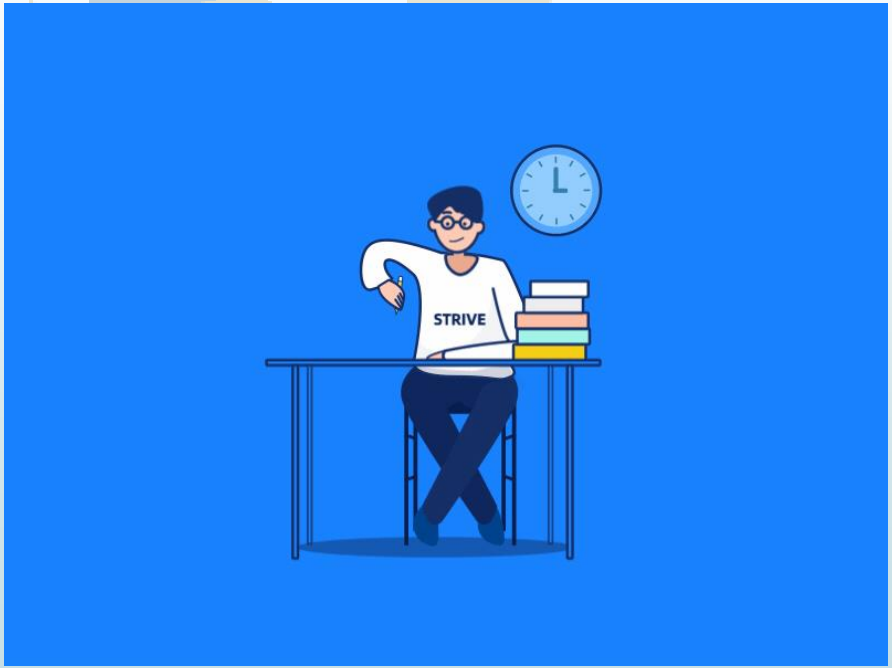
Selected Exercises of Official Exams



2013II

Exercise 4 (5 points)

Ovaries and Sexual Cycles

Ovaries are active from puberty till menopause.
In order to understand the endocrine role of ovaries on the genital activity, the following experiments are performed.

Experiment 1:
Two lots of female rats which did not reach puberty, 2 and 3, are subjected to ovariectomy with or without injection of ovarian extracts: estradiol and progesterone. The conditions and the results of the experiment are presented in document 1.

Groups	Conditions	Observed Results	
		Mass of the uterus	Uterine cycles
1	Control	710 mg	Cyclic variation
2	Ablation of two ovaries	120 mg	No variation
3	Bilateral ovariectomy + continuous and identical injections of ovarian extracts	705 mg	No cyclic variation

Document 1

1- Draw out the roles of ovaries and their mode of action as revealed in this experiment.

Part	Answer	Grade
	Exercise 4	
1	Ovaries are responsible for the development of the uterus and the cyclic variation of the uterine cycle. Ovaries act by secreting estradiol and progesterone in the blood in a variable or cyclic manner.	0.75

Experiment 2:

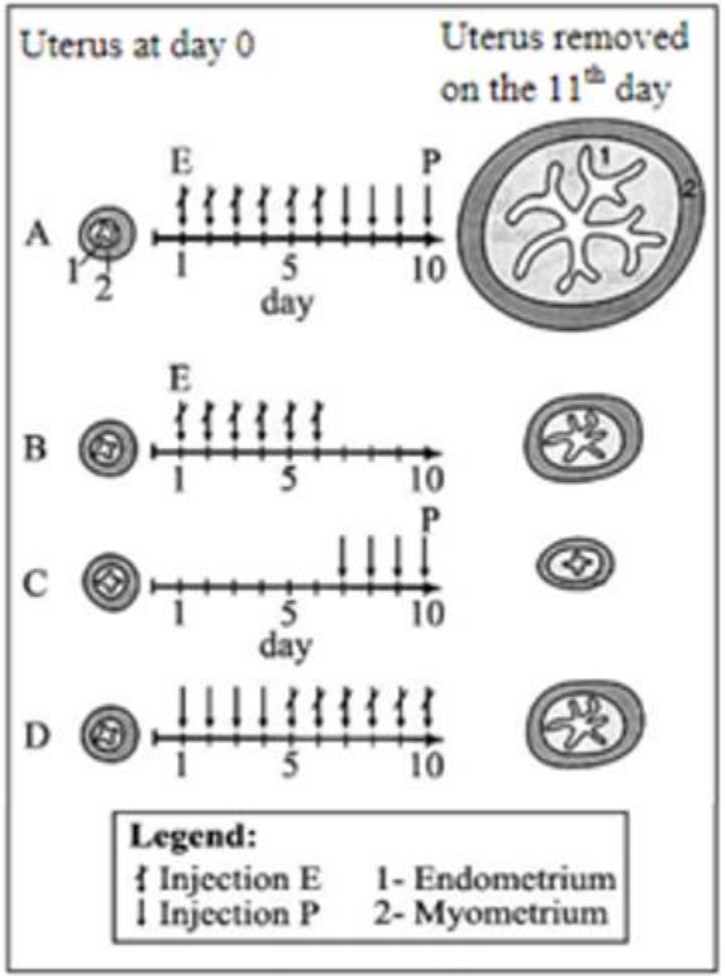
Four lots (A, B, C and D) of female rabbits that did not reach puberty receive daily injections of 5 µg of estradiol (E) and/or 200 µg of progesterone (P) during several days. Then, transverse sections of their uterus are prepared at the end of the experiment, at day 11. Document 2 presents the experimental conditions as well as the obtained results.

2- Interpret the results of document 2.

Experiment 3:

Protein receptors for progesterone were revealed at the level of endometrium cells. The injection of estradiol provokes an increase in the number of progesterone receptors in the day following the injection.

3- Explain the obtained results of lot A in experiment 2.



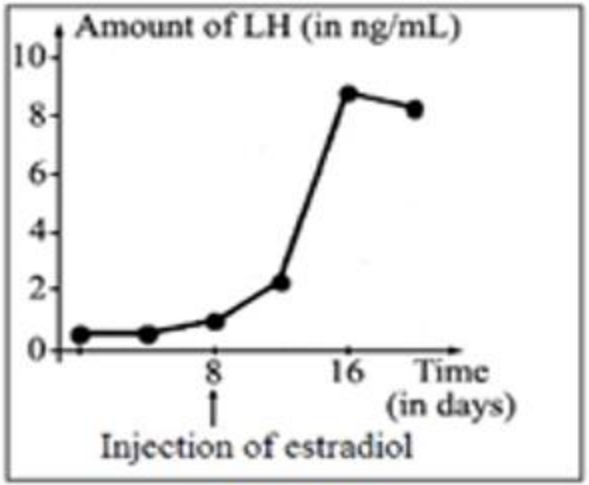
Document 2

2	There is development in the endometrium of the uterus following the injection of estradiol for 6 days followed by an injection of progesterone for 4 days (lot A). However this development is less important following the injection of estradiol for 6 days alone (lot B). Thus estradiol stimulates the development of the endometrium and progesterone amplifies this action. While there is no development of the endometrium following the injection of progesterone alone from day 7 till day 10 (lot C). Hence, progesterone alone doesn't have any effect on the endometrium. On the other hand the endometrium shows a weak development less important than that in lot A following the injection of progesterone for 4 days followed by an injection of estradiol for 6days. Thus progesterone does not act on the endometrium unless it is preceded by estradiol.	**2**
3	In lot A, the injection of estradiol at the beginning of the cycle ensures slight development of the endometrium and increases the number of progesterone specific receptors. This increases the concentration of the progesterone bound to its receptors in the nucleus of target cells. this increases the synthesis of proteins and ensures the thickening of the endometrium, leading to the important development of the endometrium in lot A.	**0.75**

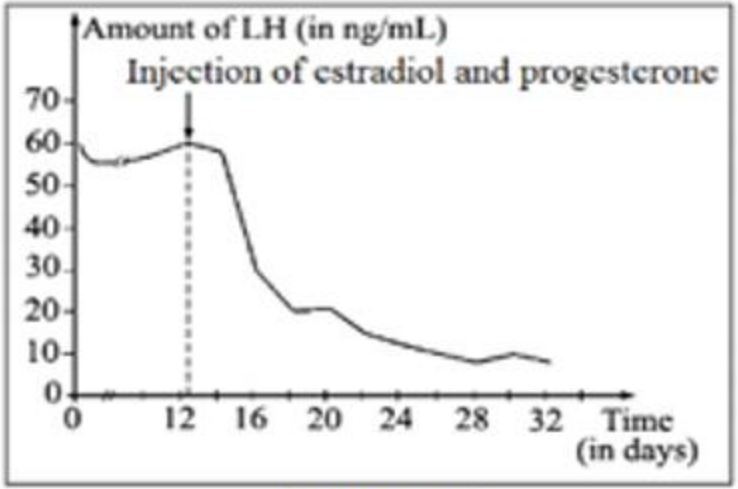
Experiment 4:

A lot of ovariectomized female mammals are subjected to injections of high amounts of estradiol with or without progesterone.

The evolution of the plasmatic concentration of the pituitary hormone LH is measure and the obtained results are shown in documents 3 and 4.



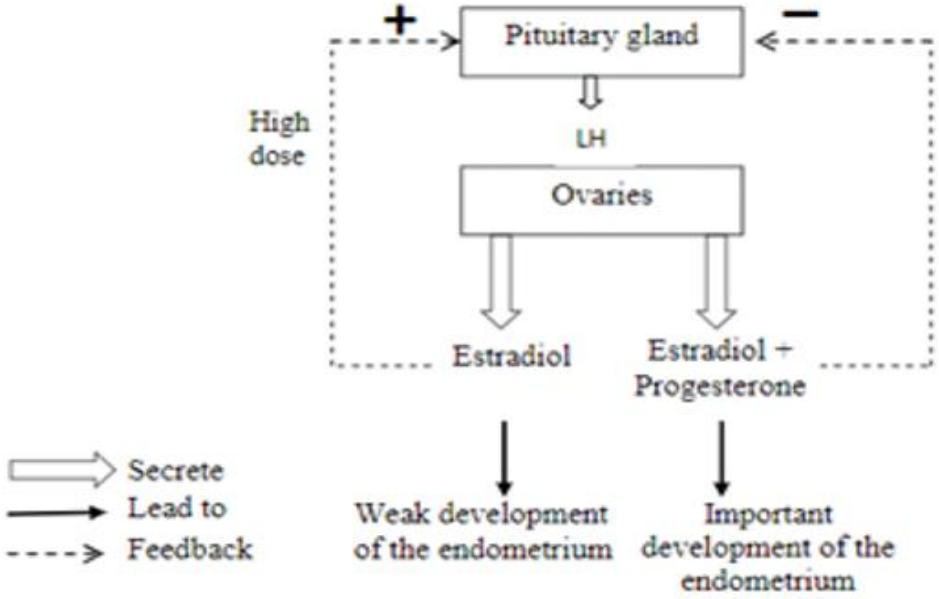
Document 3



Document 4

4- Show, by referring to documents 3 and 4, that "the activity of the pituitary gland is under the control of ovarian hormones".

5- Establish, by referring to all what precedes, a functional diagram showing the relations existing between the ovaries and the two other organs: the pituitary gland and the uterus.

4	The amount of LH increases from 0.5ng/mL to 9ng/mL between the days 8 and16 following the injection of estradiol alone on day8. This shows that estradiol exerts a positive feedback on the pituitary gland. On the contrary, the amount of LH decreases from 60ng/mL to 10ng/mL between day 12 and 28 after the injection of estradiol and progesterone at day 12. This shows that estradiol with progesterone exert a negative feedback on the pituitary gland. This shows that the activity of the pituitary gland is under the control of ovarian hormones.	0.75
5	Functional diagram showing the relations existing between the ovaries and the two other organs: the pituitary gland and the uterus  	0.75

2017 II

Exercise 4 (5 points) **Determination of Ovulation**

The first phase of the menstrual cycle is marked by important development of the follicles. Out of these follicles, only one becomes mature and ready for ovulation. In order to better understand the factors and the mechanisms that cause ovulation to occur, the following studies are performed.

Study 1: the variation of the level of estradiol, an ovarian hormone, is monitored during a sexual cycle. The results are shown in document 1.

Time(days)	0	4	10	12	14	18	21	28
Level of estradiol (pg/mL)	60	75	150	240	75	100	150	60

Document 1

1- Draw the curve which represents the variation of the level of estradiol as a function of time.

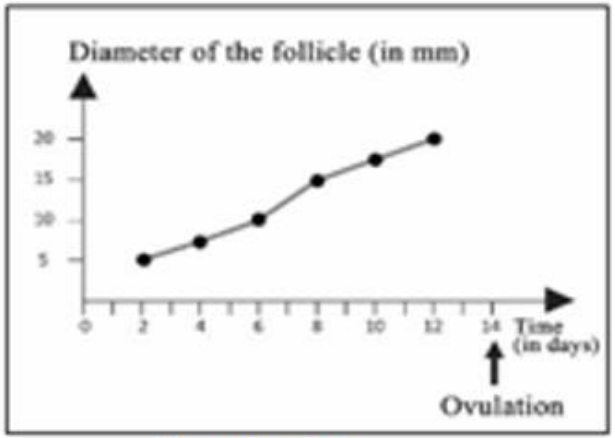
Document 2 shows the variation of the diameter of a cavitary follicle during maturation until ovulation. Note that the diameter of the follicle is proportional to the number of follicular cells.

2- Define ovulation

3- Explain how the transformation of the follicle (doc 2) leads to the variation of the level of estradiol during the follicular phase (doc 1).

Document 3 shows a follicle at two different stages of the development in the ovary during a sexual cycle.

4- Name the follicle represented in each of the photos A and B. Justify, by referring to document 2, the answer.

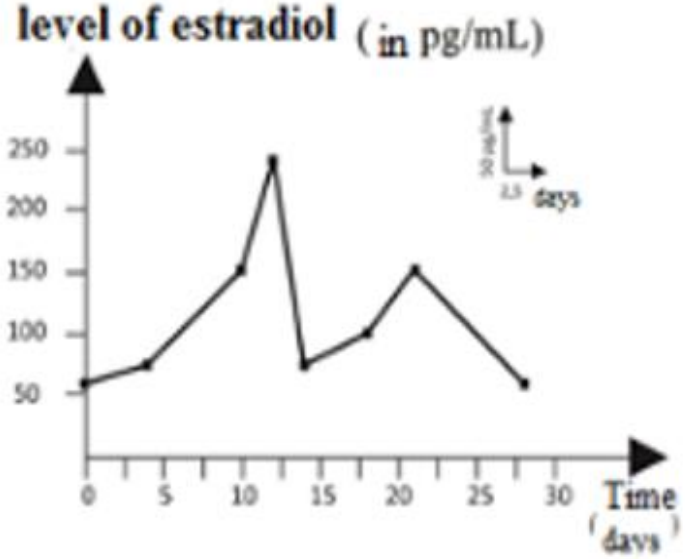


Document 2

1		11/2

Time(days)	0	4	10	12	14	18	21	28
Level of estradiol (pg/mL)	60	75	150	240	75	100	150	60

Document 1



Variation of the level of estradiol as a function of time

2	Ovulation is the liberation or release of oocyte II from the mature ruptured graafian follicle into the pavilion duct.	1/4

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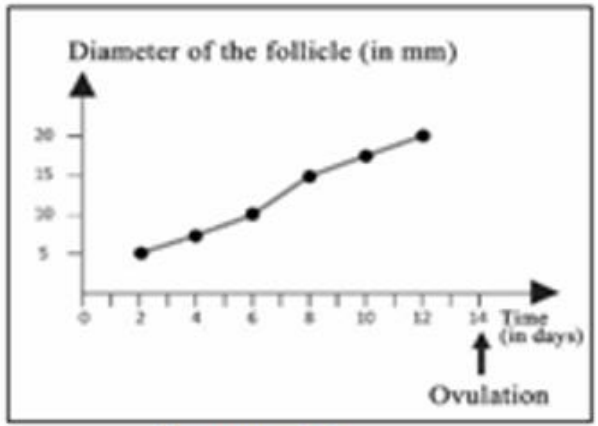


Document 2

3	The increase in the diameter of the follicle from 5mm at day 2 of the follicular phase into 20 mm at day 12 of the same phase is followed by an increase in the number of follicular cells. Knowing that these cells are responsible for estradiol secretion, as the number of these cells increases, the estradiol level increases from 60 pg/ml into 240 pg/ml between day 0 and 12 of the follicular phase (as shown in document 1)	3/4

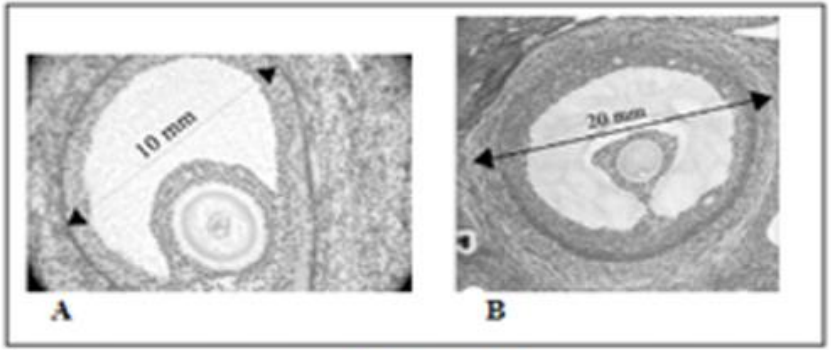
Document 3 shows a follicle at two different stages of the development in the ovary during a sexual cycle.

4- Name the follicle represented in each of the photos A and B. Justify, by referring to document 2, the answer.

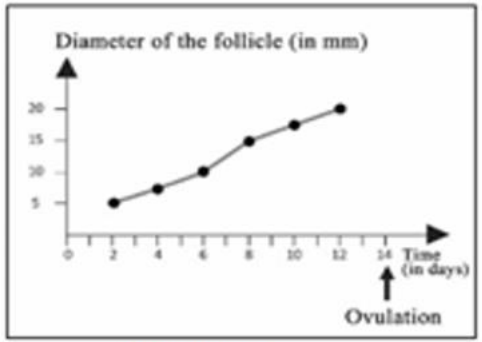
Study 2

Two lots A and B of female monkeys which are subjected to the ablation of their ovaries, receive a continuous injection of moderate level of estradiol, which keeps LH at a low level.

The monkeys of each lot receive later a unique injection of a high dose of estradiol, on a specific day. The variation of the LH level is monitored in these monkeys. The results are represented in document 4.



Document 3



Document 2

4	A= cavitary (tertiary) follicle. Since the diameter is 10 mm which corresponds to a follicle at day 6 of the cycle during its development. B= Graafian follicle. Since the diameter is 20 mm which corresponds to a follicle at day 12 of a follicular phase that's a mature follicle tends to ovulate.

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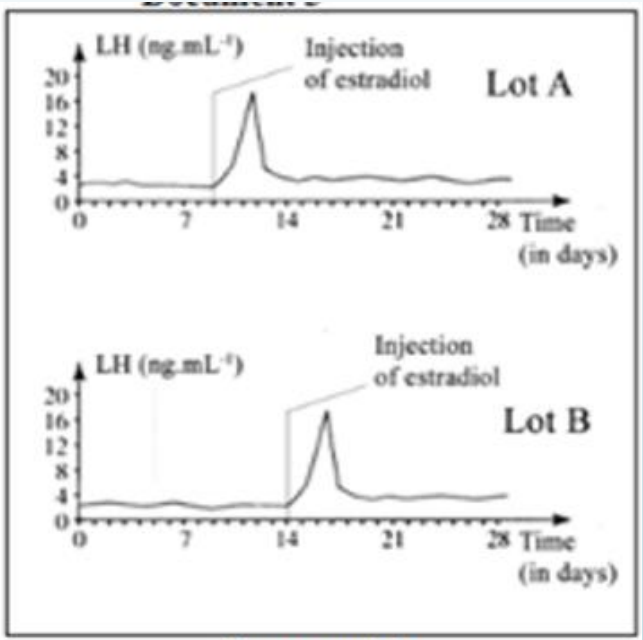
Two lots A and B of female monkeys which are subjected to the ablation of their ovaries, receive a continuous injection of moderate level of estradiol, which keeps LH at a low level.

The monkeys of each lot receive later a unique injection of a high dose of estradiol, on a specific day. The variation of the LH level is monitored in these monkeys. The results are represented in document 4.

5- Interpret the results in document 4.

6- Explain that the stimulus leading to ovulation is given by the ovarian follicle.



Document 4

5	In both ovariectomized female monkeys of lot A and B a peak of LH of 16 ng/ml at day 12 and day 17 for the females that are subjected respectively at day 9 (lot A) and day 14 (lot B) to a unique injection of high dose of estradiol. However this level of LH is constantly maintained about 3 ng/ml following the injection of a continuous moderate level of estradiol. This shows that a high quantity of estradiol favors the peak of LH.	3/4
6	The ovary secretes a high concentration of estradiol (at the level of threshold) that stimulates by positive feedback the pituitary gland. Hence the peak of LH is responsible for ovulation. Moreover the follicle undergoing mature emits a stimulus, high dose of estradiol that favors its rapturing corresponding to ovulation.	3\4

Exercise 4 (5 points) **Relations between the pituitary gland and the testis** 2011 II

The testis produces testosterone in a constant manner due to a regulatory system that we aim to discover by performing the following experiments.

Experiment 1

We inject gonadotropins (anterior pituitary hormones) into a male animal that have not reached puberty and whose testicular cells are normally inactive. The consequencesof these injections on three types of testicular cells are presented in document 1.

Pituitary hormones / Testicular cells	Injection of LH	Injection of FSH
Spermatogonia	inactive	activated
Sertoli cells	not developped	developped
Leydig cells	activated	inactive

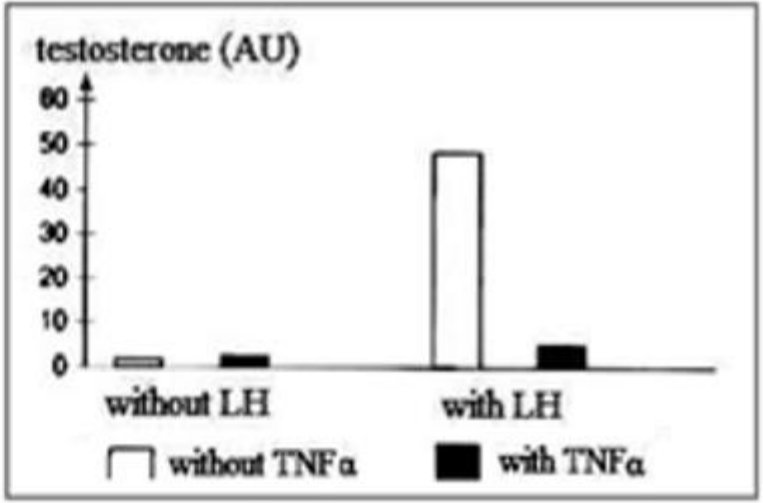
Document 1

1- Specify the role of : Sertoli cells, spermatogonia and Leydig cells.
2- Analyze the results of experiment 1 and draw out the target cells of each of the pituitary hormones LH and FSH.

Part of the Ex	Answer key	Mark
	Exercise 4 (5 points)	
1	Spermatogonium: mother cell of male gametes.**(0.25pt)** Sertoli cell: nurturing role for germ cells.**(0.25pt)** Leydig cells : produce testosterone.**(0.25pt)**	**0.75**
2	Spermatogonia are only activated by FSH similarly Sertoli cells are only developed under the effect of FSH, however Leydig cells are not activated except by LH.**(0. 5pt)**. We can draw out that the target cells of LH are Leydig cells. **(0.25pt)** Whereas Spermatogonia cells and Sertoli cells are the target cells of FSH.**(0.25pt)**	**1**

Experiment 2

Leydig cells are extracted from pig testes and cultured in vitro. We add different molecules, LH and/or TNFα, to the culture medium and we measure, at the same time, the production of testosterone. TNFα is a molecule that blocks the action of LH by binding the receptors of LH target cells. Document 2 shows the effects of LH on these cells.



Document 2

3- Determine by referring to document 2, how are Leydig cells activated.

3	The presence of LH in the culture of Leydig cells, in absence of TNFα, has strongly increased the production of testosterone, which passes from 2 a.u. (without LH) to 50 a.u. (with LH). Thus LH activates Leydig cells. However, the production of testosterone decreases 50 a.u. to 5 a.u. when TNFα is added to LH, thus the activation of Leydig cells is done by the fixation of LH to their free receptors.	**1**

Experiment 3

In order to study the action of certain types of cells on the activity of pituitary cells, we prepare three appropriate culture media and we measure the level of gonadotropins released in these media after a period of incubation (document 3).

Experimental conditions / Activity of pituitary cells	Medium 1	Medium 2	Medium 3
	Pituitary cells only	Pituitary cells + kidney cells or spleen cells	Pituitary cells + Leydig cells
Release of FSH	100%	100%	100%
Release of LH	100%	100%	60%

Document 3

4- Interpret the results of experiment 3.
5- Specify the type of feedback control revealed by experiment 3. Justify the answer.

4	The secretion of gonadotropins is 100% for FSH and LH in media 1 and 2 where the pituitary cells are alone or with kidney cells or spleen cells. However, only the level of LH decreases to 60% in the medium where the pituitary cells are with leydig cells. This shows that only Leydig cells are able to inhibit the activity of pituitary cells that secrete LH and have no effect on those that secrete FSH.	**1.25**
5	It is a negative feedback control.**(0. 5pt)** Because the level of LH (produced by pituitary cells) and the level of testosterone (produced by Leydig cells) vary in an opposite manner.**(0. 5pt)** **Or** When the level of testosterone , that is produced by Leydig cells, increases the level of LH decreases.	**1**

2012 I

Exercise 4 (5 points) **Functional relationships between ovaries and uterus**

In the frame work of studying the functional relationships between the ovaries and the uterus, many experiments are performed on female mammals.

Experiment 1: We inject increasing amounts of estradiol, to lots of ovariectomized mice at puberty; the results are shown in document 1.

Lots of mice	1 (control)	2	3	4
Amount of injected estradiol (in µg)	0	0.005	0.01	0.1
Average mass of the uterus (mg)	12	20	40	100

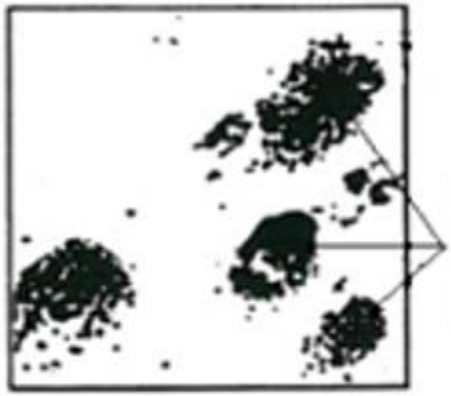
Document 1

Experiment 2: We inject only physiological doses of progesterone to an ovariectomized female mouse. No significant changes were observed at the level of the uterus.
In another ovariectomized female, 0.01 µg of estradiol is injected followed by an injection of the same previous doses of progesterone. We observe more amplified results than those represented in document 1.

1- Interpret each of the above experiments.

Part of ex.	Answer	grade
	Exercice 4	
1	**Experiment 1**: The average mass of the uterus of the ovariectomized mice without injection of estradiol is 12 mg. This mass increases from 20 mg to 100 mg when the dose of the injected estradiol increases from 0.005 mg to 0.1 mg.Thus estradiol stimulates the development of the uterus. **(3/4pt)** Experiment 2: No significant changes were observed at the level of the uterus after the injection of progesterone only, however the development is more intense compared to document 1 (above 40 mg) after the injection 0.01 µg of estradiol followed by progesterone. This means that progesterone alone has no effect on the uterus, but it enhances the development of the uterus in the presence of estradiol in an ovariectomized female. **(3/4pt)**	1 ½

Experiment 3: We perform autoradiography on a cross-section of the uterine mucosa taken from an ovariectomized female after 1 to 2 hours of being injected with estradiol marked by tritium (radioactive isotope of hydrogen) as shown in document 2.



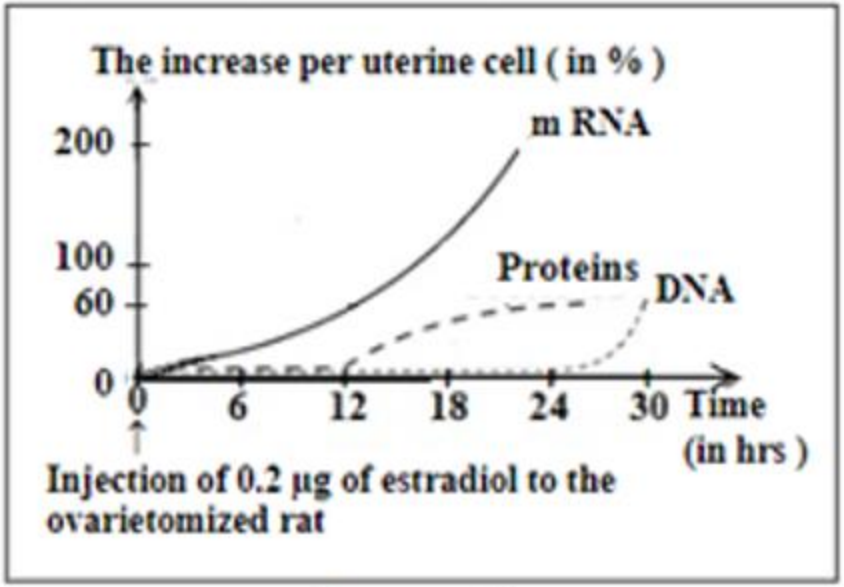
Remark: The membrane of the cell and its cytoplasm are not distinguished.

Document 2

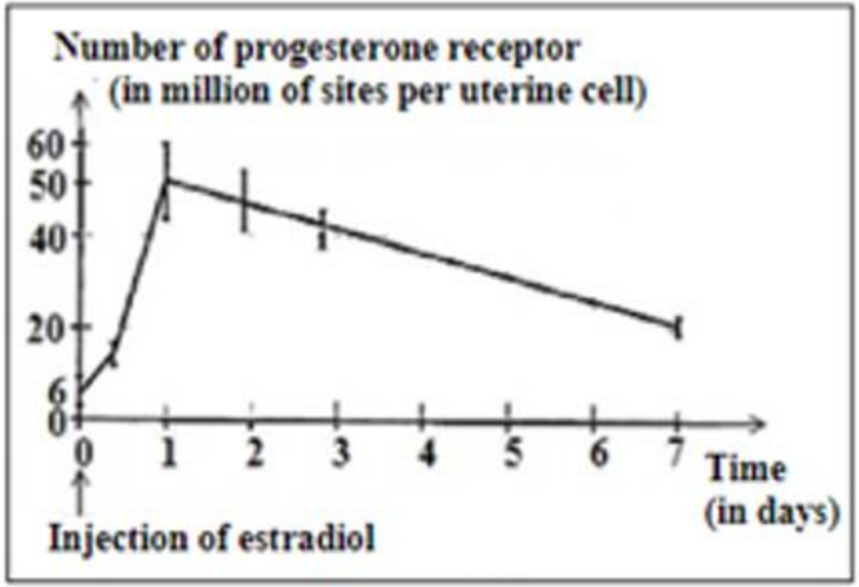
2- What can you draw out of document 2? Justify the answer.

2	We can draw out that estradiol has as targets the nuclei of uterine cells. (1/4pt) since document 2 shows the "grains" of radioactive estradiol in the nuclei of uterine cells after the injection of the tritium-labeled estradiol. (1/2pt)	**3/4**

Experiment 4: We inject estradiol to an ovariectomized rat at time 0. Then we measure the rate of certain constituents of the uterine mucosa cells. The results are represented in documents 3 and 4.



Document 3



Document 4

3- Knowing that the development of the uterine mucosa is related to mitosis, determine, using document 3 and the acquired knowledge, the mode of action of estradiol on the uterus.

4- Explain,based on document 4, the results of experiment 2.

3	After the injection of 0.2 µg of estradiol to ovariectomized rats, the increase of mRNA per uterine cell elevates from zero to 200%. (This corresponds to the phase of DNA transcription into mRNA), and the increase of proteins per uterine cell elevates from zero to 60% after a delay of 12 hours. (This corresponds to the translation phase which follows the phase transcription). So, estradiol stimulates the expression of certain genes for protein synthesis. **(3/4pt)** Also, This injection elevates the increase of DNA per uterine cell from 0 to 60% after a more delay of 24 h, indicating the replication of DNA molecules, which precedes cell division that corresponds to cellular proliferation. **(3/4pt)**	**1 ½**
4	Document 4 shows an increase in progesterone receptors in thousands of sites per uterine cell from 6 to 50 between 0 to1day after the injection of estradiol. This shows that estradiol favors the production of progesterone receptors. Therefore, when injecting progesterone alone (experiment 2) there was few progesterone receptors in uterine cells and therefore this hormone has no effect on these cells, but after the injection of estradiol, the number of progesterone receptors increases and the fixation of progesterone on the receptors also increases thus modifying the cellular function and favoring protein synthesis which explains the increase in the mass of the uterus.	**1 ¼**