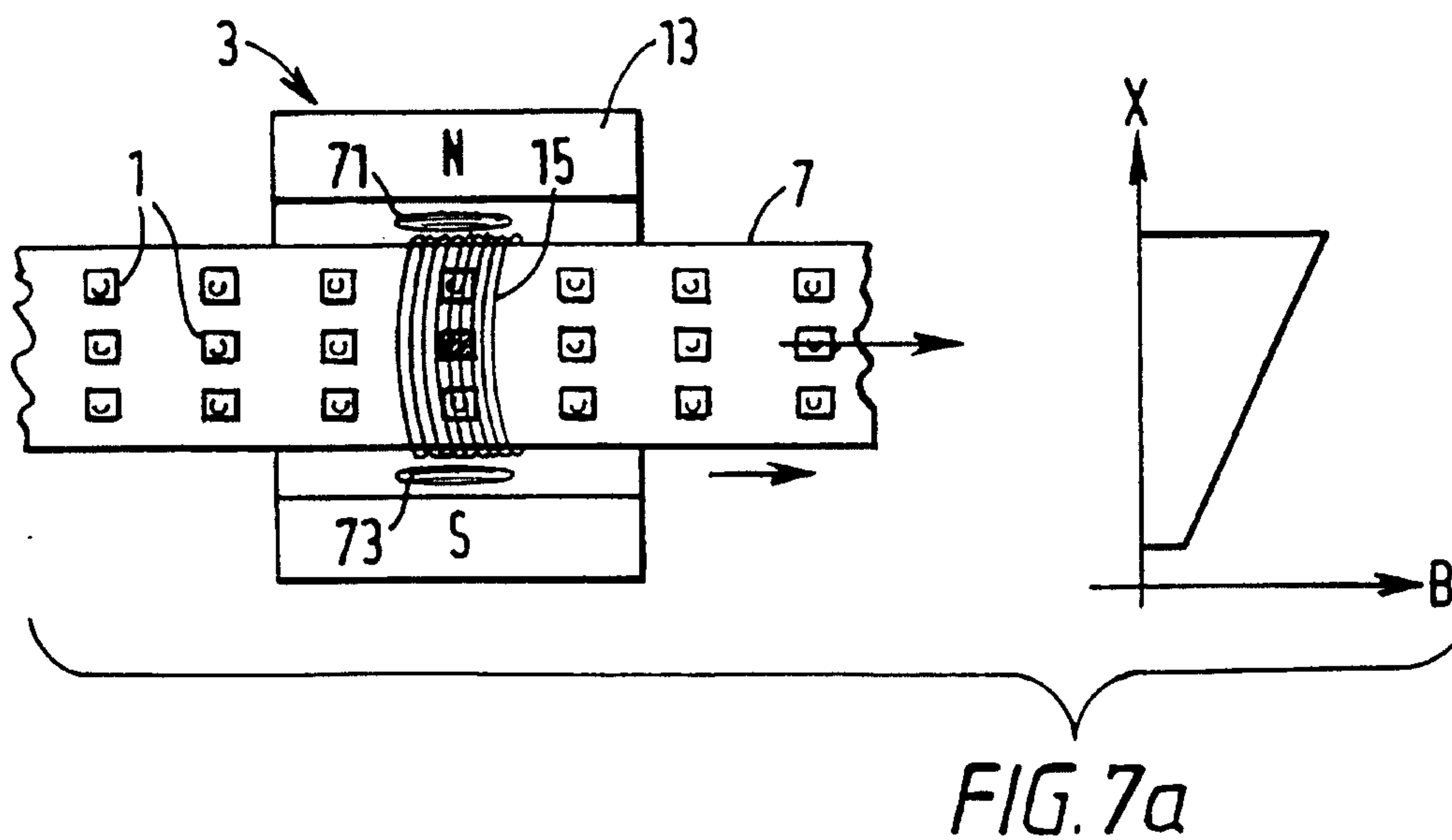
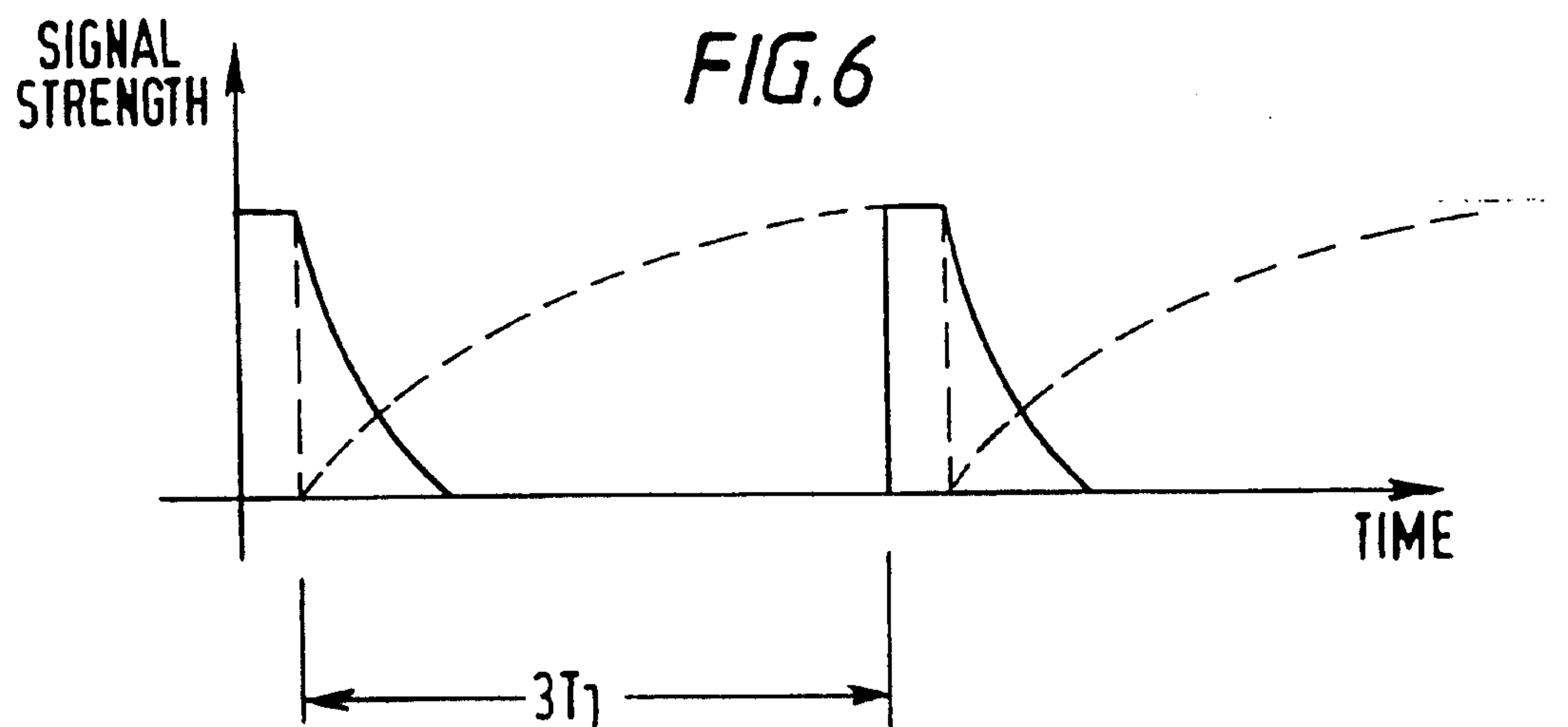


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FIG. 7b

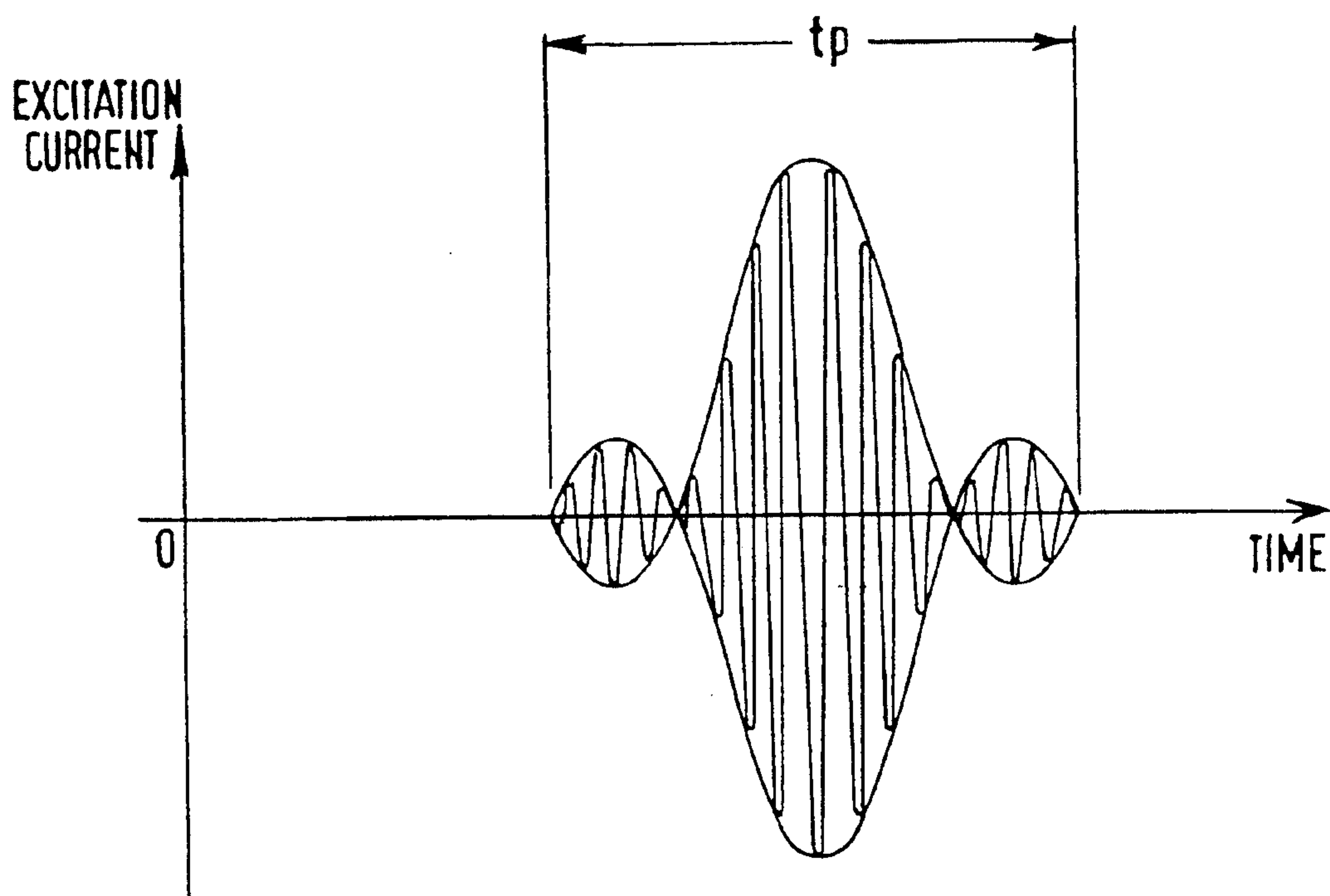
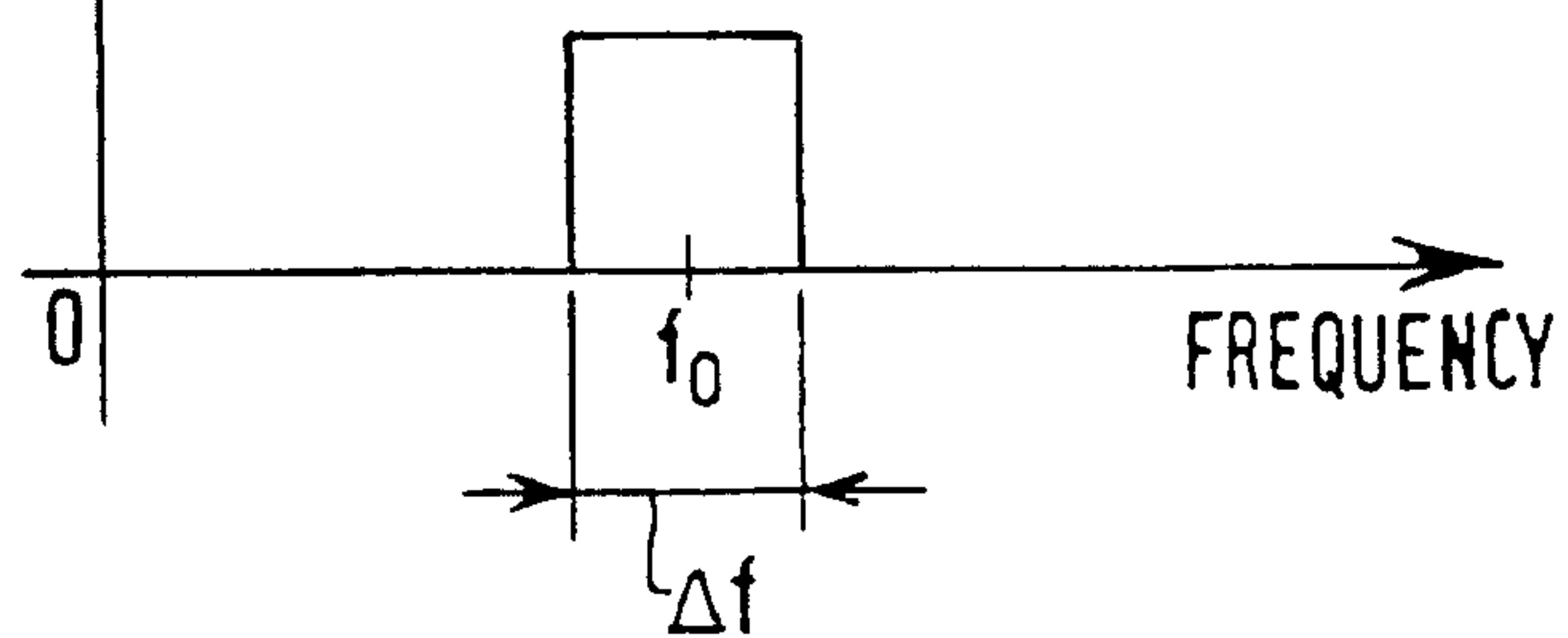
EXCITATION
CURRENT

FIG. 7c



FREQUENCY

FIG. 8

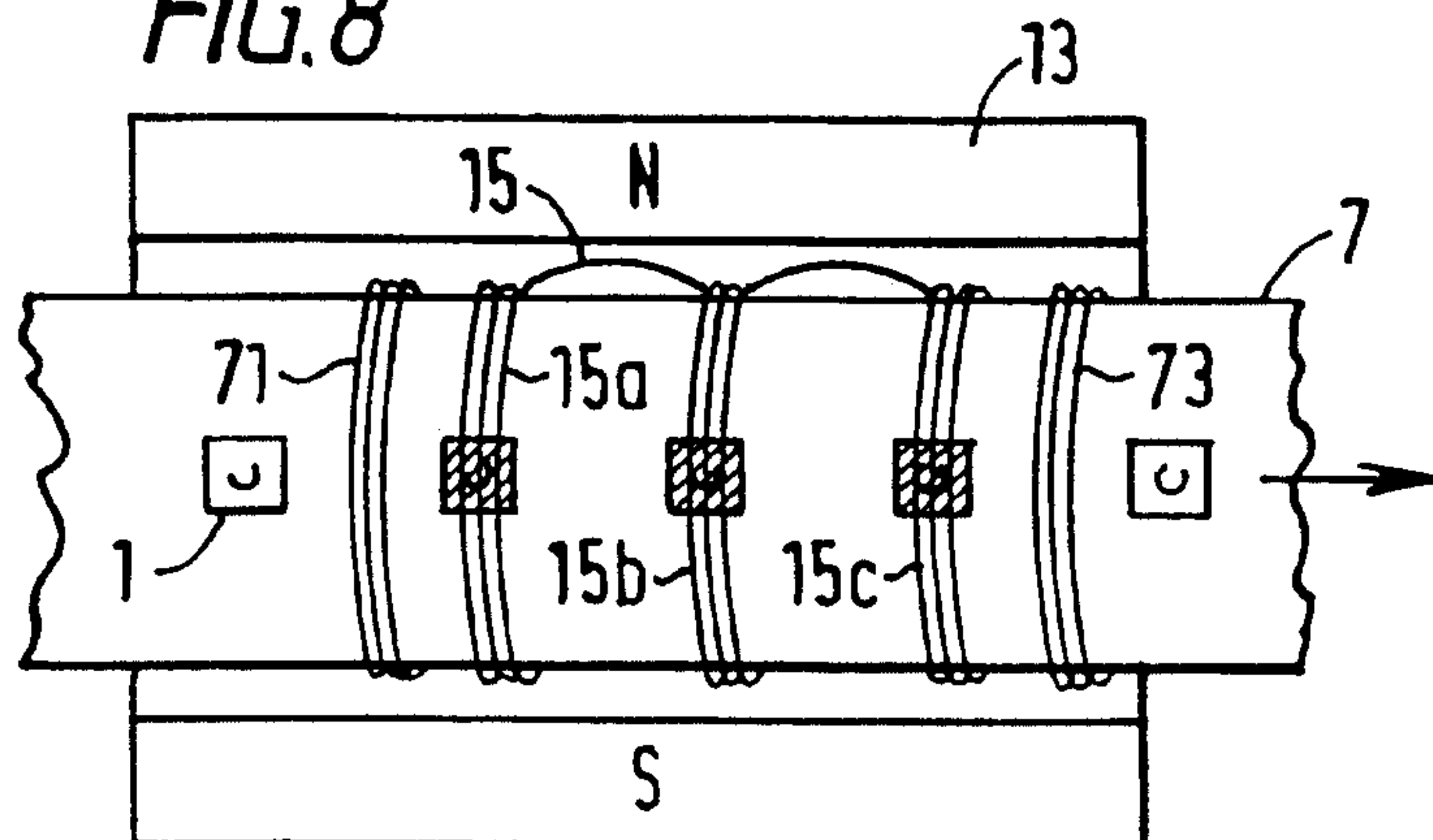


FIG. 9

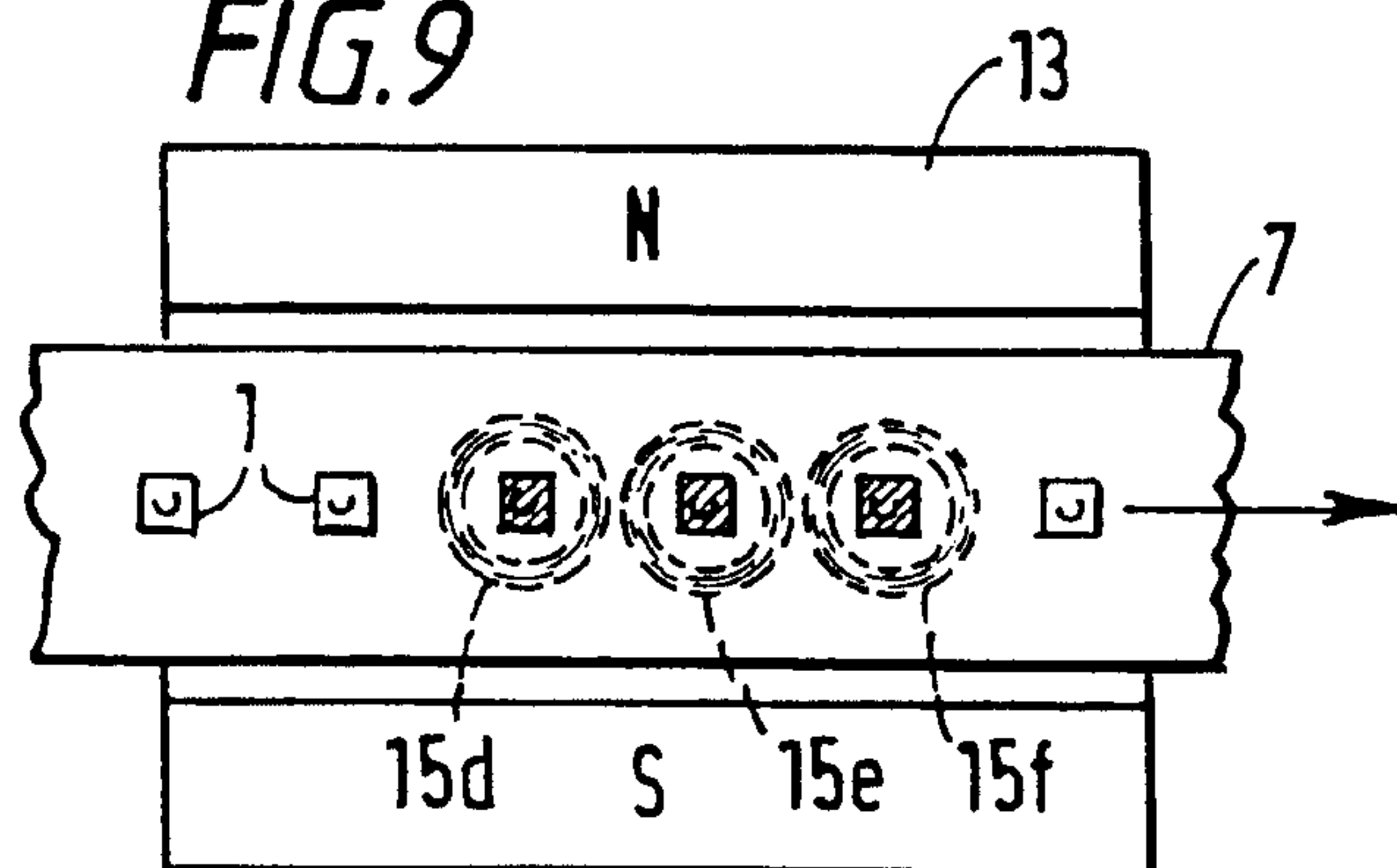


FIG. 10

